

NOVARTIS AG  
Form 6-K  
June 03, 2003

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# SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

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## 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 2003  
(Commission File No. 1-15024)

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## Novartis AG

(Name of Registrant)

Lichtstrasse 35  
4056 Basel  
Switzerland

(Address of Principal Executive Offices)

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

Form 20-F:  Form 40-F:

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

Yes  No

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Yes  No

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

Yes  No

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Enclosures:

## Edgar Filing: NOVARTIS AG - Form 6-K

1. Femara® demonstrates early survival advantage over tamoxifen in advanced breast cancer as reported in Journal of Clinical Oncology (29 May 2003)
2. Study finds Starlix® significantly improves glycemic control in rosiglitazone patients with type 2 diabetes (28 May 2003)
3. FDA approves Lescol® and Lescol® XL for secondary prevention of coronary events in patients with coronary heart disease (28 May 2003)
4. New clinical research data on Glivec® in variety of cancers to be presented at American Society of Clinical Oncology meeting (27 May 2003)
5. Zometa® significantly increased bone mineral density in men receiving hormonal therapy for non-metastatic prostate cancer, study showed (23 May 2003)
6. New data confirm Zelmac® is effective, safe and well tolerated in treating IBS (21 May 2003)
7. Return of a traditional name: Novartis Generics rebranded as Sandoz (20 May 2003)
8. New study shows Zelmac® is effective and well tolerated for chronic constipation (20 May 2003)
9. FDA advisory committee unanimously recommends approval of Xolair (16 May 2003)

2

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### **MEDIA RELEASE    COMMUNIQUE AUX MEDIAS    MEDIENMITTEILUNG**

#### **Femara® demonstrates early survival advantage over tamoxifen in advanced breast cancer as reported in Journal of Clinical Oncology**

*Femara first and only aromatase inhibitor to show significant early survival advantage over tamoxifen*

Basel, 29 May 2003 The largest study ever to evaluate a hormonal therapy in advanced breast cancer demonstrates that Femara® (letrozole), compared with tamoxifen, shows superior time to disease progression, objective tumor response rate, and reported an early survival advantage in postmenopausal women with locally advanced or metastatic breast cancer. The study is to be published in the June 2003 issue of the Journal of Clinical Oncology (JCO).

The data are from a Phase III study evaluating Femara and tamoxifen as first-line treatments in patients with advanced breast cancer. They show that, compared to tamoxifen, Femara demonstrates higher one- and two-year survival rates.

"Demonstrating a survival advantage has been an important goal of breast cancer research for a long time," said Henning Mouridsen, M.D., Rigshospitalet Department of Oncology, Copenhagen, Denmark. "Now that we have evidence that Femara offers a significant early survival

advantage over tamoxifen in the first-line setting, it may become the standard of care for patients in whom hormonal therapy is appropriate."

### **Clinical data**

The randomized, double blind study of 907 postmenopausal women was designed to compare Femara (453 patients) with tamoxifen (454 patients) as first-line therapy in women with locally advanced or metastatic breast cancer. Survival rates at one and two years show Femara offers a statistically significant survival advantage compared with tamoxifen (1 year  $P=0.0004$ ; 2 years  $P=0.02$ ). The median overall survival for Femara was 35 months vs. 32 months for tamoxifen ( $P=0.514$ ).

At the end of the trial (median follow-up of 32 months), 48% of the patients receiving first-line Femara remained free of tumor progression, compared with 27% of the patients receiving first-line tamoxifen. In addition, the odds of responding to treatment were 78% greater with Femara ( $P=0.0002$ ) than with tamoxifen, and the risk of progression was 28% less with Femara than with tamoxifen ( $P<0.0001$ ). Equally important, patients treated with Femara rather than tamoxifen experienced a significantly longer interval until they needed chemotherapy (median time-to-chemotherapy 16 vs. 9 months,  $p=0.005$ ). The reported data also confirm earlier findings that use of Femara significantly delayed progression of the disease for a median of 9.4 months, compared to a median of 6.0 months for tamoxifen ( $P<0.0001$ ).

### **Femara helps patients to maintain performance**

As breast cancer advances, it often affects a woman's ability to function and perform routine daily activities. In the reported trial, researchers measured women's daily performance by using the Karnofsky Performance Score, a standard clinical measurement tool based on a 100-point scale (100 being the top performance point). A change of 20 points or more on the KPS-scale is considered clinically relevant. The investigators found that, significantly more women taking Femara were able to

3

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maintain their original level of performance for a longer period of time than those treated with tamoxifen.

### **Additional research with Femara**

These data mark the first time a hormonal therapy has demonstrated a clear, early survival advantage over tamoxifen for advanced breast cancer patients, and are an important addition to the growing body of evidence in support of aromatase inhibitors.

