

NOVARTIS AG  
Form 6-K  
June 02, 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 May 2005  
(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:

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Yes:  No:

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### Enclosures:

1. Novartis receives European Commission approval to acquire Hexal AG, further step towards creating world leader in Generics (Basel, May 27, 2005)
  2. Xolair® halves rate of severe exacerbations and significantly improves quality of life in patients at risk of life-threatening asthma attacks (San Diego, Calif., May 26, 2005)
  3. Novartis unveils promising Phase II data for bronchodilator QAB149 (San Diego, Calif., May 23, 2005)
  4. Preliminary phase III data show Lucentis maintained or improved vision in nearly 95% of patients with wet age-related macular degeneration (Basel, May 23, 2005)
  5. Certican approved by Swissmedic to reduce risk of organ rejection in heart and kidney transplant patients (Basel, May 18, 2005)
  6. New data show Zometa® significantly improved bone mineral density in breast cancer patients receiving adjuvant therapy (Basel, Switzerland, May 16, 2005)
  7. First results from PTK/ZK CONFIRM 1 trial presented at American Society of Clinical Oncology show positive drug effects in advanced colorectal cancer (Basel, Switzerland, May 13, 2005)
  8. Femara helped significantly more women with early breast cancer live free of cancer compared with tamoxifen, study presented today shows (Basel, Switzerland, May 13, 2005)
  9. Diovan® receives EU approval for the treatment of heart attack survivors (Basel, Switzerland, May 9, 2005)
  10. Novartis files Exjade® new drug applications for treatment of chronic iron overload due to blood transfusions (Basel, Switzerland, May 3, 2005)
  11. Novartis highlights pharmaceutical research strategy, intensifying focus on molecular pathways shared by various diseases (Cambridge, Massachusetts, May 3, 2005)
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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 receives European Commission approval to acquire Hexal AG, further step towards creating world leader in Generics**

**Basel, May 27, 2005** Novartis announced today that it has received approval from the European Commission to acquire the privately-held generic pharmaceutical company Hexal AG of Germany. The acquisition is expected to be completed in early June.

"With the completion of this acquisition, Sandoz will further strengthen its ability to rapidly bring the best-quality, cost effective generic drugs to patients and physicians, offering more choices to meet their healthcare needs," said Dr. Daniel Vasella, Chairman and CEO of Novartis. "The combined company will have outstanding management talent, which combined with a dynamic, fast moving culture, will position the new Sandoz for strong growth and leadership in the generics business."

Hexal will be integrated into the Sandoz division of Novartis as part of previously announced strategic acquisitions to create the world leader in the generic drug industry.

Following the acquisitions, Sandoz will be a leader in generic pharmaceuticals in Germany and in several other key regions, and will have a strong presence in Asia and Latin America. The company will have a portfolio of more than 600 active ingredients, in more than 5,000 dosage forms. Sandoz will have a competitive, broad product portfolio and geographic presence, as well as leading development and registration capabilities. The combination will significantly strengthen its technology base, particularly in the application of transdermal patches, inhalation products, sustained-release implants and multi-particulate drug-delivery dosage forms, and expand the already strong capabilities in biopharmaceuticals.

"Thanks to the strength of our integration planning, Sandoz is fully prepared to rapidly integrate and operate as a unified company," said Dr. Andreas Rummelt, CEO of Sandoz. "Our major strategy and staffing decisions have been taken, and we are on course to meet our most ambitious timelines. We will put all our efforts towards further building our market presence to deliver our products to patients and physicians worldwide."

After the acquisition, Sandoz will employ more than 20,000 people. Its global headquarters will be located in Holzkirchen, Germany, by year-end.

On May 23, Novartis initiated a tender offer to acquire the publicly-held shares of Eon Labs, Inc. (NASDAQ: ELABS), a US generic pharmaceuticals company that has a strategic partnership with Hexal. The tender offer, set at USD 31.00 per share, is scheduled to expire on June 20, 2005, and is subject to completion of the regulatory process and the contemporaneous purchase of a 67.7 percent stake in Eon Labs from its control shareholder. Novartis is in the process of responding to a request from the US Federal Trade Commission for additional information regarding the acquisition of Eon Labs (commonly referred to as a "second request").

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This document contains "forward-looking statements" within the meaning of the US Private Securities Litigation Reform Act. Forward-looking statements are statements that are not historical facts and are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "will", or similar expressions, or by express or implied discussions regarding strategies, plans and expectations (including synergies). These statements include, but are not limited to, financial projections and estimates and their underlying assumptions, statements regarding the benefits of the business transactions described herein, including future financial and operating results. Such statements reflect the current plans, expectations, objectives, intentions or views of management with respect to future events, are based on the current beliefs and expectations of management and are subject to significant risks, uncertainties and assumptions. Management's expectations could be affected by, among other things, competition in general, the general economic environment and other risks such as, but not limited to, those referred to in Novartis AG's 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 differ materially from those set forth or implied by the forward-looking statements.

The following factors, among others, could cause actual results to differ materially from those set forth in the forward-looking statements: the ability to obtain governmental approvals for the transaction on the proposed terms and schedule; the risk that the businesses will not be integrated successfully; the risk that the cost savings and any other synergies from the transaction may not be fully realized or may take longer to realize than expected; disruption from the transaction making it more difficult to maintain relationships with customers, employees or suppliers; social and political conditions such as war, political unrest and terrorism or natural disasters; and general economic conditions and normal business uncertainty and competition and its effect on pricing, spending, third-party relationships and revenues. These forward-looking statements speak only as of the date of this press release and no undertaking has been made to update or revise them if there are changes in expectations or if any events, conditions or circumstances on which any such forward looking statement is based.

Securityholders of Eon are urged to read the tender offer statement LETTER OF TRANSMITTAL AND OTHER MATERIALS relating to the tender offer, as THEY contain important information, including the various terms of, and conditions to, the tender offer. Securityholders can obtain a copy of the tender offer statement. LETTER OF TRANSMITTAL AND OTHER RELATED MATERIALS FREE OF CHARGE at the SEC's internet site (<http://www.sec.gov>) or from the information agent for the tender offer, Georgeson Shareholder Communications Inc., by calling (877) 278-4774 (call toll-free). We urge EON securityholders to carefully read those materials prior to making any decisions with respect to the tender offer.

#### **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 a 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 approximately 81,400 people and operate in over 140 countries around the world. Further information is available at [www.novartis.com](http://www.novartis.com).

Sandoz, a Novartis company, is a world leader in generic pharmaceuticals and develops, manufactures and markets these medicines as well as pharmaceutical and biotechnological active ingredients. Decades of experience and know-how make Sandoz a renowned partner in pharmaceuticals, biogenerics and industrial products. Sandoz employs approximately 13,000 people in over 110 countries and reported sales of USD 3.0 billion in 2004.

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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 +41 61 324 53 16

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

Nina Malik +1 925 551 59 64

John Menditto +1 212 830 24 44

Jill Pozarek +1 212 830 24 45

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

**Xolair® halves rate of severe exacerbations and significantly improves quality of life in patients at risk of life-threatening asthma attacks**

***First humanised antibody for asthma could fulfill important unmet need***

**San Diego, Calif., May 26, 2005** Results of a clinical study presented at a leading international medical congress show that Xolair® (omalizumab) halved the rate of severe asthma exacerbations and reduced the rate of hospital emergency visits by 44% in patients with inadequately controlled severe persistent asthma, who are at high risk of life-threatening attacks.<sup>(1)</sup> Xolair also significantly improved patients' asthma-related quality of life, according to data from the same study presented at the centenary congress of the American Thoracic Society this week.<sup>(2)</sup>

Xolair is a first-in-class therapy that is given by injection every two or four weeks and blocks the action of IgE, the antibody responsible for triggering the cascade of allergic symptoms in patients with diseases such as allergic asthma. It offers a novel therapeutic approach to the control of asthma symptoms such as wheezing and shortness of breath, even in the most difficult-to-treat patients whose condition remains poorly-controlled despite receiving the best available therapy.

A total of 419 such patients, aged 12-75, were recruited for a double-blind, placebo-controlled, parallel-group, multicenter study called INNOVATE to assess the effect of add-on Xolair therapy on the rate of severe asthma exacerbations and emergency visits.<sup>(1)</sup> The participants all had reduced lung function and a recent history of clinically significant exacerbations, despite receiving step 4 therapy as defined in the GINA guidelines, including high-dose inhaled corticosteroids, long-acting beta2-agonists and other controller medication (including oral corticosteroids) if required.

**Severe exacerbations halved**

The severe exacerbation rate (i.e. where lung function measured by PEF or FEV1 was less than 60% of personal best, requiring systemic corticosteroids) and the rate of emergency visits (i.e. hospital admissions, emergency room visits and unscheduled doctor's visits) were calculated during the treatment phase. Results showed that add-on Xolair therapy significantly reduced both the severe exacerbation rate (0.24 vs 0.48,  $p = 0.002$ ) and emergency visit rate (0.24 vs 0.43,  $p = 0.038$ ) compared with placebo. The authors concluded: "Omalizumab should be considered as add-on therapy for patients with inadequately controlled severe persistent asthma who have a significant unmet need despite best available therapy."

