

NOVARTIS AG  
Form 6-K  
January 06, 2005

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## 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 the month of December 2004  
(Commission File No. 1-15024)

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### Novartis AG

(Name of Registrant)

Lichtstrasse 35  
4056 Basel  
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:

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Yes:  No:

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7):

Yes:  No:

Indicate by check mark whether the registrant by furnishing the information contained in this form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes:  No:

Enclosures:

1. FDA approves Enablex for treatment of overactive bladder (Basel, Switzerland, December 23, 2004)
2. Novartis ramps up Coartem® production to provide potentially life-saving medicine to more patients (Basel, Switzerland, December 22, 2004)

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3. Novartis announces commercialization collaboration in Germany for Emselex® for the treatment of overactive bladder (Basel, Switzerland, December 17, 2004)
  4. Landmark study in New England Journal of Medicine shows Exelon® may help people suffering from dementia associated with Parkinson's disease (Basel, Switzerland, December 9, 2004)
  5. Novartis investigational drug ICL670 demonstrates positive results in treating chronic iron overload, a potentially life-threatening condition (Basel, Switzerland, December 7, 2004)
  6. Results from two new multi-center trials confirm efficacy and tolerability of Prexige 100 mg once daily in treatment of osteoarthritis (Basel, Switzerland, December 6, 2004)
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7. New Glivec data: Prolonged efficacy with approved 400 mg daily dose and potential for improved response at higher dose (Basel, Switzerland, December 6, 2004)
  8. Novartis Foundation for Sustainable Development celebrates 25th anniversary with symposium on the "Right to Health: A Duty for Whom?" (Basel, Switzerland, December 2, 2004)
  9. Diovan® receives approval in Sweden to treat high-risk heart attack patients (Basel, Switzerland, December 1, 2004)
  10. Certican® European Union Mutual Recognition Procedure expanded to include 10 new EU Member States (Basel, Switzerland, December 1, 2004)
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Investor Relations

Novartis International AG  
CH-4002 Basel  
Switzerland

Novartis Corporation  
608 Fifth Avenue  
New York, NY 10020  
USA

**Investor Relations Release**

**FDA approves Enablex for treatment of overactive bladder**

*New option offers unique M3 profile with proven efficacy, safety and tolerability*

**Basel, December 23, 2004** Novartis Pharma AG announced that the U.S. Food and Drug Administration (FDA) has approved Enablex® (darifenacin) extended-release tablets (7.5mg and 15mg) for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency and frequency. Enablex, a once-daily medication, is expected to launch in the U.S. in early 2005.

Enablex works by blocking the M3 receptor, which is primarily responsible for bladder muscle contraction. It is a potent muscarinic receptor antagonist that helps reduce incontinence episodes, increases the amount of urine the bladder can hold, reduces the frequency of urination episodes, and decreases the pressure or urgency associated with the urge to urinate.

"The M3 profile of Enablex is unique among all overactive bladder medications," said David Chaikin, MD, clinical assistant professor of urology at New York Hospital/Cornell Medical Center. "By combining sustained efficacy with a low incidence of central nervous system and cardiovascular side effects, Enablex will be especially useful as a new treatment option for overactive bladder."

The FDA approval of Enablex was based on efficacy data from four pivotal studies and safety data from studies in which more than 7,000 patients with a mean age of 58 years were treated with varying doses of Enablex. In these studies, patients taking Enablex experienced decreased frequency of incontinence and urination episodes, increased bladder capacity, and decreased feelings of urgency. Enablex was shown to reduce weekly incontinence episodes by up to 83 percent and results were seen within two weeks of beginning treatment. Efficacy was sustained throughout the 12-week treatment period, and long-term safety was studied for up to one year.

"Many patients with overactive bladder do not seek treatment for this condition and many of those who do remain unsatisfied. As we make Enablex available in the United States, we have the potential to bring unique benefits to these patients whose needs are not currently met," stated Paulo Costa, president and CEO, Novartis Pharmaceuticals Corporation.

OAB, a condition that affects an estimated 33 million Americans, is caused by the untimely contraction of the bladder muscle. At least 16 percent of the population over the age of 40 suffers from the chronic and troublesome symptoms of OAB. Although prevalence increases with age, the problem affects people of all ages. People with OAB often limit travel, social and even work activities to avoid potentially embarrassing episodes that can occur with this condition.

"Millions of patients and their families can be profoundly affected by overactive bladder. It is important that we continue to advance technology to bring new options to people with overactive bladder to help them manage this condition," said Nancy Muller, executive director, National Association for Continence.

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In total, Enablex has been studied in 98 clinical trials involving more than 10,000 people. In clinical trials, the most frequently reported adverse events associated with Enablex were dry mouth and constipation, however patient discontinuation rates due to these events were low. The majority of adverse events in Enablex treated subjects were mild or moderate and mostly occurred during the first two weeks of treatment. As with other OAB medications, Enablex is contraindicated in patients with urinary retention, gastric retention or uncontrolled narrow-angle glaucoma and in patients who are at risk for these conditions. Enablex is also contraindicated in patients with known hypersensitivity to the drug or its ingredients.

This release contains certain forward-looking statements relating to Novartis Pharmaceuticals Corporation's business, which can be identified by the use of forward-looking terminology, such as "is expected," "will be," and "have the potential to" or similar expressions, or by express or implied discussions regarding potential future sales of Enablex. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause the actual results with Enablex to be materially different from any future results, performance, or achievements expressed or implied by such statements. There can be no guarantee that Enablex will reach any particular level of sales. 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 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** Novartis AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2003, the Group's businesses achieved sales of USD 24.9 billion and a net income of USD 5.0 billion. The Group invested approximately USD 3.8 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 81,000 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

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**Novartis Global Investor Relations**

**Karen J. Huebscher, Ph.D.** +41 61 324 84 33

**International office**

Richard Jarvis +41 61 324 43 53

Nafida Bendali +41 61 324 35 15

Silke Zentner +41 61 324 86 12

Katharina Ambühl (maternity leave until end April 2005)

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

Fax: +41 61 324 84 44

[www.novartis.com](http://www.novartis.com)

---

**North American office**

Ronen Tamir +1 212 830 24 33

John Menditto +1 212 830 24 44

Sabine Moravi +1 212 830 24 56

Jill Pozarek +1 212 830 24 45

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

Fax: +1 212 830 24 05

[www.novartis.com](http://www.novartis.com)

**Novartis International AG**

Novartis Communications  
CH-4002 Basel  
Switzerland  
Tel +41 61 324 2200  
Fax+ 41 61 324 3300  
Internet Address:  
<http://www.novartis.com>

**MEDIA RELEASE COMMUNIQUE AUX MEDIAS MEDIENMITTEILUNG**

**Novartis ramps up Coartem® production to provide potentially life-saving medicine to more patients**

*Capacity increased to five million Coartem treatments per month*

**Basel, December 22, 2004** Novartis announced today that production capacity for its artemisinin-based combination therapy Coartem® (artemether-lumefantrine) has been expanded to reach the level of five million treatments per month. The World Health Organization (WHO) expects in 2005 patient needs will reach 60 million treatments, an exponential increase over three years ago when only 100,000 treatments were produced.

"The introduction of artemisinin-based combination therapy (ACT) is of highest priority for malaria control in Africa and Coartem is the only therapy currently available as a fixed-dose combination providing both active ingredients in a single tablet," said Professor Marcel Tanner, Director of the Swiss Tropical Institute. "Due to the fact that many African countries now recommend Coartem as first line treatment, demand for Coartem has risen dramatically and Novartis has moved admirably to ramp up production capacity. This move will certainly help to reduce the malaria burden for millions of people, especially children, and prevent malaria deaths and severe and complicated malaria episodes."

Novartis has also concluded agreements for supply of 11.6 tons of artemether by its Chinese partner Kunming Pharmaceuticals Corporation (KPC) and 15 tons of artemisinin by several other suppliers, most prominently Chongqing Holley. This is an amount sufficient to produce 60 million Coartem treatments. Final Coartem production in 2005 is highly dependent on the timely delivery of sufficient quantities of the key raw materials artemisinin and artemether by Chinese suppliers who currently dominate the world market. Most deliveries to Novartis will occur in the second half of the year, resulting in a production forecast of 30 million Coartem treatments in 2005.

"In partnership with WHO since 2001, we have provided at cost six million treatments of Coartem for malaria patients, many of whom are children. Based on the escalation of WHO estimates of the number of treatments needed, we have invested in new production capacity and supply agreements with our Chinese partners," said Dr. Daniel Vasella, Chairman and CEO of Novartis. "In addition, we are committing additional resources to work together with governments in the developing world and NGOs to research how to help those most vulnerable to malaria, especially pregnant women and children. To help ensure that the medicine is broadly accessible to needy patients, we make Coartem available at cost to the WHO for supply to the public sector of malaria endemic developing countries. Up to now we have been subsidizing Coartem and do not anticipate ever making a profit from future sales."

Artemether-lumefantrine is on the WHO's Essential Medicines list and is the only ACT pre-qualified by the WHO for use in countries experiencing high levels of resistance to conventional anti-malaria drugs.

The immense scale up of ACTs requires strong collaboration between the WHO, other stakeholders in the Roll Back Malaria partnership, the manufacturers of ACTs and raw material suppliers.

"The effort of Novartis to expand its manufacturing capacity will make it possible for tens of millions of malaria patients to benefit from this highly effective treatment in 2005," said Dr. Jack C. Chow, WHO Assistant Director-General HIV/AIDS, TB and Malaria.

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Artemisinin, the active ingredient in Coartem and all other ACTS, is a plant derived raw material and crops of *Artemisia annua* must be planted one growing season ahead of harvesting and extraction for use in production. The cultivation of *Artemisia annua* requires a minimum of six months. The supply chain for manufacturing ACTs is particularly complex and time-consuming, adding an additional two to five months to production timelines depending on product formulation.

"Artemisinin-based combination therapies like artemether-lumefantrine are central to our fight against malaria. We have seen remarkable results with this new class of drugs. In some regions the number of malaria cases dropped by more than 90% when ACTs were used in combination with other malaria control measures," said Professor Nick White, Wellcome Trust Research Laboratories, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand. "The demand for artemether-lumefantrine has risen dramatically. Production capacity has been ramped up as usage has risen exponentially, but we need to ensure sufficient agricultural production of artemisinin to sustain this progress."

#### **About malaria**

Worldwide, experts estimate that there are between 300 and 500 million new cases of malaria each year, resulting in over one million deaths annually, 90% of which occur in children in Africa. Malaria morbidity and mortality rates are rising in developing countries, largely due to the emergence of drug resistant parasites rendering traditional antimalarial drugs, such as chloroquine, sulfadoxine-pyrimethamine (SP) ineffective.

In addition to the devastating toll malaria takes on human life in terms of morbidity and mortality, the disease also has substantial negative impacts on the economic development of nations in which the disease is endemic. The drain on African economies alone is estimated to be USD 12 billion each year (WHO, 2000) and the threat of malaria can be a serious deterrent to tourism, further hampering economic development and growth.

#### **About Coartem**

Coartem is a highly effective and well tolerated antimalarial that achieves cure rates of up to 95%, even in areas of multi-drug resistance. It is indicated for the treatment of falciparum malaria, the most dangerous form of malaria. Coartem is the only pre-qualified, fixed-dose ACT combining artemether, an artemisinin derivative, and lumefantrine.

Artemisinin is a compound derived from the sweet wormwood plant and has been used for centuries in traditional Chinese medicine to treat fever. An artemisinin-based combination therapy is a combination of two or more drugs (one of which is an artemisinin derivative) that have different modes of action and different targets. Studies have shown that using two or more drugs in combination has the potential to delay the development of resistance in areas of low transmission. Artemisinin-based combination therapies in particular have been found to be highly effective in treating malaria and their potential to delay resistance in areas of intense transmission is under investigation.

Coartem was co-developed by Novartis in collaboration with Chinese partners who also supply the active ingredients (artemether and lumefantrine) and is produced in China by Novartis. Coartem is currently registered in 77 countries worldwide and more than four million patients have benefited from this innovative treatment since its first registration in October 1998. Coartem has been extensively studied in multi-center clinical trials involving more than 3,000 patients.

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This release contains certain forward-looking statements that can be identified by the use of forward-looking terminology, such as "will occur", "help alleviate", "continue", "remain committed", "will benefit", "will evaluate" or similar expressions, or by express or implied discussions regarding Novartis' ability to satisfy the WHO's requirements for Coartem production in the future. Such forward looking statements reflect the current views of the Company or WHO, as the case may be, regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause the actual results with Coartem to be materially different from any future results, performance, or achievements expressed or implied by such statements. There can be no guarantee that Novartis will be able to achieve any particular level of Coartem production in the future. Any such results can be affected by, among other things, the ability to obtain the necessary raw materials, uncertainties relating to regulatory actions or government regulation generally, 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.

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Investor Relations

Novartis International AG  
CH-4002 Basel  
Switzerland

Novartis Corporation  
608 Fifth Avenue  
New York, NY 10020  
USA

### Investor Relations Release

#### Novartis announces commercialization collaboration in Germany for Emselex® for the treatment of overactive bladder

**Basel, December 17, 2004** Novartis Pharma AG announced today the start of a collaboration between Novartis Pharma GmbH and Bayer Vital AG for the commercialization and distribution of Emselex® (darifenacin hydrobromide) 7.5 mg and 15 mg in Germany. Emselex, a new once-daily M3 selective receptor antagonist (M3 SRA) recently received marketing approval from the European Commission in 25 European member states as well as Norway and Iceland for the treatment of overactive bladder (OAB).

"Bayer Vital has significant expertise of the German urology market, so collaborating with them helps to ensure that Emselex will reach physicians quickly and ultimately benefit patients who suffer from overactive bladder," said Kurt Graves, Chief Marketing Officer of Novartis Pharma AG. "Emselex is a new effective drug for the treatment of OAB that is selective for the M3 receptors in the bladder, with proven efficacy, good tolerability and with a well established central nervous system and cardiovascular safety profile."

Under the terms of the collaboration, Novartis remains the owner of the EU marketing authorization for darifenacin, while Bayer Vital gains exclusive commercialization rights for Emselex in Germany.