The rate of clinically significant asthma exacerbations (i.e. those requiring rescue systemic corticosteroid therapy) was significantly reduced by 26% ( $p = 0.043$ ), when adjusted for an observed imbalance in asthma exacerbation history prior to randomisation into the trial. Without taking this baseline imbalance into account, a similar magnitude of effect was seen (i.e. a 19% reduction) but this did not reach statistical significance.<sup>(3)</sup>

Around 300 million people in the world have asthma,<sup>(4)</sup> of whom an estimated 15 million suffer from severe persistent disease.<sup>(5)</sup> Their health and quality of daily life are severely affected, and asthma is estimated to cause more than 180,000 deaths worldwide each year.<sup>(6)</sup> Until now there have been few additional therapeutic options available for these patients.

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A further analysis of data from the INNOVATE study evaluated the impact of Xolair treatment on patients' quality of life, measured by the Asthma QoL Questionnaire (AQLQ) (i.e. individual domains, overall score and clinically meaningful  $\geq 0.5$ -point improvement).<sup>(2)</sup> Add-on Xolair therapy produced significantly greater improvements than placebo for each individual AQLQ domain ( $p < 0.002$ ) and overall score ( $p < 0.001$ ). In addition, a significantly greater proportion of patients receiving Xolair achieved a clinically meaningful  $\geq 0.5$ -point improvement from baseline in their AQLQ score than patients receiving placebo (60.8% vs 47.8%,  $p = 0.008$ ).

#### **Well-tolerated in children**

Another study presented at the ATS congress evaluated the long-term safety and tolerability of Xolair in children aged 6-12 years at entry, who were eligible to join a three-year multicenter, open-label extension on completion of a one-year clinical trial (28-week double-blind core trial and 24-week open-label extension).<sup>(7)</sup>

The percentage of patients who experienced adverse events (AEs) in the core trial was similar in the Xolair and placebo groups (89.3%,  $n = 201$  and 87.2%,  $n = 95$  respectively). Of the 309 patients who entered the 24-week extension of the core trial, 244 (79.0%) experienced an AE. A total of 188 patients continued into the three-year extension, of whom 103 completed the study. Of the 85 patients who discontinued, the majority withdrew consent due to study duration and maintaining study commitments.

Xolair was generally well-tolerated and most AEs were mild to moderate in severity. When evaluated by 28-week increments, the incidence of AEs was generally comparable or lower than that seen in the 28-week core trial. No AEs suggestive of immunological reactions were reported. Overall, there were 13 AEs that investigators suspected were drug-related. There were eight serious AEs of which only one (dyspnea) was considered to be drug-related. No evidence of clinically significant changes in vital signs, spirometry or laboratory parameters, including platelets, were observed following Xolair treatment.

Xolair was launched in the US in July 2003, and is also approved in Australia, Brazil, Canada, Dominican Republic, Guatemala, Israel, New Zealand and Venezuela. It has been developed under an agreement between Novartis Pharma AG, Genentech, Inc., and Tanox, Inc. The European Medicines Agency (EMA) is due to announce its decision on Xolair approval later this year.

The foregoing release contains certain forward-looking statements that can be identified by terminology such as "could fulfill," "should be considered," "is due to," or similar expressions, or by discussions regarding the potential that Xolair will be approved for marketing, or regarding any potential 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 market. In particular, management's expectations regarding commercialization of Xolair could be affected by, among other things, uncertainties relating to clinical trials; new clinical data; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; 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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## About Novartis

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## References

- (1) Korenblat P, Levy R, Slavin R, Hedgecock S, Fox H, Surrey K, Reisner C. Add-on omalizumab therapy significantly reduces severe asthma exacerbations and emergency visits in patients with inadequately controlled severe persistent asthma despite GINA 2002 step 4 therapy: INNOVATE. ATS, May 2005.
- (2) Matz J, Melamed I, Ledford D, Hedgecock S, Fox H, Surrey K, Reisner C. Add-on omalizumab therapy significantly improves quality of life in patients with inadequately controlled severe persistent asthma despite GINA 2002 step 4 treatment: INNOVATE. ATS, May 2005.
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- (4) GINA. The Global Burden of Asthma Report 2004.
- (5) American Thoracic Society. Proceedings of the ATS workshop on refractory asthma. Current understanding, recommendations, and unanswered questions. Am J Respir Crit Care Med 2000;162:2341-2351.
- (6) World Health Organization, <http://www.who.int/mediacentre/factsheets/fs206/en/>
- (7) Milgrom H, Miller SD, Lanier BQ, Fowler-Taylor A, Chen H, Gupta N. Long-term omalizumab therapy is well tolerated in children with moderate-to-severe IgE-mediated asthma. ATS, May 2005.

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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 unveils promising Phase II data for bronchodilator QAB149**

***QAB149 provides 24-hour bronchodilation with once-daily dosing***

**San Diego, Calif., May 23, 2005** Novartis announced today that its development compound indacaterol (QAB149) may provide a new standard for beta2-agonist therapy in patients with asthma and chronic obstructive pulmonary disease (COPD), according to data presented at the centenary meeting of the American Thoracic Society (ATS). The collective data from Phase II studies show indacaterol provides effective and well-tolerated bronchodilation for up to 24-hours, with convenient once-daily dosing.

"The release of these first clinical data on indacaterol show that it offers significant therapeutic potential for patients with asthma and COPD, either as a single agent or in combination with drugs such as the long-acting anti-muscarinic AD 237, which was recently licensed by Novartis," said Joerg Reinhardt, Global Head of Development, Novartis Pharma AG. "Tackling respiratory diseases is one of our major priorities for the future, and we have designed an ambitious development program for these and other compounds."

**Results in patients**

A randomized, double-blind, dose-ranging study (50, 100, 200, 400 g or placebo) in 42 patients with intermittent or mild to moderate persistent asthma demonstrated effective 24-hour bronchodilation within five minutes and a favorable safety profile with once-daily dosing. Improvements in efficacy were generally dose-dependent, while safety and tolerability were similar to the effects reported for placebo. Beeh K-M, Schelfout V, Grönke L, Kanniess F, Cameron R, van As A. Indacaterol (QAB149): the first once-daily  $\beta_2$ -agonist with 24-hour bronchodilation. Abstract 1314, poster board number G34.

"Despite advances in the management of these chronic conditions, the numbers of individuals affected by asthma and COPD are large and growing," said James Donohue, M.D., Professor of Medicine, Chief, Division of Pulmonary Critical Care, University of North Carolina School of Medicine. "These data show indacaterol has significant therapeutic potential, including single-dose 24-hour control for asthma and COPD patients."

A further randomized, double-blind, placebo-controlled, parallel-group, multicenter study involving 156 patients aged 13-75 demonstrated that indacaterol was shown to have a favorable cardiovascular safety profile, with no clinically significant effect on ECG measurements, vital signs or laboratory tests commonly affected by long-duration beta2-agonists. No clinically notable changes occurred in the mean QTc intervals for any treatment group at any time point (calculated using Fridericia's formula). No clinically or statistically significant changes in serum potassium and blood glucose, or evidence of dose-related increases in adverse events, were detected. In addition, no serious adverse events occurred in any active treatment group. Chuchalin AG, Tsoi AN, Richter K, Arieovich H, Cameron R, Bao W, van As A. Cardiovascular safety of indacaterol (QAB149), a novel 24-hour  $\beta_2$ -agonist, in patients with asthma. Abstract 1316, poster board number G35.

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### Indacaterol pre-clinical studies

In addition, extensive pre-clinical studies involving indacaterol were also presented, demonstrating that in isolated human bronchi, indacaterol provides effective bronchodilation with a longer duration of action than albuterol and formoterol and an onset of action more rapid than salmeterol and comparable to albuterol. At resting tone, the onset of action of indacaterol ( $9.2 \pm 1.5$ min,  $n = 8$ ) was not significantly different from that of formoterol ( $5.8 \pm 0.8$ min,  $n = 8$ ) and albuterol ( $11.0 \pm 3.6$ min,  $n = 8$ ) but was significantly faster than that of salmeterol ( $18.0 \pm 3.5$ min,  $n = 8$ ;  $p < 0.05$ ). Naline E, Molimard M, Fairhurst R, Trifilieff A, Advenier C. Duration and onset of action of indacaterol (QAB149), a novel 24-hour  $\beta_2$ -agonist, on the isolated human bronchus. Abstract 1296, poster board number G32. In addition, indacaterol was shown to be a potent  $\beta_2$ -agonist that, in contrast to salmeterol, does not antagonize the bronchorelaxant effect of a short-acting  $\beta_2$ -agonist.