#### About Emselex

Emselex is a once-daily M3 selective receptor antagonist (M3 SRA) oral treatment that works by selectively inhibiting the M3 receptor, the primary mediator of detrusor contraction, while sparing the M1 and M2 receptors that are located in various body organs, including the brain and heart. Emselex has been shown to effectively reduce the number of weekly incontinence episodes by up to 77% versus placebo.<sup>1</sup> Additional clinical trials comparing Emselex with placebo showed Emselex does not impair cognitive function and has a cardiovascular safety profile similar to placebo.

To date, 98 clinical trials with Emselex have been completed involving more than 10,500 subjects and patients, of whom 7,146 were treated with darifenacin. Across a range of pivotal endpoints, Emselex has been shown to significantly improve all other key symptoms of OAB, including the number of times patients had to visit the bathroom each day, bladder capacity, frequency of urgency, severity of urgency and the number of incontinence episodes leading to a change in clothing or pads.<sup>2</sup>

Emselex 7.5mg and 15mg was granted approval by the European Commission for the treatment of overactive bladder (OAB) in all 25 European member states as well as Norway and Iceland on October 27, 2004. Novartis is able to market Emselex throughout these countries. This product is known as Enablex in the US. The US Food and Drug Administration issued an approvable letter in October 2003 for the approval of Enablex in the US, and discussions with the FDA are progressing according to schedule.

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## About OAB

Symptoms of overactive bladder include urinary urgency (a sudden and compelling desire to pass urine, which is difficult to defer) with, or without, urge incontinence (involuntary leakage accompanied by urgency), usually with urinary frequency (voiding the bladder too often) and nocturia (waking at night one or more times to void the bladder).

## Disclaimer

This release contains certain forward-looking statements that can be identified by the use of forward-looking terminology, such as "will reach", or similar expressions, or by express or implied discussions regarding potential additional marketing approvals or future sales of Emselex. 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 Emselex to be materially different from any future results, performance, or achievements expressed or implied by such statements. There can be no guarantee that Emselex will receive any additional marketing approvals in any other countries, or that it 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.

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**Novartis Global Investor Relations**

**Karen J. Huebscher, Ph.D.** +41 61 324 84 33

**International office**

Richard Jarvis +41 61 324 43 53

Nafida Bendali +41 61 324 35 15

Jill Pozarek +1 212 830 24 45

Katharina Ambühl (maternity leave until end April 2005)

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

Fax: +41 61 324 84 44

[www.novartis.com](http://www.novartis.com)

**North American office**

Ronen Tamir +1 212 830 24 33

John Menditto +1 212 830 24 44

Sabine Moravi +1 212 830 24 56

Silke Zentner +41 61 324 86 12

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

Fax: +1 212 830 24 05

[www.novartis.com](http://www.novartis.com)

---

**Novartis International AG**

Novartis Communications  
CH-4002 Basel  
Switzerland  
Tel +41 61 324 2200  
Fax+ 41 61 324 3300  
Internet Address:  
<http://www.novartis.com>

**MEDIA RELEASE COMMUNIQUE AUX MEDIAS MEDIENMITTEILUNG**

**Landmark study in New England Journal of Medicine shows Exelon® may help people suffering from dementia associated with Parkinson's disease**

*Exelon provided significant benefits on a wide range of symptoms such as loss of memory, concentration and behavioral problems*

*Patients were also able to cope better with activities of daily living*

**Basel, Switzerland, December 9, 2004** Exelon® (rivastigmine tartrate) can provide significant benefits in dementia associated with Parkinson's disease (PD), according to a study published in the New England Journal of Medicine this month.

The study, known as EXPRESS (**EXelon in PaRkinson's disEaSe dementia Study**), is the first large-scale clinical trial assessing the efficacy and safety of an Alzheimer's disease treatment in PD patients with dementia.<sup>1</sup> Exelon has been widely used in Alzheimer's disease dementia since its approval in 1997.

Patients taking Exelon showed statistically significant benefits on a range of symptoms, such as loss of memory, concentration and behavioral problems. They were also able to cope better with everyday activities like watching TV or talking about current events.

"The findings of the EXPRESS study could have important implications for clinical practice," said Dr Murat Emre, Professor of Neurology at the Istanbul University in Turkey, lead investigator of the EXPRESS study.

"With current treatments we are able to manage the movement symptoms of Parkinson's disease quite well, but dementia has been an area which could not be treated up to now. Rivastigmine is a therapy that has been shown to improve symptoms frequently seen in patients suffering from dementia associated with PD and thus offers hope to provide a better quality of life," Dr. Emre said.

Dementia is one of the complications most feared by PD patients.<sup>2</sup> In addition to cognitive impairment, neuro-psychiatric symptoms like depression, hallucinations, anxiety and apathy, are also common.<sup>3</sup> These symptoms are important determinants of the patient's quality of life, course of the disease and caregiver distress.<sup>3</sup> Two out of five people with PD develop dementia over the course of their illness.<sup>4,5</sup> Patients with PD have a six-fold increase in the risk of developing dementia compared with elderly people without PD.

"Dementia associated with Parkinson's disease places a significant emotional, economic and social burden on patients and their families," said Mary Baker, President of the European Parkinson's Disease Association, which is based in the United Kingdom.

"As the person with PD becomes increasingly dependent, watching someone that you care for start to deteriorate in this way is heart breaking, and the future becomes an uncertain abyss for all the family. Sometimes institutional care is the only option and this places a significant economic burden on the family and the state. Results like this give new hope to families caring for a loved one with dementia and may improve the quality of life of the whole family,"

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## EXPRESS Study Results

Over a 24-week study period, patients were randomly assigned to a daily dose of 3-12 mg Exelon or placebo. Investigators used two measures regularly applied in clinical studies of patients with dementia: the Alzheimer's Disease Assessment Scale-cognition (ADAS-cog) to evaluate patients' cognitive function; and the Alzheimer's Disease Cooperative Study-Clinician's Global Impression of Change (ADCS-CGIC) to assess the patients' overall functioning.

Patients who were treated with Exelon showed a mean 2.1-point improvement (versus a 0.7-point decline in placebo) on the ADAS-cog scores ( $p < 0.001$ ) at week 24 of the study. Mean ratings on the ADCS-CGIC were 3.8 on rivastigmine versus 4.3 on placebo ( $p = 0.007$ ). Additional specific tests for memory, attention, behavioral symptoms and verbal fluency consistently showed significantly better outcomes for Exelon versus placebo (all  $p < 0.05$ ). Since patients receiving placebo declined by nearly 1 point on the ADAS-cog over 24 weeks, an improvement of 2.1 points in the rivastigmine group might represent approximately one year's advantage.

The side effects associated with Exelon during this study were mild to moderate in nature and included nausea and vomiting. Importantly, motor scale assessments showed that Parkinsonian symptoms were not worsened overall relative to baseline or placebo. Mild to moderate tremor was reported in Exelon-treated patients, but this rarely resulted in withdrawal from the study.

## About Exelon

Exelon is a treatment for mild to moderate Alzheimer's disease. It belongs to a class of drugs known as cholinesterase inhibitors (ChEI's) which increase neurotransmitter activity in the brain. It was approved for the treatment of Alzheimer's disease in 1997 and is currently used in over 70 countries.

Among the widely used ChEI's, Exelon is the only treatment that inhibits both enzymes involved in the breakdown of the neurotransmitter acetylcholine: acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE). This may offer additional benefits over treatments which inhibit AChE alone. Exelon can maintain both memory and thinking, help with behavioral problems and affect how patients cope with the activities of daily living. It may help them communicate better, interact socially, participate in hobbies and eat and dress independently.<sup>6,7</sup>

## About Parkinson's Disease, Alzheimer's Disease and Dementia

**Parkinson's disease (PD)** is a chronic and progressive neurological condition estimated to affect 6.3 million people worldwide.<sup>8</sup> Dementia occurs in around 40 percent of patients diagnosed with PD and may affect up to 80 percent of Parkinson's patients as the disease further progresses.<sup>3,9</sup> Like Alzheimer's disease, dementia associated with Parkinson's disease is thought to result from a cholinergic deficit, which causes decreased transmission of signals between nerves in the brain, especially those that rely on the neurotransmitter acetylcholine. This deficit contributes to the cognitive and behavioral problems observed in these patients. Patients with dementia associated with Parkinson's disease typically have problems with memory, concentration, activities of daily living, as well as depression, anxiety, apathy and hallucinations.<sup>5,10</sup>

**Alzheimer's disease (AD)** is a progressive, degenerative disease that alters the brain, causing impaired memory, thinking and behavior. Affecting approximately 10 million people worldwide and two to six percent of those over 65 years of age, it is the most common form of dementia and the third leading cause of death in this age group behind cardiovascular disease and cancer.<sup>11</sup>

**Dementia** occurs in different forms such as Alzheimer's disease, vascular dementia, dementia associated with Parkinson's disease, dementia with Lewy bodies, and is currently estimated to affect nearly 18 million people worldwide.<sup>12</sup> As the mean age of the population increases, this number is steadily increasing.

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#### 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 2003, the Group's businesses achieved sales of USD 24.9 billion and a net income of USD 5.0 billion. The Group invested approximately USD 3.8 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 80,000 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

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1. Emre M *et al.* Rivastigmine for the dementia associated with Parkinson's Disease. *N Engl J Med* 2004;351:29-38.
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Investor Relations

Novartis International AG  
CH-4002 Basel  
Switzerland

Novartis Corporation  
608 Fifth Avenue  
New York, NY 10020  
USA

### Investor Relations Release

#### **Novartis investigational drug ICL670 demonstrates positive results in treating chronic iron overload, a potentially life-threatening condition**

*Phase III trial in regularly transfused patients shows doses of 20 and 30 mg/kg/day to be highly effective while doses of 5 and 10 mg/kg/day not effective*

*Treatment with ICL670 results in highly statistically significant ( $p < 0.001$ ) absolute reduction of liver iron concentration*

*Global submission anticipated for first half 2005 with Orphan Drug status in US and EU*

**Basel, Switzerland, December 7, 2004** The investigational drug ICL670, an oral, once-daily iron chelator, demonstrated significant efficacy at maintaining or reducing absolute liver iron concentration (LIC), an accepted indicator for total body iron content, when used at doses of 20 and 30 mg/kg/day in a Phase III trial. However, the overall trial primary endpoint of non-inferiority to deferoxamine was not met because doses of 5 and 10 mg/kg/day were not effective. Data from three studies were presented at the annual meeting of the American Society of Hematology in San Diego, California.

As a once-daily oral treatment, ICL670 is designed to be easier to use and more convenient than deferoxamine (Desferal®), the current standard iron chelation therapy, which typically requires slow infusion by pump over eight to 12 hours for at least five days a week. Additionally, ICL670 was generally well tolerated in both adults and children as young as age two years, with most adverse events being mild to moderate in severity. The ICL670 global clinical trials program is the largest ever prospectively implemented for an investigational iron chelator.

Iron overload is a cumulative, potentially life-threatening condition that may result from repeated blood transfusions required to treat certain types of anemias, including sickle cell disease, thalassemia and myelodysplastic syndromes. Over time, if left undiagnosed or untreated, iron overload can lead to debilitating and life-threatening consequences, including damage to the liver, heart and endocrine glands.

"This is a wonderful potential advancement in the treatment of chronic iron overload and could extend the benefits of chelation therapy to many patients who are not currently being treated," said Diane Young, MD, vice president and global head of Phase II/III Clinical Development at Novartis Oncology. "Additionally, as the first once-daily oral treatment, ICL670 has the promise to free patients from the burden of daily subcutaneous infusions of therapy."

#### **Study Details**

The international, open-label, randomized, multicenter Phase III study included 586 patients with beta-thalassemia and transfusion-related iron overload who were randomized to receive ICL670 or deferoxamine according to a fixed dosing regimen. According to LIC at baseline, patients were randomized in a 1:1 ratio to receive either oral ICL670 once daily at doses of 5, 10, 20 or 30 mg/kg, or subcutaneous deferoxamine at doses of 20-60 mg/kg/day for 5 days/week.

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The primary endpoint of the trial was the achievement of a specified reduction in liver iron concentration (LIC) after one year of therapy. Those with lower initial LIC values on the deferoxamine arm were permitted to remain on their pre-study doses and were compared to patients receiving the lower doses of 5 or 10 mg/kg/day of ICL670. Therefore, many of these individuals received significantly higher doses of deferoxamine relative to ICL670.

Because of the disproportionately low dosing of patients with ICL670 at 5 and 10 mg/kg/day when compared to deferoxamine, non-inferiority was not achieved in the overall population. Non-inferiority was demonstrated, however, in those patients treated with ICL670 at 20 and 30 mg/kg/day.

The ICL670 trial showed a highly statistically significant ( $p < 0.001$ ) absolute reduction of LIC in the overall patient population studied. Data demonstrated that after one year of treatment, the mean overall change in LIC from baseline was  $-5.3 \pm 8.0$  mg Fe/g dry weight (dw) for patients taking doses of 20 and 30 mg/kg/day of ICL670. Patients being treated with comparable doses of deferoxamine achieved a reduction in LIC of  $-4.3 \pm 5.8$  mg Fe/g dw.

In a related, open-label Phase II trial presented at ASH, data from a study of 184 patients with myelodysplastic syndrome (MDS), other rare anemias, and patients with thalassemia unable to take deferoxamine therapy, also demonstrated maintenance or reduction of absolute LIC values in patients treated with ICL670 at doses of 20 and 30 mg/kg/day.

In these studies, ICL670 was generally well tolerated with the most frequently reported adverse events being nausea, vomiting, diarrhea, abdominal pain, skin rash and mild stable increases in serum creatinine, usually within the normal range. No unmanageable toxicities have been observed. No cases of agranulocytosis, a potentially life-threatening hematological adverse event, were reported in the ICL670 trials (more than 800 patients received ICL670). In the Phase III trial, four patients (1.4%) in the deferoxamine group and eight patients (2.7%) in the ICL670 group had discontinued therapy due to any adverse events.

Based on the positive results of these studies, Novartis anticipates submitting ICL670 in the first half of 2005 for registration with health authorities worldwide for the treatment of patients with chronic iron overload due to blood transfusions. The U.S. Food and Drug Administration granted fast-track status in 2003 for ICL670 in this patient population. A drug designated as a fast-track product is intended for the treatment of a serious or life-threatening condition and demonstrates the potential to address unmet medical needs for the condition.

Additionally, ICL670 was granted Orphan Drug status in the US and EU in 2002. In the US, the term "Orphan Drug" refers to a product that treats a disease that affects fewer than 200,000 people in the US. In the EU, the term "Orphan Drug" refers to a product that treats a serious or life-threatening disease that affects fewer than five people per 10,000 population. The intent of the Orphan Drug designation is to stimulate the research, development, and approval of products that treat rare diseases.