Other pre-clinical data demonstrate that indacaterol provides a long duration of action and fast onset *in vitro* and *in vivo* in animals. The risk of tachyphylaxis, or rapidly decreasing response to a drug, was assessed in once-daily intratracheal (IT) dosing of indacaterol compared with formoterol and salmeterol. Animals in the study were then challenged with aerosolized 5-HT (175g/mL, 1 min) two hours after  $\beta_2$ -agonist exposure following both single and five daily IT treatments, and bronchoconstriction was quantified by plethysmography. No tachyphylaxis was observed with indacaterol, formoterol or salmeterol. Battram CH, Mok J, Lewis CA. Once-daily administration of indacaterol (QAB149) does not induce tachyphylaxis *in vivo*. Abstract 2569, poster board number G37.

### Significant disease burden

COPD incurs a significant burden on the US healthcare system in terms of number of visits and medications prescribed. Among the papers presented at the ATS meeting was an analysis of data from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey conducted by a team of researchers from Novartis Pharmaceuticals, Rutgers University and Duke University that assessed the disease burden. Results showed that during 2002, 9.9 million ambulatory visits were made to physician offices, outpatient departments and emergency departments in the US, representing a 50.1% increase from 2001. In addition, the annual rate of visits for COPD across all settings was 34.4 visits per 1,000 persons in the US population. Lau H, Valiyeva E, Suh D, Mahajan S. Characteristics of ambulatory care visits for chronic obstructive pulmonary disease in 2002 in a national sample of the US population. Abstract 3636, poster board number J115.

### About asthma and COPD

Exploring new treatments for asthma and COPD is critical. Despite a wide range of currently available therapeutic options, respiratory diseases affect millions of patients around the world. For example, asthma affects more than 23 million people in the US and is the sixth most common chronic condition overall. [http://www.ncqa.org/somc2001/asthma/somc\\_2001\\_asthma.html-en4#en4](http://www.ncqa.org/somc2001/asthma/somc_2001_asthma.html-en4#en4). In addition, the estimated number of asthma-related deaths is approximately 5,000 per year. [http://www.ncqa.org/somc2001/asthma/somc\\_2001\\_asthma.html](http://www.ncqa.org/somc2001/asthma/somc_2001_asthma.html). COPD is presently the fourth leading cause of death worldwide and is expected to become the third leading cause of death by 2020. While COPD death rates are very low under age 45, complications and deaths increase steeply with age. <http://www.thoracic.org/COPD/2/epidemiology.asp>.

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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 +41 61 324 53 16

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

Nina Malik +1 925 551 59 64

John Menditto +1 212 830 24 44

Jill Pozarek +1 212 830 24 45

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

Fax: +1 212 830 24 05

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

**Preliminary phase III data show Lucentis maintained or improved vision in nearly 95% of patients with wet age-related macular degeneration**

**Basel, May 23, 2005** Novartis announced today that a Phase III clinical study of the investigational new drug Lucentis (ranibizumab) met its primary efficacy endpoint of maintaining vision in patients with wet age-related macular degeneration (AMD).

Approximately 95 percent of patients maintained or improved vision (defined as a loss of less than 15 letters in visual acuity) at one year when treated with Lucentis injections compared to approximately 62 percent of those treated in the control arm (p<0.0001).

Patients treated with Lucentis for 12 months had, on average, a significant improvement in visual acuity compared to their visual acuity at study entry, an important secondary endpoint, while the control group demonstrated a substantial decrease in mean visual acuity from baseline to 12 months. One-year data from the trial will be presented at the 23rd Annual Meeting of the American Society of Retina Specialists (ASRS), July 16 to 20 in Montreal, Canada.

"We are delighted that these results show vision improvement which is an important objective for AMD therapy, and exceeded our expectations. Lucentis will be the first therapeutic antibody which achieves a statistically significant improvement in visual acuity," commented Flemming Ørnkov, M.D., President, the Novartis Ophthalmics Business Unit. "We look forward to sharing these data with the health authorities in due course."

A preliminary analysis of the data showed that adverse events were similar to those seen in earlier trials of Lucentis. Common side effects occurring in the Lucentis arms more frequently than in the control group were mild to moderate and included conjunctival hemorrhage, eye pain and vitreous floaters. Serious ocular adverse events occurring more frequently in Lucentis-treated patients were rare (<1%) and included uveitis and endophthalmitis. There appeared to be no imbalance in serious non-ocular adverse events.

Lucentis is a humanized antibody fragment developed at Genentech and designed to bind and inhibit Vascular Endothelial Growth Factor A (VEGF-A), a protein that plays a critical role in angiogenesis (the formation of new blood vessels).

**About the study**

Minimally classic/occult trial of the Anti-VEGF antibody Ranibizumab (formerly, RhuFab) In the treatment of Neovascular AMD (MARINA) is a Phase III study of 716 patients in the United States with minimally classic or occult wet AMD who were randomized 2:1 to receive intravitreal Lucentis injections or a control regimen. The control regimen consisted of a sham injection meaning the treating physician prepares and anesthetizes the patient's eye but does not perform an injection. Patients treated with Lucentis were further randomized to receive either a 0.3 mg or 0.5 mg dose of Lucentis once a month for two years. Exclusion criteria included prior subfoveal laser treatment, verteporfin photodynamic therapy, or experimental treatments for wet AMD. Visual acuity was measured using the Early Treatment of Diabetic Retinopathy (ETDRS) chart, the standard method of quantifying visual acuity.

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### **Ongoing phase III studies**

Genentech and Novartis are conducting two additional Phase III studies of Lucentis. ANCHOR (ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularization in AMD) is a randomized, multi-center, double-masked, active treatment controlled, Phase III study comparing two different doses of Lucentis to verteporfin photodynamic therapy in 423 patients. The trial is ongoing in the United States, Europe and Australia in patients with predominantly classic wet AMD. Results from this study are expected in Q4 2005.

A Phase IIIb study of 184 patients, PIER (A Phase IIIb, Multicenter, Randomized, Double-Masked, Sham Injection- Controlled Study of the Efficacy and Safety of Ranibizumab in Subjects with Subfoveal Choroidal Neovascularization with or without Classic CNV Secondary to Age-Related Macular Degeneration), is also underway. In this trial, Lucentis is administered once per month for the first three doses followed thereafter by doses once every three months for two years. Results from this study are expected in the first half of 2006.

### **About Lucentis**

Lucentis (ranibizumab) is a humanized antibody fragment developed at Genentech and designed to bind and inhibit VEGF-A, a protein that plays a critical role in angiogenesis (the formation of new blood vessels). Lucentis is designed to block new blood vessel growth and leakiness, which are thought to lead to wet AMD disease progression and vision loss.

Lucentis is being developed by Genentech and the Novartis Ophthalmics Business Unit. Genentech retains commercial rights for Lucentis in North America (United States, Canada and Mexico). Novartis has exclusive commercialization rights for the rest of the world.

### **About AMD**

AMD is a major cause of painless central visual loss and is the leading cause of blindness for people over the age of 50. It affects over 25 million people worldwide. AMD occurs in two forms: dry and wet. The dry form is associated with atrophy of the central retina or macula, which is required for fine vision used for activities such as reading, driving or recognizing faces. The wet form is caused by growth of abnormal blood vessels also known as choroidal neovascularization (CNV) or ocular angiogenesis under the macula. These vessels leak fluid and blood and cause scar tissue that destroys the macula. This results in a deterioration of sight over a period of months to years.

### **About angiogenesis**

Genentech is a leader in research and product development in the area of angiogenesis, the process by which new blood vessels are formed. In 1989 Napoleone Ferrara, M.D., and a team of scientists at Genentech conducted seminal work in the field, which resulted in the identification and cloning of a gene termed Vascular Endothelial Growth Factor (VEGF), now known as VEGF-A. The VEGF protein plays a critical role in angiogenesis, and serves as one of the key contributors to physiological or pathological conditions that can stimulate the formation of new blood vessels. The process of angiogenesis is normally regulated throughout development and adult life, and the uncontrolled growth of new blood vessels is an important contributor to a number of pathologic conditions, including wet AMD.

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The foregoing press release contains certain forward-looking statements that can be identified by terminology such as "investigational", "will be", "preliminary", "look forward to", "ongoing", "are expected", "exceeded", or similar expressions, or by express or implied discussions regarding potential marketing approvals of Lucentis, or regarding any potential revenues from Lucentis. Such forward-looking statements involve known and unknown risks, uncertainties or 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 Lucentis will be approved for sale in any market or that it will reach any particular sales levels. In particular, management's expectations relating to Lucentis could be affected by, among other things, uncertainties relating to clinical trials; unexpected 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. 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 Ophthalmics**

With worldwide headquarters in Basel, Switzerland, the Novartis Ophthalmics Business Unit is a global leader in research, development and manufacturing of leading ophthalmic pharmaceuticals that assist in the treatment of age-related macular degeneration, eye inflammation, glaucoma, ocular allergies and other diseases and disorders of the eye. Novartis Ophthalmics products are available in more than 110 different countries. Novartis Ophthalmics products are made in Switzerland, France, the United States and Canada. For more information, visit [www.novartisophthalmics.com](http://www.novartisophthalmics.com) or [www.novartisophthalmics.com/us](http://www.novartisophthalmics.com/us).