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The foregoing release contains forward-looking statements that can be identified by terminology such as "investigational drug," "potentially," "anticipated," "designed to," "can lead," "potential advancement," "could extend," "has the promise to free," "anticipates," or similar expressions, or by discussions regarding potential regulatory approvals of ICL670, potential revenues from ICL670, or regarding the long-term impact of a patient's use of ICL670. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with ICL670 to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that ICL670 will be approved for any indications, or will achieve any particular level of revenues, in any market. Neither can there be any guarantee regarding the long-term impact of a patient's use of ICL670. In particular, management's ability to ensure satisfaction of the health authorities' requirements is not guaranteed and management's expectations regarding commercialization of ICL670 could be affected by, among other things, additional analysis of ICL670 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; and other risks and factors referred to in the Company'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.

#### **Additional Information**

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

#### **About Novartis**

Novartis Oncology is a business unit within Novartis AG (NYSE: NVS), is a world leader in pharmaceuticals and consumer health. In 2003, the Group's businesses achieved sales of USD 24.9 billion and a net income of USD 5.0 billion. The Group invested approximately USD 3.8 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 80,000 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

###

#### **Novartis Global Investor Relations**

**Karen J. Huebscher, Ph.D.** +41 61 324 84 33

##### **International office**

Richard Jarvis +41 61 32443 53

Nafida Bendali +41 61 324 35

Silke Zentner +41 61 324 86 12

Katharina Ambühl (materinty leave until end April 2005)

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

Fax: +1 212 830 24 05

[www.novartis.com](http://www.novartis.com)

##### **North American office**

Ronen Tamir +1 212 830 24 33

John Menditto +1 212 830 24 44

Sabine Moravi +1 212 830 24 56

Jill Pozarek +1 212 830 24

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

Fax: +41 61 324 84 44

[www.novartis.com](http://www.novartis.com)

---

Investor Relations

Novartis International AG  
CH-4002 Basel  
Switzerland

Novartis Corporation  
608 Fifth Avenue  
New York, NY 10020  
USA

### Investor Relations Release

#### Results from two new multi-center trials confirm efficacy and tolerability of Prexige 100 mg once daily in treatment of osteoarthritis

*Data reinforce favorable tolerability and safety profile of Prexige 1,2*

**Basel, December 6, 2004** New data from two studies provide strong evidence that the selective COX-2 inhibitor Prexige (lumiracoxib), taken daily at 100 mg offers reduced pain intensity while improving the functional status of patients' osteoarthritis (OA) of the knee. These data were presented at the Osteoarthritis Research Society International (OARSI) annual meeting in Chicago on December 4.

The data shows that over the 13-week study Prexige 100 mg once daily significantly reduced OA pain intensity in the target knee compared to placebo and was comparable to celecoxib 200 mg once daily<sup>1,2,3</sup>. In the first study, Prexige demonstrated significant improvements in pain intensity from the first measurement at Week 2 with a significant reduction of 42% in pain intensity at study end ( $p < 0.01$  vs placebo)<sup>1</sup>.

A similar decrease was observed in the second study with significant improvements throughout the study and a 38% decrease in pain intensity by study end ( $p < 0.001$  vs placebo)<sup>2</sup>. Throughout the study Prexige and celecoxib demonstrated significant improvements in functional status in both studies compared with placebo, with no statistically significant difference observed between active treatment groups<sup>1,2,3</sup>.

In both trials, the number of patients discontinuing treatment due to adverse events, including serious adverse events, was similar between placebo and the active treatment groups<sup>1,2,3</sup>. Furthermore, no significant difference was observed between all treatment groups for the incidence of liver enzyme elevations, defined as alanine aminotransferase/aspartate amino-transferase levels above three times the upper limit of normal. In the first study enzyme elevations with Prexige were 0.2%, celecoxib 0.5% and placebo 0.5%, and Prexige/celecoxib 0.3% and placebo 0.0% in the second study<sup>1,2,3</sup>. These data reinforce the existing body of evidence showing a favorable safety and tolerability profile for Prexige.

Though data regarding gastrointestinal (GI) and cardiovascular (CV) adverse events were not evaluated separately in these trials, results from the landmark TARGET (Therapeutic Arthritis Research & Gastrointestinal Event Trial of lumiracoxib), which were published in August 2004 in *The Lancet*, demonstrated a significant 79% reduction in the incidence of upper gastrointestinal (GI) ulcer complications without compromising cardiovascular (CV) safety. The TARGET trial demonstrated that Prexige has a cardiovascular profile similar to conventional non-steroidal anti-inflammatory drugs (NSAIDs) ibuprofen and naproxen.

The two similarly designed 13-week, randomized, placebo and active-controlled trials compared Prexige 100 mg once daily, Prexige 100 mg once daily with a loading dose of 200 mg once daily for the first two weeks and celecoxib 200 mg once daily to placebo. Both trials were designed using three co-primary efficacy variables including functional status assessment criteria: OA pain intensity in the target knee, patient's global assessment of disease activity and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC ) questionnaire. Improvement in patient's functional status was further assessed using the OMERACT-OARSI functional status criteria.

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Novartis has filed applications for regulatory approval throughout the world based on data from more than 40 pre-clinical and clinical studies in OA, rheumatoid arthritis, acute pain and primary dysmenorrhea involving more than 31,000 adult patients around the world (including TARGET). In addition to the United Kingdom, Prexige has been approved in 21 countries to date, including Australia, New Zealand and several countries in Latin America, including Argentina, Brazil and Mexico. On November 30, 2004, Novartis announced that it had temporarily withdrawn the dossier for Prexige from the Mutual Recognition Procedure in Europe to await the outcome of the EMEA cardiovascular safety review of all COX-2 inhibitors.

The foregoing press release contains forward-looking statements that can be identified by express or implied discussions regarding potential future regulatory filings, approvals or future sales of Prexige (lumiracoxib). 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 any current or future regulatory filings will satisfy the FDA's and other health authorities' requirements regarding Prexige, that Prexige will be approved by the FDA or by any additional country's health authorities for any indication, or that Prexige will be brought to market in the US or any other country, or will reach any particular level of sales. In particular, management's expectations regarding Prexige could be affected by, among other things, regulatory actions or delays or government regulation generally; the public debate and regulatory activity regarding COX-2 inhibitors like Prexige which has followed Merck's withdrawal of Vioxx® from the market; uncertainties relating to clinical trials and product development; and competition in general; 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 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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**Novartis Global Investor Relations**

**Karen J. Huebscher, Ph.D.** +41 61 324 84 33

**International office**

Richard Jarvis +41 61 32443 53

Nafida Bendali +41 61 324 35

Silke Zentner +41 61 324 86 12

Katharina Ambühl (maternity leave until end April 2005)

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

Fax: +1 212 830 24 05

[www.novartis.com](http://www.novartis.com)

**North American office**

Ronen Tamir +1 212 830 24 33

John Menditto +1 212 830 24 44

Sabine Moravi +1 212 830 24 56

Jill Pozarek +1 212 830 24

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

Fax: +41 61 324 84 44

[www.novartis.com](http://www.novartis.com)

---

Investor Relations

Novartis International AG  
CH-4002 Basel  
Switzerland

Novartis Corporation  
608 Fifth Avenue  
New York, NY 10020  
USA

**Investor Relations Release**

**New Glivec data: Prolonged efficacy with approved 400 mg daily dose and potential for improved response at higher dose**

*IRIS 42-month data show remarkable 91% overall survival in patients taking 400 mg recommended daily dose*

*Subset analysis shows 98% progression-free survival in patients achieving major molecular response*

*Second study shows patients on 800 mg daily achieved greater molecular response than patients on currently recommended 400 mg daily dose*

*Patients in both studies were newly diagnosed patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase*

**Basel, Switzerland, December 6, 2004** New data on Glivec (imatinib) demonstrated that newly diagnosed patients with a certain form of leukemia<sup>2</sup> receiving 400 mg daily maintained their response to therapy long term. A separate study found patients receiving 800 mg daily had better outcomes compared to patients receiving 400 mg daily. Patients receiving 800 mg daily were found to be more likely to achieve a major molecular response.