#### **About Novartis**

Novartis AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2004, the Group's businesses achieved sales of USD 28.2 billion and pro forma net income of USD 5.8 billion. The Group invested approximately USD 4.2 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 81,400 people and operate in over 140 countries around the world. Further information is available at [www.novartis.com](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 +41 61 324 53 16

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

Nina Malik +1 925 551 59 64

John Menditto +1 212 830 24 44

Jill Pozarek +1 212 830 24 45

e-mail: [investor.relations@novartis.com](mailto:investor.relations@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 approved by Swissmedic to reduce risk of organ rejection in heart and kidney transplant patients**

*Swiss approval supports expanded global regulatory submissions to bring innovative therapy to patients in Asia and Europe*

**Basel, May 18, 2005** Certican (everolimus) was recently approved by Swissmedic for the prophylaxis of organ rejection in heart and kidney transplant patients.\* This decision not only provides access to an innovative new therapy for Swiss transplant patients, but also supports expanded regulatory submissions in Asia and Europe.

"The positive Swissmedic decision on Certican will not only make this innovative and valuable therapy available to Swiss patients, but will also allow us to start approval procedures in many countries that require home country approval as a prerequisite for local regulatory reviews," said Giacomo Di Nepi, Head of the Transplantation and Immunology Business Unit, Novartis Pharma AG. "This is very positive news for heart and kidney transplant patients in countries throughout the world."

The countries that require Swissmedic approval as a precursor to submission are China, Hong Kong, Malaysia, Sri Lanka, Vietnam, Bahrain, Belarus, Croatia, Iraq, Jordan, Kazakhstan, Kuwait, Lebanon, Libya, Morocco, Nigeria, Oman, Pakistan, Palestine, Qatar, Russia, Saudi Arabia, United Arab Emirates, Uzbekistan, Yemen North, Yugoslavia.

Certican is now approved in over 40 countries and recently was launched in Spain, with additional positive recommendations for approval received in Australia, South Africa and Israel continuing the momentum of world-wide approvals.

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 an indication for both heart and kidney transplant recipients. Prophylaxis of allograft dysfunction or late graft loss remains a major unmet medical need in transplantation.

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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 "will", "positive recommendations", "continuing", 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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#### **References**

Eisen HJ et al. Everolimus for the Prevention of Allograft Rejection and Vasculopathy in Cardiac-Transplant Recipients. N Engl J Med 2003; 349: 847-858.

Vitko S et al. Everolimus with Optimized Cyclosporine Dosing in Renal Transplant Recipients: 6-Month Safety and Efficacy of Two Randomized Studies. Am J Transplant 2004; 4: 626-635.

\* Certican is indicated for prevention of rejection in adult patients at low to moderate immunological risk receiving an allogenic renal or cardiac transplant. Certican should be used in combination with ciclosporin for microemulsion and corticosteroids. In longterm Certican should be used with a reduced dose of Ciclosporin for microemulsion.

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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**

**New data show Zometa® significantly improved bone mineral density in breast cancer patients receiving adjuvant therapy**

*Bone loss is a well-documented side effect in breast cancer patients treated with aromatase inhibitors*

**Basel, May 16, 2005** Zometa® (zoledronic acid), an intravenous bisphosphonate administered to more than one million patients worldwide, was shown to inhibit aromatase inhibitor-induced bone loss in postmenopausal women treated with Femara® (letrozole) in the adjuvant breast cancer setting.

Final data of the primary endpoint of 12-month bone mineral density (BMD) demonstrate a significant increase in BMD for those breast cancer patients treated with Femara and upfront Zometa compared with those who received Femara and delayed Zometa. These data were presented at the American Society of Clinical Oncology (ASCO) annual meeting in Orlando, Florida.

Several studies have shown that women treated with hormonal therapy in the adjuvant breast cancer setting are at risk of bone loss. New data from the Z-FAST (Zometa-Femara Adjuvant Synergy Trial) study offer evidence that Zometa may prevent bone loss in these patients. These data are particularly important given that aromatase inhibitors are a widely prescribed hormonal therapy for newly diagnosed breast cancer.

"These are valuable and encouraging data for the medical community and breast cancer patients," said Adam Brufsky, M.D. Ph.D., co-director, Magee Women's Hospital/UPCI Comprehensive Breast Cancer Center in Pittsburgh, PA, USA, and assistant professor of Medicine at the University of Pittsburgh, principal investigator. "It is exciting that Zometa has shown activity against bone loss in breast cancer patients receiving adjuvant treatment with an aromatase inhibitor."

**Study results**

The Z-FAST study showed that at the 12-month follow-up, the group of patients receiving upfront Zometa had a mean increase of lumbar spine BMD of 1.9% vs. a decrease of 2.4% in the group of patients who received delayed Zometa ( $p < 0.0001$ ). This represents a 4% relative difference in lumbar spine BMD in favor of the upfront Zometa group. Total hip BMD was also significantly higher in the upfront group, compared with the delayed group. Significantly, 8% of patients in the delayed group had decreases in BMD at the 12-month follow-up, which required initiation of Zometa.

Zometa is generally well tolerated in nonmetastatic cancer patients, as supported by several trials in this setting. The following adverse events occurred in more than 5% of patients in the Z-FAST study: arthralgia (30% in upfront group, 29% in delayed group); hot flashes (25.3%, 25.7%); fatigue (17.3%, 15.3%); myalgia (12.7%, 9.7%); bone pain (11.3%, 4%); headache (9%, 7.3%); nausea (8%, 5.7%); pain in extremities (8%, 4.3%); insomnia (7%, 5.3%); depression (5.7%, 9%); back pain (6%, 5.7%).

The Z-FAST study is part of a wider clinical program that includes the international sister trial Zo-FAST. Zo-FAST, which will include more than 900 patients in 30 countries outside the U.S., is investigating the same primary and secondary endpoints and will add to this body of clinical evidence.

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"We are committed to developing innovative treatments for patients with cancer," said Diane Young, M.D., vice president, global head, Clinical Development, Novartis Oncology. "We are pleased that these data suggest that Zometa may offer breast cancer patients receiving aromatase inhibitors and their physicians an important new option in the treatment of bone loss."

### Study design

The landmark study, Z-FAST, is a multicenter trial designed to help address two important and previously unanswered clinical questions facing the breast cancer community: 1) Does adjuvant treatment of breast cancer with an aromatase inhibitor cause bone loss? 2) Can potential bone loss be prevented by including an IV bisphosphonate in the treatment paradigm?

This open-label, randomized, multicenter trial enrolled 602 postmenopausal women with stage I, II, IIIa, estrogen receptor (ER) and/or progesterone receptor (PR) positive breast cancer who have undergone complete tumor resection, and have no clinical or radiological evidence of recurrent or metastatic disease.

Patients will remain in the study and be treated for a maximum of five years, or until disease progression, with Femara as their adjuvant therapy beginning day one. Patients were randomized to one of two Zometa treatment arms, receiving either an upfront 4 mg, 15-minute infusion of Zometa every six months beginning on day one, or a delayed start 4 mg, 15-minute infusion of Zometa every six months. The delayed start group received Zometa when researchers detected a post-baseline bone mineral density T score below -2.0 SD (standard deviation) or after a bone complication has occurred. Patients will be followed for bone complications including fractures.

### About Zometa

An intravenous bisphosphonate, Zometa is the first therapy of its kind to demonstrate efficacy in reducing or delaying bone complications across a broad range of tumor types such as breast, prostate, lung and renal cell cancers in patients with metastatic disease. Prior to Zometa, intravenous bisphosphonates had only been indicated for use in multiple myeloma and breast cancer patients with bone metastasis. Zometa offers patients, nurses and clinicians a convenient 4 mg, 15-minute infusion.

Zometa was granted marketing authorization by the FDA in February 2002 for the treatment of bone complications in patients with advanced malignancies involving bone. This indication was based on data from three large pivotal trials of more than 3,000 patients that evaluated the drug for a treatment period of approximately one year.

Zometa is indicated for the treatment of patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. In prostate cancer, patients should have progressed after treatment with at least one hormonal therapy. The solid tumors studied included, among others, prostate, breast, lung, renal and colon. Zometa also is indicated for the treatment of hypercalcemia of malignancy (HCM), the most common life-threatening metabolic complication of cancer.

### About Femara

Femara is a leading once-a-day oral aromatase inhibitor currently available in more than 90 countries worldwide. Femara is approved for extended adjuvant treatment of early breast cancer in postmenopausal women who have completed standard adjuvant tamoxifen therapy in 57 countries worldwide, now including member countries of the EU as well as the United States. In addition, it is indicated for first-line treatment of postmenopausal women with hormone receptor-positive or hormone receptor-unknown locally advanced or metastatic breast cancer and for the treatment of advanced breast cancer in postmenopausal women with disease progression following antiestrogen therapy, and as neo-adjuvant (pre-operative) therapy. Not all indications are available in every country.

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#### **Femara contraindications, warnings and adverse events**

In previous clinical trials, the most common adverse events experienced with Femara have been hot flushes, arthralgia/arthritis and myalgia. Other commonly reported adverse reactions are: nausea, fatigue, anorexia, appetite increase, peripheral oedema, headache, dizziness, vomiting, dyspepsia, constipation, diarrhea, alopecia, increased sweating, rash, myalgia, bone pain, arthritis/arthralgia, weight increase, osteoporosis, and bone fracture.

Femara is contraindicated in women who are pregnant or breast-feeding as well as in premenopausal women. Femara is contraindicated in patients with known hypersensitivity to Femara or any of its excipients.

#### **Zometa contraindications, warnings and adverse events**

In clinical studies, the safety profile with Zometa was similar to that of pamidronate or placebo. Zometa has been associated with reports of renal insufficiency. Patients should have serum creatinine assessed prior to receiving each dose of Zometa. Caution is advised when Zometa is used in aspirin sensitive patients, or with aminoglycosides, loop diuretics, and other potentially nephrotoxic drugs. Due to the risk of clinically significant deterioration in renal function, single doses of Zometa should not exceed 4 mg and the duration of infusion should be no less than 15 minutes in 100 ml of diluent.

In clinical trials in patients with bone metastases and hypercalcemia of malignancy (HCM), Zometa had a safety profile similar to other intravenous bisphosphonates. The most commonly reported adverse events included flu-like syndrome (fever, arthralgias, myalgias, skeletal pain), fatigue, gastrointestinal reactions, anemia, weakness, cough, dyspnea and edema. Zometa should not be used during pregnancy. Zometa is contraindicated in patients with clinically significant hypersensitivity to zoledronic acid or other bisphosphonates, or any of the excipients in the formulation of Zometa.

Osteonecrosis of the Jaw (ONJ): ONJ has been reported in patients with cancer receiving treatment including bisphosphonates, chemotherapy, and/or corticosteroids. The majority of reported cases have been associated with dental procedures such as tooth extraction. A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors. While on treatment, these patients should avoid invasive dental procedures if possible. No data are available as to whether discontinuation of bisphosphonate therapy reduces the risk of ONJ in patients requiring dental procedures.

The foregoing release contains forward-looking statements that can be identified by terminology such as "new data," "was shown," "may prevent," "encouraging data," "has shown activity," "potential," "suggest," "may offer" or similar expressions, or by express or implied discussions regarding potential future sales of Femara and/or Zometa. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Femara and/or Zometa to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Femara and/or Zometa will reach any particular sales levels. In particular, management's expectations regarding commercialization of Femara and/or Zometa could be affected by, among other things, additional analysis of Femara and/or Zometa 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 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.

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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 +41 61 324 53 16

e-mail: [investor.relations@novartis.com](mailto:investor.relations@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  
Nina Malik +1 925 551 59 64  
John Menditto +1 212 830 24 44  
Jill Pozarek +1 212 830 24 45

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

Fax: +1 212 830 24 05  
[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**

**First results from PTK/ZK CONFIRM 1 trial presented at American Society of Clinical Oncology show positive drug effects in advanced colorectal cancer**

*Preplanned analysis of progression-free survival, as assessed by investigators, demonstrated a significant 17% reduction in risk of disease progression*

*Central review assessment of primary endpoint showed a 12% reduction in risk that did not achieve statistical significance*

*An exploratory analysis of patients with high LDH levels found this group benefited the most from PTK/ZK treatment (40% reduction in risk of disease progression)*

*CONFIRM 1 & 2 studies ongoing to assess overall survival*

**Basel, May 13, 2005** First results from the Phase III CONFIRM 1 trial showed PTK/ZK, a new oral targeted therapy designed to block the growth of blood and lymphatic vessels, demonstrated positive drug effects in patients with metastatic colorectal cancer combined with FOLFOX chemotherapy as first-line therapy.

Patients who received the PTK/ZK-FOLFOX combination had a 17% reduction in risk of disease progression ( $p = 0.026$ ) compared to FOLFOX alone when assessed by the patients' physicians. Assessment by central review showed a 12% reduction in risk of disease progression; however, the difference did not achieve statistical significance ( $p = 0.118$ ).

In the study, patients were divided into four subgroups based on two prognostic factors, serum lactate dehydrogenase (LDH) and performance status. An exploratory analysis announced by J. Randolph Hecht, M.D., Clinical Professor of Medicine, Director, Gastrointestinal Oncology Program, Jonsson Comprehensive Cancer Center, University of California, Los Angeles School of Medicine, and lead investigator, showed that patients with high LDH levels showed a 40% reduction in risk of disease progression independent of performance status. Further research is ongoing to determine the relevance of these findings.

These data from the first analysis of the ongoing CONFIRM 1 trial will be presented in full during a plenary presentation on May 14 at the American Society of Clinical Oncology (ASCO) meeting in Orlando, Florida. Further analysis of the CONFIRM 1 data, including detailed evaluations of overall survival endpoints, is expected in the second half of 2006.

"These new data show that PTK/ZK may improve outcomes for colorectal cancer patients," Dr. Hecht said. "We eagerly await the findings on overall survival, which will enable us to see how this compound may advance treatment for these patients."

**Study details**

In the study, PTK/ZK was given in combination with the chemotherapy regimen oxaliplatin/5-fluorouracil/leucovorin, called FOLFOX-4, in patients previously untreated for metastatic colorectal cancer (mCRC). FOLFOX-4 is the most commonly used treatment for patients with mCRC. CONFIRM 1 is a multinational study in which 1,168 patients were randomly assigned to receive FOLFOX-4 with either PTK/ZK or a placebo between February 2003 and May 2004. The CONFIRM 1 study design is powered to include two analyses: progression-free survival and overall survival.

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## **Safety data**

In the CONFIRM 1 trial, the overall side effects that were seen were generally consistent with those of FOLFOX chemotherapy and anti-angiogenic therapy. The most frequently reported grade 3 adverse events in the two treatment arms (PTK/ZK with FOLFOX-4 vs. placebo with FOLFOX-4), greater than 5%, were as follows: hypertension (21% vs. 6%), neutropenia (17% vs. 21%), diarrhea (15% vs. 10%), nausea (9% vs. 5%), peripheral neuropathy (9% vs. 7%), vomiting (7% vs. 6%), venous thrombosis (7% vs. 4%), dizziness (7% vs. 2%), and thrombocytopenia (6% vs. 4%). The most frequently reported grade 4 events, greater than 5% in both arms, were neutropenia (14% vs. 11%) and pulmonary embolism (6% vs. 1%).

The independent Data Safety Monitoring Board (DSMB) reviewed all safety data and recommended continuation of the trial.

Another ongoing Phase III trial, CONFIRM 2, compares the PTK/ZK combination regimen to FOLFOX-4 alone in patients with metastatic colorectal cancer who have progressed after irinotecan-based first line chemotherapy. An interim analysis is planned in mid-2005, and final overall survival data are expected in mid-2006.

Novartis and Schering anticipate filing for approval of PTK/ZK with the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) in early 2007.

"Our analysis of this trial is helping us understand how PTK/ZK may be used to treat patients with metastatic colorectal cancer," said David Epstein, Head of Specialty Medicines and of Novartis Oncology. "We look forward to the final results of the CONFIRM clinical research program and exploring PTK/ZK in other tumor types."

## **About PTK/ZK**

PTK/ZK, an investigational oral multi-VEGF receptor tyrosine kinase inhibitor, blocks tumor angiogenesis and lymphangiogenesis by inhibiting all known VEGF receptors. Targeting all the VEGF receptors rather than a single VEGF type may provide a new approach for inhibiting tumor growth and spread.

## **About colorectal cancer**

In 2002, according to the World Health Organization, there were more than one million cases of colorectal cancer worldwide, almost 65% of which were in more developed countries. The Colorectal Cancer Network reports that only lung cancer is responsible for more cancer-related deaths in the US. In 2004, according to the International Agency for Research on Cancer, it was estimated that 270,000 new cases were diagnosed and more than 22,000 deaths occurred in the EU.

Novartis and Schering have been jointly researching and co-developing PTK/ZK since 1995. Under a commercialization agreement executed in January 2005, the companies will partner on promotion and further development of the product for oncology indications including metastatic colorectal cancer in all major markets. The value of the agreement to Schering and Novartis is designed to be equal based on the co-promotion terms and territory allocations. Novartis will lead North American co-promotion activities and Schering will lead European co-promotion activities with both companies sharing co-promotion activities equally in Japan. Novartis will exclusively promote the product in Asia (excluding Japan) and Middle East. Schering will exclusively promote PTK/ZK in Latin America, Africa and Australia.