An update to the landmark International Randomized Interferon versus STI571 (IRIS) study was presented on December 5 at the American Society of Hematology (ASH) annual meeting in San Diego. The study results demonstrated a link between rapid, early cytogenetic response and long-term outcome during treatment with Glivec in newly diagnosed patients with chronic-phase Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML). Patients who achieved cytogenetic responses early in the study had improved rates of progression-free survival compared to those who did not achieve early responses.

In a separate study also presented at ASH, researchers at the M.D. Anderson Cancer Center in Houston, Texas, found that patients with newly diagnosed chronic phase Ph+ CML who took an 800 mg daily dose of Glivec were more likely to achieve a complete cytogenetic response (CCR) than patients taking the approved 400 mg daily starting dose. In addition to a higher rate of CCR, the study found 67% of patients taking 800 mg daily achieved a major molecular response (MMR) at a median follow-up of 19 months compared to 47% of patients taking 400 mg daily at a median follow-up of 36 months. MMR is defined as the near absence of disease at a molecular level. Molecular response may prove a possible new benchmark for evaluating effectiveness of drug therapy and disease prognosis. "The more data we see on Glivec, the more it appears that patients obtain better long-term outcomes when they reduce their leukemic loads rapidly, which we know can be achieved in more patients with an optimised dose," said Jorge Cortes, MD, Department of Leukemia, M.D. Anderson Cancer Center. "These new data show that patients who have good early responses may have the greatest protection from relapse."

**Study details**

Abstract # 21: *Guilhot F on behalf of the IRIS Study Group. Sustained durability of responses plus high rates of cytogenetic responses result in long-term benefit for newly diagnosed chronic-phase chronic myeloid leukemia treated with imatinib therapy: update from the IRIS study*

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The study was conducted in 1,106 patients. At the 42-month follow-up, 98% of newly diagnosed patients treated with Glivec had achieved complete hematologic response (CHR), while 91% had achieved a major cytogenetic response (MCR) and 84% had achieved a complete cytogenetic response (CCR).

For patients who had achieved CCR and a thousand-fold (3 log) or greater reduction in Bcr/Abl transcript level a molecular response at 12 months, the probability of remaining progression-free was 98% at 42 months compared with 90% for patients with CCR and less than a thousand-fold reduction in Bcr-Abl transcript level and 75% for patients who had not achieved CCR.

Responses to Glivec were found to be durable at the 42-month follow-up, with an estimated 91% of patients maintaining CHR, 91% of patients maintaining MCR and 87% of patients maintaining CCR.

In CML, a molecular response is the disappearance or reduction in the quantity of Bcr-Abl transcripts that produce the abnormal protein responsible for driving the proliferation of white blood cells that occurs in CML patients. CHR refers to the normalization of blood counts, lasting for at least four weeks. However, the cells containing the Philadelphia chromosome (the genetic abnormality that characterizes most cases of CML) may still be present. In MCR, less than 35% of cells containing the Philadelphia chromosome are detected.

The most common adverse events to first-line treatment with Glivec in this study were hemtologic and hepatic toxicities and included severe (NCI Grades 3/4) neutropenia (16.2%), anemia (4.0%), thrombocytopenia (9.3%) and elevated liver enzymes (5.4%). Other drug-related adverse events occurred in 15.8% of patients.

Abstract #999: Cortes J, et al. High-dose imatinib mesylate treatment in patients with previously untreated early chronic phase chronic myeloid leukemia

The second study, conducted by researchers at the M.D. Anderson Cancer Center in Houston, Texas, consisted of three consecutive trials. In these trials, a total of 222 previously untreated early chronic phase CML patients were split into two groups. In one group, patients were treated with the 400 mg daily dose of Glivec, while another group was treated with 800 mg daily. Median follow-up of patients on 400 mg daily was 36 months and median follow-up of patients on 800 mg daily was 19 months.

Patients in the higher dose group had an estimated progression-free survival rate of 99% at 12 months compared with 92% in the standard dose group. Researchers concluded that the 800 mg daily Glivec dose resulted in higher rates of complete cytogenetic and molecular remissions.

Extramedullary toxicity (toxicity outside the bone marrow) was similar in the two groups, but myelosuppression was more common with high dose. Severe (NCI Grades <sup>3/4</sup>) anemia, neutropenia and thrombocytopenia occurred in 7%, 39% and 27% of patients receiving the high dose, respectively, and 4%, 20% and 12% of patients receiving the standard dose, respectively. At 12 months, the median actual dose for the high-dose group was still 800 mg daily, with 40 of 112 (36%) evaluable patients having required dose reduction. This compared with 7 of 43 (14%) of those treated with the standard dose.

## **About Glivec**

Glivec is indicated in the EU for the treatment of patients with newly diagnosed Ph+ CML for whom bone marrow transplantation is not considered as the first line of treatment. Glivec is approved in the U.S. for newly diagnosed adult patients with Ph+ chronic phase CML and pediatric patients with Ph+ chronic phase CML whose disease has recurred after stem cell (an unspecialized cell that gives rise to differentiated cells) transplant or who are resistant to interferon-alpha treatment. In Japan, Glivec is approved for adult patients in all phases of Ph+ CML. In addition, Glivec is already approved for the treatment of adult patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha treatment in more than 80 countries worldwide.

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Glivec is approved in the EU, US and other countries for the treatment of patients with Kit (CD117) positive gastrointestinal tumors (GISTs), which cannot be surgically removed and/or have already spread to other parts of the body (metastasized). In Japan, Glivec is approved for the treatment of patients with Kit (CD117) positive GISTs.

The effectiveness of Glivec is based on overall hematologic and cytogenetic response rates and progression-free survival in CML and objective response rates in GIST. There are no controlled trials demonstrating increased survival.

### **Contraindications, warnings and adverse events<sup>3</sup>**

In the first-line study (IRIS), the safety profile with Glivec was similar to that of previous Phase II studies in other CML patients. The majority of patients treated with Glivec experienced adverse events at some time. Most events were of mild to moderate grade and treatment was discontinued for adverse events only in 2% of patients in chronic phase, 3% in accelerated phase and 5% in blast crisis. The most common side effects included nausea, superficial edema, muscle cramps, skin rash, vomiting, diarrhea, hemorrhage, fatigue, headache, joint pain, cough, dizziness, dyspepsia and dyspnea, as well as neutropenia and thrombocytopenia.