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The foregoing release contains certain forward-looking statements that can be identified by terminology such as "show positive drug effects," "progression-free survival," "research is ongoing," "is expected," "may improve outcomes," "eagerly await," "will enable," "may advance treatment," "is planned," "are expected," "anticipate filing," "may be used," "look forward," "may provide," "will partner," "will lead," "will exclusively promote," or similar expressions, or by discussions regarding the potential that PTK/ZK will be approved for marketing, or regarding any potential revenues from PTK/ZK. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with PTK/ZK to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that PTK/ZK will be approved for sale in any market. In particular, management's expectations regarding commercialization of PTK/ZK could be affected by, among other things, uncertainties relating to clinical trials; new clinical data; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; 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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###

---

**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 +41 61 324 53 16

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

Nina Malik +1 925 551 59 64

John Menditto +1 212 830 24 44

Jill Pozarek +1 212 830 24 45

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

Fax: +1 212 830 24 05

[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**

**Femara helped significantly more women with early breast cancer live free of cancer compared with tamoxifen, study presented today shows**

*Femara demonstrated significant advantage in disease free survival vs. tamoxifen, particularly in subgroups of postmenopausal women at increased risk of breast cancer recurrence (29% reduction in node-positive patients; 30% in those who had received prior chemotherapy)*

*Femara greatly reduced the risk of cancer spreading to other parts of the body (distant metastases)*

**Basel May 13, 2005** Femara® (letrozole) treatment of postmenopausal women with early breast cancer prolonged disease free survival by reducing risk of recurrence an additional 19% ( $p = 0.003$ ) over that offered by tamoxifen when used as initial treatment after surgery, according to data from the Breast International Group (BIG) 1-98 study.

Even more importantly, use of Femara resulted in greater disease free survival in two subgroups of women who are at particularly increased risk of recurrence those whose cancer had already spread to the lymph nodes at the time of diagnosis (node positive) and those who had received chemotherapy. The risk reductions in these subgroups were 29% and 30%, respectively.

The results also showed that for all women in the study, Femara reduced, by 27%, the risk that cancer would spread to other parts of the body (distant metastases), compared with the reduction offered by tamoxifen ( $p = 0.0012$ ). This is important because women who develop distant metastases are at greater risk of dying from breast cancer. These findings were presented today at the annual meeting of the American Society for Clinical Oncology in Orlando, Florida.

"Women with early breast cancer are at highest risk of recurrence during the first five years after surgery," said PD Dr. Beat Thürlimann, MD, Scientific Secretary General, Therapy of Early Breast Cancer Senology Center of Eastern Switzerland, Kantonsspital, St. Gallen. "The BIG 1-98 study showed that Femara offered postmenopausal women with hormone-sensitive early breast cancer increased benefit compared with tamoxifen by reducing the risk of recurrence and by decreasing the risk of distant metastasis, a risk factor for death."

Further, there was a statistically significant reduction of 17% in the risk of systemic failure. That is, a recurrence of cancer in sites other than the breast, or death without recurrence ( $p = 0.017$ ). There was a 14% reduction in risk of death in favor of Femara that was not statistically significant ( $p = 0.15$ ). Patients will continue to be monitored to track disease status, survival and long-term tolerability of their treatment.

"These data, like those in the extended adjuvant setting, show that Femara reduces recurrence of distant metastatic disease and offers increased protection for women most at risk for breast cancer recurrence. More women are living free of breast cancer recurrence on Femara compared with tamoxifen. We look forward to updated results from the sequential arms of the BIG 1-98 study," said Diane Young MD, Vice President and Global Head, Clinical Development, Novartis Oncology.

**Study details**

This Phase III, randomized, double-blind, controlled clinical trial enrolled more than 8,000 postmenopausal women with early breast cancer in 27 countries. The median follow-up time was 26 months. The study was supported by Novartis.

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Disease free survival (DFS), the primary efficacy endpoint in this study, was defined as the time from randomization to invasive loco-regional recurrence, distant metastasis, invasive contralateral breast cancer, a second non-breast primary tumor or death from any cause, whichever occurred first.

These data complement those of the landmark MA-17 trial for the use of Femara in the extended adjuvant setting. The term *extended adjuvant* describes the period following standard adjuvant treatment with tamoxifen. Femara is the only aromatase inhibitor shown to be effective in both the adjuvant and extended adjuvant settings.

#### **About BIG 1-98**

Initial results from the final analysis of the head-to-head comparison of Femara with tamoxifen in study BIG 1-98 were presented at the Primary Therapy of Early Breast Cancer 9th International Conference in St. Gallen, Switzerland, in January 2005. The trial was conducted by the International Breast Cancer Study Group (IBCSG), with participation of the Danish Breast Cancer Group, the French FNCLCC group, the Yorkshire Group and many independent centers.

BIG 1-98 is the only clinical trial designed to incorporate both a head-to-head comparison of Femara with tamoxifen during the first five years following breast cancer surgery and a sequencing of both agents to determine the most effective approach to minimizing the risk of recurrence. Patients were randomized to the following arms: tamoxifen for five years; Femara for five years; tamoxifen for two years followed by Femara for three years; and Femara for two years followed by tamoxifen for three years. Results from the ongoing arms of the study, which are expected to determine whether monotherapy or sequential therapy is more effective, and if sequential therapy, which sequence is more effective, are expected in 2008. Based on these data, Novartis expects to submit regulatory submissions globally for Femara monotherapy in the adjuvant setting by mid-2005.

The spectrum of adverse events found in the study is consistent with published data. In this trial, patients treated with Femara had significant reductions in vaginal bleeding (3.3% vs. 6.6%); hot flushes (33.5% vs. 38%); endometrial biopsies (2.3% vs. 9.1%); invasive endometrial cancer (0.2% vs. 0.5%); and, thromboembolic disorders, both overall (1.5% vs. 3.5%) and severe events (0.8% vs. 2.1%) when compared to tamoxifen. Average non-fasting blood levels of cholesterol were slightly higher in the letrozole arm than in the tamoxifen arm. There were more severe ischemic cardiovascular disorders (1.1% vs. 0.6%) including myocardial infarction (0.5% vs. 0.3%) in patients treated with Femara than with tamoxifen. As expected with estrogen deprivation, the number of women reporting new bone fractures to date was 5.7% on Femara and 4.0% on tamoxifen.

Overall, more deaths were reported on tamoxifen (n = 192) than on letrozole (n = 166). More patients on tamoxifen (n = 135) died from breast cancer than Femara (n = 100). In patients whose breast cancer did not recur, more deaths due to cardiac causes were reported in Femara treated patients (n = 13) than tamoxifen treated patients (n = 6). Further analysis of these preliminary data is ongoing.

#### **About Femara**

Femara is a leading once-a-day oral aromatase inhibitor currently available in more than 90 countries worldwide. Femara is approved for extended adjuvant treatment of early breast cancer in postmenopausal women who have completed standard adjuvant tamoxifen therapy in 57 countries worldwide, now including member countries of the EU as well as the United States. In addition, it is indicated for first-line treatment of postmenopausal women with hormone receptor-positive or hormone receptor-unknown locally advanced or metastatic breast cancer and for the treatment of advanced breast cancer in postmenopausal women with disease progression following anti-estrogen therapy, and as neo-adjuvant (pre-operative) therapy. Not all indications are available in every country.

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### **Contraindications, warnings and adverse events**

In previous clinical trials, the most common adverse events experienced with Femara have been hot flushes, arthralgia/arthritis and myalgia. Other commonly reported adverse reactions are: nausea, fatigue, anorexia, appetite increase, peripheral oedema, headache, dizziness, vomiting, dyspepsia, constipation, diarrhea, alopecia, increased sweating, rash, myalgia, bone pain, arthritis/arthralgia, weight increase, osteoporosis and bone fracture.

Femara is contraindicated in women who are pregnant or breast-feeding as well as in premenopausal women. Femara is contraindicated in patients with known hypersensitivity to Femara or any of its excipients.

The foregoing release contains forward-looking statements that can be identified by terminology such as "helped," "expects," "first," "demonstrated," "shown effective," "continued," "offered," "potentially," "may be," "more likely," "look forward," or similar expressions, or by express or implied discussions regarding potential future sales of Femara. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Femara to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Femara will reach any particular sales levels. In particular, management's expectations regarding commercialization of Femara could be affected by, among other things, additional analysis of Femara 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 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.

### **For more information**

Additional information regarding Femara or Novartis Oncology can be found on the websites [www.femara.com](http://www.femara.com) or [www.novartisoncology.com](http://www.novartisoncology.com). Additional media information can be found at [www.novartisoncologyvpo.com](http://www.novartisoncologyvpo.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 +41 61 324 53 16

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

Nina Malik +1 925 551 59 64

John Menditto +1 212 830 24 44

Jill Pozarek +1 212 830 24 45

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

Fax: +1 212 830 24 05

[www.novartis.com](http://www.novartis.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 EU approval for the treatment of heart attack survivors**

*Leading antihypertensive agent Diovan is first in its class to receive approval to treat people after heart attacks; also being evaluated in EU to treat heart failure*

**Basel, May 9, 2005** Novartis announced today that it has successfully completed the EU Mutual Recognition Procedure (MRP) in 14 countries for Diovan® (valsartan) for the treatment of heart attack survivors. Diovan, a proven, powerful antihypertensive agent, is now indicated as a potentially life-saving therapy for the more than 750,000 people in the EU who are at risk of a recurrent heart attack or other serious outcomes such as cardiovascular mortality, hospitalization for heart failure, resuscitated cardiac arrest or stroke. Diovan is also being evaluated by EU regulatory authorities for people with heart failure.