The most common undesirable effects experienced during Glivec treatment in GIST are: headache, nausea, vomiting, diarrhea, dyspepsia, myalgia, muscle spasm and cramps, joint swelling, dermatitis, eczema, rash, edema, fluid retention, neutropenia, thrombocytopenia or anemia.

Glivec is contraindicated in patients with known hypersensitivity to imatinib or any of its excipients. Women of childbearing potential should be advised to avoid becoming pregnant while taking Glivec.

The foregoing release contains forward-looking statements that can be identified by terminology such as "long-term," "prolonged efficacy," "potential for improved response," "remarkable overall survival," "progression-free survival," "greater response," "better outcomes," "more likely to achieve," "improved rates," "it appears", "possible new benchmark," "greatest protection," "found to be durable," "estimated", or similar expressions, or by express or implied discussions regarding potential new indications for Glivec or potential future sales of Glivec, or regarding the long-term impact of a patient's use of Glivec. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Glivec to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Glivec will be approved for any additional indications in any market. Nor can there be any guarantee regarding potential future sales of Glivec. Neither can there be any guarantee regarding the long-term impact of a patient's use of Glivec. In particular, management's expectations regarding commercialization of Glivec could be affected by, among other things, additional analysis of Glivec 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; government, industry, and general public pricing pressures; and 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 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.

### **For more information**

Information about Glivec is available at [www.Glivec.com](http://www.Glivec.com). Reporters interested in more information regarding Glivec or Novartis Oncology can visit the Novartis Oncology Virtual Press Office at [www.novartis oncologyVPO.com](http://www.novartis oncologyVPO.com). The site features background information on Novartis Oncology products.

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## References

1. Known as Gleevec in the US
2. The studies were conducted in patients with newly diagnosed chronic phase Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML)
3. Numbers indicate the range in percentages in four studies among patients with CML in blast crisis, accelerated phase and chronic phase

###

## Novartis Global Investor Relations

**Karen J. Huebscher, Ph.D.** +41 61 324 84 33

### International office

Richard Jarvis +41 61 32443 53

Nafida Bendali +41 61 324 35

Silke Zentner +41 61 324 86 12

Katharina Ambühl (maternity leave until end April 2005)

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

Fax: +1 212 830 24 05

[www.novartis.com](http://www.novartis.com)

### North American office

Ronen Tamir +1 212 830 24 33

John Menditto +1 212 830 24 44

Sabine Moravi +1 212 830 24 56

Jill Pozarek +1 212 830 24

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

Fax: +41 61 324 84 44

[www.novartis.com](http://www.novartis.com)

---

**Novartis International AG**

Novartis Communications  
CH-4002 Basel  
Switzerland  
Tel +41 61 324 2200  
Fax+ 41 61 324 3300  
Internet Address:  
<http://www.novartis.com>

**MEDIA RELEASE    COMMUNIQUE AUX MEDIAS    MEDIENMITTEILUNG**

**Novartis Foundation for Sustainable Development celebrates 25th anniversary with symposium on the "Right to Health: A Duty for Whom?"**

**Basel, December 2, 2004** The Novartis Foundation for Sustainable Development (NFSD) today reinforced its 25-year commitment to sustainable development and stakeholder-dialogue with a landmark symposium exploring the roles and responsibilities of key societal players in ensuring the right to human health.

The symposium focused on the complexity of healthcare issues facing the developing world and the need for public-private partnerships to combine the unique expertise and capacities of various stakeholders in creating viable and sustainable solutions.

"In development politics, there are no solutions that are easy and persuasive at one and the same time," said Professor Dr. Klaus M. Leisinger, President and CEO of the Novartis Foundation for Sustainable Development and host of the symposium. "Though it might be an uncomfortable way to go, we are convinced that dialogue with critics and constructive engagement are essential to finding common ground for progress."

The symposium brought together over 500 international experts and stakeholders involved in healthcare and development issues, including: Paul Hunt, U.N. Special Rapporteur on the Right to Health; Joan Kaufman, Director of AIDS Public Policy Training Project Asia Programs, Harvard University; Ioanna Kuçuradi, President of the National Committee for the "UN Decade for Human Rights Education"; and Daniel Vasella, Chairman and CEO of Novartis.

One key topic was the role of pharmaceutical companies in ensuring access to medicines for people who cannot afford treatment. Participants explored the importance of creating basic health infrastructure like sanitation, transportation, distribution and education in addition to providing access to affordable and effective medicines.

"One vital way of improving health conditions for poor people of the world is to establish strong partnerships involving all parties – governments, NGOs, the private sector and international organizations," said Paul Hunt, U.N. Special Rapporteur on the Right to Health. "The cooperation between The World Health Organization (WHO), the NFSD and Novartis to eliminate leprosy exemplifies this form of partnership."

The Novartis Foundation for Sustainable Development has worked for decades with governments and international partners such as the WHO and other United Nations organizations on disease prevention and treatment programs and other basic healthcare services to promote economic, social and cultural human rights in developing nations.

The results of this commitment include providing over three million multi-drug therapy treatments free of charge to cure leprosy patients around the world and donating 500,000 tuberculosis treatments to the WHO.

**For further information**

For more background information and pictures please access the electronic media kit at:  
<http://novartis.imagedirector.net/album?album-code=trcucrqn6mkz>

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For the first time, the symposium was web cast. The web cast will be available during 3 months at:  
<http://www.novartisfoundation.com/en/symposia/2004>

For more information on the Novartis Foundation for Sustainable Development please consult <http://www.novartisfoundation.com>.

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Investor Relations

Novartis International AG  
CH-4002 Basel  
Switzerland

Novartis Corporation  
608 Fifth Avenue  
New York, NY 10020  
USA

**Investor Relations Release**

**Diovan® receives approval in Sweden to treat high-risk heart attack patients**

*First-in-class approval solidifies already established cardio-protective benefits of leading high blood pressure agent*

*Paves the way for further approvals of this indication throughout the EU*

**Basel, December 1, 2004** Diovan® (valsartan), a powerful, first-line high blood pressure agent, has received its first European marketing authorization from the Medical Products Agency (MPA) of Sweden to treat patients at high risk following a recent heart attack.

Diovan is the first drug in its class to obtain such an indication, which was based on the positive results of a major international trial proving Diovan to be as effective at preventing death of heart attack survivors as a current standard of care. The approval provides a new treatment for these patients, half of whom are not receiving recommended therapies, and marks a major step toward attaining authorization of Diovan for this new indication throughout the European Union (EU). This indication was nationally approved in the UK earlier this year.

"Combined with Diovan's well established double-digit blood pressure reduction efficacy and proven cardio-protective benefits, the approval in Sweden secures Diovan's place on the forefront of cardiovascular medicine," said Dr. Jörg Reinhardt, Head of Development, Novartis Pharma AG. "We look forward to acquiring similar indications across the European Union to provide heart attack survivors a protective treatment that may be life-saving."

Novartis is pursuing this indication in 13 additional member states of the EU as well as Iceland based on the approval by Sweden through the Mutual Recognition Procedure (MRP). Novartis has also submitted a marketing application at the national level in France, and additional filings have been made in the US and Australia as well as in certain Asian and Latin American countries. Under the MRP, a EU member state is expected to recognize the marketing authorization granted by another member state within 90 days of the start of the process. To date, 23 countries around the world, including the UK and a number of Latin American countries, have approved Diovan to treat post-heart attack patients.

Heart attack remains one of the world's deadliest conditions. Every year, more than three million people from EU countries and 1.2 million Americans suffer a heart attack. High blood pressure is a major risk factor for heart attacks. While progress has been made in treating heart attacks in the emergency room, people who survive the acute (emergency) phase of a heart attack have permanently damaged hearts and are at greatly increased risk for repeat attacks, heart failure or other deadly complications. One in three will die within a year after surviving a first heart attack, and half of all heart attacks are repeat attacks. There is a critical need for new treatments given such a high risk of death.

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### **New approvals based on landmark VALIANT trial**

The new approval for Diovan is based on the positive results of VALIANT (VALsartan In Acute myocardial iNfarcTion), one of the largest long-term studies ever conducted in people who have survived a heart attack. VALIANT demonstrated that Diovan preserved 99.6% of the benefit of captopril, which is currently a standard of care in these patients, meaning it reduced death to the same degree as the proven treatment. This finding translates into a 25% reduction in premature death by Diovan in patients at high risk following a heart attack. Diovan is the only cardiovascular agent ever demonstrated by a head-to-head trial to have matched the proven benefits of an ACE inhibitor in these patients.

VALIANT was a rigorous comparison of Diovan vs. the ACE inhibitor captopril in 14,703 patients at the highest risk for death following a heart attack for an average of two years. VALIANT also studied the effects of combination treatment with Diovan and captopril. An active-controlled trial, VALIANT compared Diovan to a proven treatment instead of a placebo or sugar pill and was statistically powered to prove whether the effects of Diovan on all-cause mortality were comparable to captopril. The patient population and dosing regimen were intentionally modeled after studies which established the benefits of ACE inhibitors vs. placebo so that a statistical comparison (imputed placebo analysis) could be made of the findings.

VALIANT demonstrated that Diovan is well-tolerated in post-heart attack patients. Adverse events were generally related to the underlying disease.

### **About Diovan**

One of the fastest-growing high blood pressure drugs on the market today, Diovan is a powerful first-line treatment of high blood pressure approved in more than 80 countries and in more than 50 for the treatment of heart failure in patients who also take usual therapy including diuretics, digitalis and either beta blockers or ACE inhibitors, but not both. In the US and Switzerland, among other countries, Diovan is indicated for the treatment of heart failure in patients who cannot tolerate ACE inhibitors. Additional approvals are pending in the European Union for Diovan for the treatment of heart failure.

This new indication for Diovan in Sweden is for the treatment of clinically stable patients with symptomatic heart failure or asymptomatic left ventricular dysfunction after a recent myocardial infarction (heart attack).

Novartis is focused on improving the care of patients with high blood pressure and heart disease through world-class research and unprecedented public health initiatives. The Diovan clinical trial program represents an impressive research commitment across the cardiovascular continuum, involving approximately 50,000 patients. Recently completed Diovan trials include VALUE in high blood pressure patients at risk for cardiovascular complications, VALIANT in post-heart attack patients and Val-HeFT in heart failure patients. Ongoing studies include the NAVIGATOR trial, the largest outcomes trial ever conducted on the prevention of cardiovascular disease and type 2 diabetes in patients with impaired glucose tolerance.

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The foregoing release contains forward-looking statements that can be identified by terminology such as "marks a major step toward", "secures... on the forefront", "look forward to", "is pursuing", "is expected", 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 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 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 2003, the Group's businesses achieved sales of USD 24.9 billion and a net income of USD 5.0 billion. The Group invested approximately USD 3.8 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 81,000 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

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#### **Novartis Global Investor Relations**

**Karen J. Huebscher, Ph.D.** +41 61 324 84 33

##### **International office**

Richard Jarvis +41 61 324 43 53

Nafida Bendali +41 61 324 35

Silke Zentner +41 61 324 4586 12

Katharina Ambühl (materinty leave until end April 2005)

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

Fax: +41 61 324 84 44

[www.novartis.com](http://www.novartis.com)

##### **North American office**

Ronen Tamir +1 212 830 24 33

John Menditto +1 212 830 24 44

Sabine Moravi +1 212 830 24 5615

Jill Pozarek +1 212 830 24

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

Fax: +1 212 830 24 05

[www.novartis.com](http://www.novartis.com)

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**Novartis International AG**

Novartis Communications  
CH-4002 Basel  
Switzerland  
Tel +41 61 324 2200  
Fax+ 41 61 324 3300  
Internet Address:  
<http://www.novartis.com>

**MEDIA RELEASE    COMMUNIQUE AUX MEDIAS    MEDIENMITTEILUNG**

**Certican® European Union Mutual Recognition Procedure expanded to include 10 new EU Member States**

*Could offer transplant recipients a welcome new tool to improve long-term survival following cardiac and kidney transplantation*

**Basel, December 1, 2004** Novartis Pharma AG announced today that the 10 new European Union Member States have completed the Mutual Recognition Procedure (MRP) for Certican® (everolimus) for the prophylaxis of organ rejection in adult kidney and cardiac transplant patients at low to moderate immunological risk.

The 10 new EU member states participating in the second wave of MRP included Cyprus, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, Slovakia and Slovenia. All of these countries agreed to issue a national marketing authorization based on the assessment of Sweden as the reference member state.

"The completion of the expanded MRP for Certican reinforces the value of Certican as a new agent in transplantation," said Tony Rosenberg, Head of the Novartis Transplantation and Immunology Business Unit, Novartis Pharma AG. "Certican could offer transplant patients and physicians a welcome new tool to improve long-term survival through its ability to reduce the incidence and severity of the primary causes of rejection."

Certican is a proliferation signal inhibitor that targets the primary causes of allograft dysfunction (also known as chronic rejection) following organ transplantation, including acute rejection and vascular remodelling. Certican is the first drug in its class to receive the indication for both heart and kidney transplant recipients. Preventing allograft dysfunction or late graft loss remains a major unmet medical need in transplantation.

The decision by these European countries is based on data from studies comprising 634 heart transplant patients over 24 months and more than 1,700 kidney transplant patients for up to 36 months. Results from these studies showed Certican effectively prevented graft rejection when given with low-dose Neoral® (cyclosporin for microemulsion) and corticosteroids.

At the completion of MRP in December 2003, the following 15 countries initially provided their endorsement: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Italy, Luxembourg, Netherlands, Norway, Portugal, Spain and Sweden. Certican received its first approval from the Swedish Medical Products Agency in July 2003 for the prevention of rejection in heart and kidney transplant patients in combination with Neoral and corticosteroids. Sweden served as the reference member state for MRP.

Since the completion of the initial MRP in the EU in December 2003, Certican is now available in Germany, Austria, Portugal, the Netherlands, Greece, the Nordic countries and most recently in several Latin American countries.

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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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 "could offer", "committed to developing", or similar expressions, or by express or implied discussions regarding potential additional marketing approvals or future sales of Certican. 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 Certican to be materially different from any future results, performance, or achievements expressed or implied by such statements. There can be no guarantee that Certican will receive any additional marketing approvals in any other countries, or that it 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.

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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: January 5, 2005

By:           /s/ MALCOLM B. CHEETHAM          

Name: Malcolm B. Cheetham

*Title: Head Group Financial Reporting and Accounting*

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