"The most widely prescribed ARB globally, Diovan provides a unique range of benefits to patients with cardiovascular disease that is unlike any other agent of its class," said Joerg Reinhardt, Head of Development, Novartis Pharma AG. "Already trusted as a highly effective and powerful high blood pressure agent, physicians can now prescribe Diovan to help reduce mortality in patients who have suffered a heart attack."

This approval provides physicians with a proven life-saving treatment for these high-risk patients who have suffered a heart attack. Despite continual improvements, mortality after heart attack is still high. Now, Diovan can help prolong the life of these high-risk heart attack survivors in addition to providing them with excellent blood pressure lowering efficacy. This indication is based on the VALIANT study which demonstrated that Diovan improved survival and reduced cardiovascular events in high risk patients following a heart attack.

High blood pressure is a major risk factor for heart attacks, which remains one of the world's deadliest conditions. Every year, more than three million people from EU countries suffer a heart attack. World Health Organization, European Health for All Database, Hospital discharges, ischemic heart disease.<sup>(1)</sup> Available at <http://hfadb.who.dk/hfa/>, World Health Organization, International Classification of Diseases, Diseases of the Circulatory System.<sup>(2)</sup> One in three will die within a year after surviving a first heart attack, American Heart Association, Heart Disease and Stroke Statistics 2004 Update<sup>(3)</sup> and half of all heart attacks are repeat attacks. National, Heart, Lung and Blood Institute, National Institutes of Health, Morbidity & Mortality: 2004 Chart Book on Cardiovascular, Lung, and Blood Diseases.<sup>(4)</sup> While progress has been made in treating heart attacks in the emergency room, people who survive the acute phase of a heart attack are at greatly increased risk for repeat attacks and are in critical need for new treatments given such a high risk of death.

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### **EU approval based on landmark VALIANT trial**

The only drug of its kind to receive such an indication, Diovan has now been approved in more than 50 countries to reduce mortality of high-risk patients following a heart attack. The post-heart attack indication for Diovan is based on the positive results of the 14,703 patient trial known as VALIANT (VALsartan In Acute myocardial iNfarcTion) which was one of the largest long-term studies ever conducted in people who have survived a heart attack. VALIANT demonstrated that Diovan preserved the benefit of captopril, which is one essential component of the currently recommended standard of care in these patients, meaning it reduced death to the same degree as the proven treatment. This finding can translate 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. 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.<sup>(5)</sup> VALIANT also showed that Diovan is well-tolerated in post-heart attack patients. Adverse events were generally related to the underlying disease. 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 [ $p < 0.05$ ].

### **About Diovan**

The most prescribed ARB globally and one of the fastest-growing high blood pressure drugs on the market today, Diovan is available as a powerful first-line treatment for high blood pressure in more than 90 countries and in more than 60 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.

This new indication for Diovan is for the treatment of clinically stable patients with symptomatic heart failure or asymptomatic left ventricular systolic 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. 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 "is being evaluated" 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.

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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 +41 61 324 53 16

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

Nina Malik +1 925 551 59 64

John Menditto +1 212 830 24 44

Jill Pozarek +1 212 830 24 45

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

Fax: +1 212 830 24 05

[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**

**Novartis files Exjade® new drug applications for treatment of chronic iron overload due to blood transfusions**

*Innovative, once-a-day oral formulation offers life-altering treatment option to broad range of iron overload patients*

*Filings based on data from largest prospective clinical trials program for iron chelation therapy*

**Basel, Switzerland, May 3, 2005** Novartis has filed regulatory submissions for Exjade® (deferasirox), the first and only once-daily oral iron chelator for the treatment of chronic iron overload due to blood transfusions, in the United States and the European Union (EU). Submissions in other countries will follow shortly.

Exjade, also known as investigational agent ICL670, has been granted fast-track status in the US and Switzerland. Priority review has been requested in the US. Furthermore, Exjade has received Orphan Drug status in the US, EU and Australia.

An easy to administer novel oral iron chelator, Exjade is simply taken once daily, after dispersing tablets in a glass of water. Exjade was developed to extend the benefits of iron chelation to a greater number of patients receiving blood transfusions and to address the needs of thousands of adult and pediatric patients who have been using Desferal® (deferoxamine). Patients have been frustrated for years by the inconvenience and pain that can result from daily insertion of the deferoxamine infusion needle. In many patients, the need for transfusion and chelation therapy may be life-long.

"Novartis has demonstrated a long-term commitment to help improve the lives of patients at risk for iron overload. First by developing a highly effective drug, deferoxamine, and then by conducting research on hundreds of new compounds to find an easy-to-take oral alternative to this product." said Diane Young, MD, vice president and global head of Clinical Development at Novartis Oncology. "We understand the needs of patients and know that the burdensome administration of deferoxamine limits its use. In an effort to bring the benefits of effective iron chelation to more patients, we will work diligently with health authorities to expedite the approval of this important advancement."

Iron overload is a life-threatening cumulative toxicity which results from lifesaving blood transfusions required to treat certain types of anemias and other disorders, including thalassemia, sickle cell disease, other rare anemias, and myelodysplastic syndromes. If left undiagnosed or untreated, iron overload can lead to damage to the liver, heart and endocrine glands. Transfused patients may require concomitant removal of excess iron with a type of drug therapy called iron chelation, to treat iron overload. Deferoxamine, the current standard of care in iron chelation, is effective but 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.

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"Desferal infusion therapy is difficult for children, who dislike needles and fear the pain. But it is extremely burdensome for older teens and young adults, who often will not comply with therapy, even though they see first-hand the risks of iron overload including deformities, organ failure, and premature death," said Durhane Wong-Rieger, PhD, president and chief executive officer, Anemia Institute for Research and Education. "For many patients, the infusions, lasting up to 12 hours per day, stigmatize them, severely limit their social activities and interfere with intimate relationships. Patients and caregivers are very hopeful for a once-daily oral chelator that will enable them to continue to treat iron overload."

#### **Filing data**

The Exjade global clinical trials program enrolled more than 1,000 patients, and is the largest ever prospectively implemented for an investigational iron chelator. The filings are based on the results of pivotal clinical trials, including a Phase III head-to-head trial vs. deferoxamine, which showed that Exjade significantly reduced liver iron concentration (LIC), an accepted indicator for body iron content, in adult and pediatric patients receiving blood transfusions. Findings from the clinical trial program were presented in December 2004 at the annual meeting of the American Society of Hematology. The studies demonstrated that Exjade led to the maintenance or reduction of absolute LIC in regularly transfused patients with different underlying diseases. Additional data on Exjade will be presented this month at three important meetings: the annual meeting of the American Society of Pediatric Hematology/Oncology in Washington, D.C. (May 14-16, 2005); the 8th International Symposium on Myelodysplastic Syndromes in Nagasaki, Japan (May 12-15, 2005); the First Congress of the International BioIron Society in Prague, Czech Republic (May 22-27, 2005); and in June at the 10th Congress of the European Hematology Association in Stockholm, Sweden (June 2-5, 2005).

In the clinical studies in both adults and children as young as two years of age, Exjade 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.

#### **Orphan drug designation and fast-track status**

In the EU, the filing for Exjade was submitted to the European Medicines Agency under the centralized procedure. Exjade was granted Orphan Drug status in both the US and EU in 2002. The intent of the Orphan Drug designation is to stimulate the research, development, and approval of products that treat rare diseases. 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. In the US, the term "Orphan Drug" refers to a product that treats a disease that affects fewer than 200,000 people in the country. Exjade also was granted fast-track status in the US and Switzerland. The fast-track designation is generally reserved for drugs intended for the treatment of a serious or life-threatening condition that demonstrate the potential to address unmet medical needs for that condition.

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**Additional information**

Exjade is still in clinical development and not yet approved for marketing. Some patients may be eligible to enroll in ongoing clinical trials. To learn more about Exjade clinical trials, patients, caregivers and their health care providers can call either 0800 328 9875 or +44 (0) 1506 814895. The foregoing release contains forward-looking statements that can be identified by terminology such as "easier," "more convenient," "potentially," "important advancement," "will be," "would represent," "significant advance," "would make it possible," "fast-track designation pending," "innovative," "life-altering," "lifesaving," or similar expressions, or by express or implied discussions regarding potential additional 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 additional marketing approvals in any other countries, 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 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.

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

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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 +41 61 324 53 16

e-mail: [investor.relations@novartis.com](mailto:investor.relations@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  
 Nina Malik +1 925 551 59 64  
 John Menditto +1 212 830 24 44  
 Jill Pozarek +1 212 830 24 45

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

Fax: +1 212 830 24 05  
[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**

**Novartis highlights pharmaceutical research strategy, intensifying focus on molecular pathways shared by various diseases**

*Transforming the "grammar" of drug discovery by focusing on molecular pathways and patient stratification*

*Redefining Research-to-Development transition through fast and rigorous "proof-of-concept" trials*

*More than 60 new molecular entities have potential to enter trials by end of 2008*

*Development pipeline progressing well, key data planned for second half of 2005*

**Cambridge, Massachusetts, May 3, 2005** At an investor conference to highlight progress at the Novartis Institutes for BioMedical Research (NIBR), senior Novartis scientists presented their new research strategy focused on molecular pathways that may be shared by various diseases as an organizing concept in the search for novel compounds that address unmet needs of patients.

NIBR is the global pharmaceutical research organization of Novartis that was created in May 2002 to enhance the company's long tradition of drug discovery research that has produced breakthrough therapies such as Gleevec®/Glivec® for cancer patients, Sandimmun®/Neoral® for use in transplantation and helping those with schizophrenia with Clozaril®. More than 2,800 research scientists are now working worldwide within various NIBR institutes, including at the global headquarters in Cambridge, Massachusetts, to redefine drug discovery in the genomic era.

A key aspect of the NIBR strategy is to target key cellular pathways that may be part of the underlying mechanism causing various diseases. Traditional pharmaceutical development has relied heavily on identifying appropriate drug "targets," such as single genes or proteins. However, following the decoding of the genome, drug discovery is moving quickly toward focusing on interacting pathways of proteins, which may be at the root of several diseases and inventing compounds that target critical nodes within the signaling pathways to alter the disease-causing mechanism.

Dr. Mark Fishman, President of NIBR and a member of the Executive Committee of Novartis, and his leadership team have instituted several new fundamental discovery platforms, ranging from those focused on specific gene families to those intended to integrate key molecular pathways that cause disease and identify "drugable nodes." These platforms are already delivering targets under consideration for transition to full-scale clinical development.

"Unmet patient needs and scientific tractability, driven by an understanding of the mechanistic underpinning of a disease are the driving factors for project selection and resourcing in our research endeavors. The focus on disease pathways provides an organizational framework for studying diseases creating the foundation to discover exciting novel medicines," said Dr. Daniel Vasella, Chairman and CEO of Novartis.

**"Proof-of-concept" trials to rigorously test compounds early**

As part of the drug discovery transformation, compounds developed at NIBR enter full-scale clinical development only after successfully completing "proof-of-concept" trials.

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These trials, which are typically done with a small group of patients, are designed to rapidly assess a compound's efficacy in humans to provide a foundation for early decisions to advance or terminate projects. This approach stands in contrast to traditional, sequential Phase I and early Phase II studies, which are primarily used to assess safety in healthy volunteers and determine dosage for pivotal Phase III studies.

"All of our drug discovery efforts begin and end with the patient. By focusing early on the experience of patients alongside a commitment to understanding the mechanism of action of a particular disease, our science is geared toward improving both the patient's medical condition as well as their quality of life," said Dr. Mark Fishman. "We are harnessing the power of the genome to invent a "new grammar" of drug discovery that will translate breakthroughs in biology and chemistry into innovative medicines for patients."

For example, Novartis scientists recently completed a successful proof-of-concept trial of a novel antibody, **ACZ885**, for inflammatory conditions. This trial examined patients with a rare inherited inflammatory condition called Muckle-Wells syndrome, which is manifested by rash, joint aches, fevers and migraine headaches. All of these symptoms were relieved within days by a single injection of the antibody, which was directed to an inflammatory signal known as IL-1 beta. The positive findings in Muckle-Wells patients may be indicative of efficacy in other related illnesses, such as rheumatoid arthritis.

In another positive proof-of-concept clinical trial, the success of **LBM642**, a dual agonist of PPAR alpha and gamma, in a dyslipidemia study suggests that the molecule has the potential for efficacy in metabolic syndrome, a disease cluster including diabetes, high cholesterol, and obesity. The results show this compound may overcome many of the disadvantages of other PPAR alpha/gamma dual agonists, in particular weight gain and edema.

In Oncology, Novartis is best known for introducing **Gleevec/Glivec**, which targets the Bcr-Abl kinase in certain forms of chronic myeloid leukemia (CML) and gastrointestinal stromal tumors (GIST). Another novel oral compound is **AMN107**, which has now entered a Phase II clinical trial for patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) who are resistant or intolerant of Gleevec as well as patients with relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL), system mastocytosis or hypereosinophilic syndrome/chronic eosinophilic leukemia. The decision to proceed to Phase II was based on Phase I clinical data that showed more than 90% of patients with chronic phase Ph+ CML achieved a hematologic response, and more than 60% of patients in the advanced stages of Ph+ CML achieved similar responses.

Novartis has expanded its oncology research activities to include other mechanisms of action, particularly inhibition of cell proliferation/survival pathways and activation of apoptosis (cell death) pathways. One approach being studied is exposing cancer cells to a first-in-class **SMAC mimetic**, which is a small molecule that blocks the anti-apoptotic protein IAP, to induce cell death. Multiple cancer models have shown that this compound has reduced the size of tumors in animals.

#### **Valued and open partner to the research community**

NIBR is developing a research strategy based on excellent cooperation with the company's Development team as well as external partners. In 2004, NIBR established approximately 150 collaborations, including 50 with major biotechnology companies, to complement internal research activities. Novartis recognizes the value of scientific advances made by partners and seeks to source the best technologies and early-stage compounds.

Novartis recognizes the importance of open exchange of information. For example, NIBR and the Broad Institute of MIT and Harvard will collaborate on a joint project to decipher the genetic causes of diabetes. This initiative establishes a research partnership of physicians, geneticists, computational scientists, pharmaceutical researchers and others to identify inherited risk factors for developing the disease and its complications. All findings will be made available to the public for free on the Internet.

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NIBR is also complemented by the company's Corporate Research activities, which aim to leverage the specific scientific knowledge from the three institutes the Novartis Institute for Tropical Disease (NITD) in Singapore, the Genomics Institute (GNF) in La Jolla, California; and the Friedrich Miescher Institute (FMI) in Basel. Corporate Research contributes basic biomedical knowledge in neuroscience, growth control and epigenetics through the FMI, new therapeutic targets and technologies through the GNF, and will contribute drugs for neglected diseases through drug discovery research at NITD.

### **Strong pipeline set for dynamic progress**

NIBR has a group of 63 new molecular entities currently in advanced pre-clinical development, of which 16 are antibodies and support the ability to deliver therapies against a broader set of novel molecular targets. These compounds are spread across eight key therapeutic areas, including a particular focus on oncology and cardiovascular/metabolism.

Novartis is consistently ranked as having one of the strongest pipelines in the industry, with 75 projects in clinical development and 55 of them in Phase II, III or registration. Some of these projects have been highlighted by industry experts for being truly innovative drugs, including **SPP100** (hypertension), **LAF237** (diabetes), **FTY720** (multiple sclerosis) and **QAB149** (asthma and COPD).

"All of our late-stage projects are progressing well in an increasingly challenging industry environment marked by an intensified focus on drug safety," said Dr. Joerg Reinhardt, Head of Development, Novartis Pharma AG. "This year will be one with strong newsflow with Phase III data and regulatory submissions expected for key products. We expect to see dynamic progress in our pipeline."

Recent developments include the submission of **Exjade®** (deferasirox), a once-daily oral iron chelator, for US and EU approval. Formerly known as ICL670, *Exjade* offers the potential to revolutionize the treatment of iron overload, providing a once-daily oral formulation to replace a cumbersome infusion therapy for the treatment of this potentially life-threatening condition associated with blood transfusions.

A number of additional submissions are planned for 2005, including the Phase III compound **LDT600** for the treatment of hepatitis B as well as new indications for **Gleevec/Glivec®** for Philadelphia-chromosome-positive(Ph+) acute lymphoblastic leukemia and the breast cancer agent **Femara®** for use in the early adjuvant (post-surgery) setting. Phase III data for **LAF237** (vildagliptin) as a monotherapy and in combination with other anti-diabetic agents is expected at the end of 2005.

This release contains certain forward-looking statements relating to the Group's business, which can be identified by the use of forward-looking terminology such as "potential", "pipeline", "search", "strategy", "may be", "intended to", "designed to", "geared toward", "suggests", "will", "aim", "expect", "potential", "planned", or similar expressions, or by express or implied discussions regarding potential new products or potential future sales of such new products, or by other discussions of strategy, plans or intentions. Such statements reflect the current views of the Group with respect to future events and are subject to certain risks, uncertainties and assumptions. There can be no guarantee that any new products will be approved for sale in any market, or that any products will reach any particular sales levels. In particular, management's expectations could be affected by, among other things, unexpected research results; new clinical data; unexpected clinical trial results; unexpected regulatory actions or delays or government regulation generally; the Group'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 Group'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 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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**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>.

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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 +41 61 324 53 16

e-mail: [investor.relations@novartis.com](mailto:investor.relations@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  
Nina Malik +1 925 551 59 64  
John Menditto +1 212 830 24 44  
Jill Pozarek +1 212 830 24 45

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

Fax: +1 212 830 24 05  
[www.novartis.com](http://www.novartis.com)

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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

**Novartis AG**

Date: June 1, 2005

By:           /s/ MALCOLM B. CHEETHAM          

Name: Malcolm B. Cheetham

Title: *Head Group Financial Reporting and Accounting*

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