Aromatase inhibitors, such as Femara, are also becoming more widely studied in early breast cancer in the adjuvant setting. Novartis is conducting Femara clinical trials, involving more than 13,000 postmenopausal women to advance the body of data in this setting. These include studies evaluating not only the efficacy of Femara in early breast cancer either upfront or in sequence with tamoxifen (BIG 1-98) or in delayed use after 5 years of tamoxifen (MA-17) but also the prevention of cancer treatment-related bone loss in postmenopausal women with early breast cancer (Z-FAST/ZO-FAST). Collectively, these trials comprise one of the largest evaluations of an aromatase inhibitor in the adjuvant setting. Results of BIG 1-98 are expected to be available in late 2004, results of MA-17 in late 2005.

### **About Femara**

Femara, a leading aromatase inhibitor, is a once-a-day oral, first-line treatment for postmenopausal women with hormone receptor positive or hormone receptor unknown locally advanced or metastatic breast cancer. It is also approved for the treatment of advanced breast cancer in postmenopausal women with disease progression following antiestrogen therapy, and as neo-adjuvant (pre-operative) therapy. Femara is currently available in more than 75 countries worldwide. Not all indications are available in every country.

### **Femara contraindications and adverse events**

Femara is contraindicated in patients with known hypersensitivity to Femara or any of its excipients. Femara is generally well tolerated and adverse reaction rates in the first-line study in which Femara was compared with tamoxifen were similar with those seen in second-line studies. The most commonly reported adverse events for Femara vs. tamoxifen were bone pain (22% vs. 21%), hot flushes (19% vs. 16%), back pain (18% vs. 19%), nausea (17% vs. 17%), dyspnea or labored breathing (18% vs. 17%), arthralgia (16% vs. 15%), fatigue (13% vs. 13%), coughing (13% vs. 13%), constipation (10% vs. 11%), chest pain (6% vs. 6%) and headache (8% vs. 6%). Femara may cause fetal harm when administered to pregnant women. There is no clinical experience to date on the use of Femara in combination with other anticancer agents. The incidence of peripheral thromboembolic events, cardiovascular events, and cerebrovascular events was 3-4% in each treatment arm.

The foregoing release contains forward-looking statements that can be identified by terminology such as "to be published," "may become," "are also becoming," "are expected," or similar expressions, or by discussions regarding potential new indications for Femara or potential future sales of Femara, or regarding the long-term impact of a patient's use 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 be approved for any additional indications in any market, or that sales of Femara will increase as a result of the aforementioned study. Neither can there be any guarantee regarding the long-term impact of a patient's use of Femara. In particular, management's expectations regarding 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

4

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obtain or maintain patent or other proprietary intellectual property protection; competition in general; increased government 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.

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5

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**MEDIA RELEASE    COMMUNIQUE AUX MEDIAS    MEDIENMITTEILUNG**

**Study finds Starlix® significantly improves glycemic control in rosiglitazone patients with type 2 diabetes**

*Combination therapy with a Thiazolidinedione significantly and safely reduces HbA<sub>1c</sub>*

Basel, 28 May 2003 Results of a new study to be published in the June edition of *Diabetes Care* find that the addition of Starlix® (nateglinide) improves glycemic control and is well-tolerated in patients whose type 2 diabetes is inadequately controlled by taking rosiglitazone alone. The double-blind study demonstrated that the addition of nateglinide to rosiglitazone (Avandia®) monotherapy significantly reduced both HbA<sub>1c</sub> and post-prandial glucose levels and also restored insulin levels, with a favorable safety and tolerability profile.

"The study showed that nateglinide produced a meaningful improvement in overall glycemic exposure in patients inadequately controlled with rosiglitazone alone, without exacerbating known side-effects of this class of medication, the thiazolidinediones," said Vivian Fonseca, M.D., Medical Director from Tulane University Medical Center New Orleans, Louisiana and the lead investigator of the study.

Previous research has shown that over time there is a progressive need for multiple therapies in order to treat type 2 diabetes and maintain a target HbA<sub>1c</sub> of less than 7.0%.<sup>1</sup>

The team of researchers from 30 centers in North America carried out the 24-week double blind randomized study to compare the efficacy of nateglinide (120mg) and placebo added to ongoing open-label rosiglitazone (8mg) in patients with type 2 diabetes, who had an HbA<sub>1c</sub> level

between 7% and 11%. The 402 patients taking part in the trial had been diagnosed with type 2 diabetes at least six months previously and treated with rosiglitazone monotherapy (8 mg), diet and exercise for at least three months prior to the trial.

In patients randomized to nateglinide there was a clinically and statistically significant decrease in HbA<sub>1c</sub> from the baseline of 8.3% to 7.5% (p<0.0001). Target HbA<sub>1c</sub> (<7.0%) was achieved by 38% of patients treated with nateglinide/rosiglitazone combination therapy and by 9% of patients remaining on rosiglitazone monotherapy (p<0.001).

"The two agents work in a complementary way to address the dual defect in type 2 diabetes," explained Dr. Fonseca. "While rosiglitazone reduces insulin resistance, nateglinide stimulates insulin secretion at mealtime and targets post-prandial blood glucose."

In nateglinide-treated patients, there were clinically and statistically significant reductions in fasting plasma glucose (FPG) and 2- hour post-prandial glucose (PPG) levels. In contrast, in patients maintaining rosiglitazone monotherapy, there were no changes in either FPG or PPG.

Previous studies have shown the effects of nateglinide on meal-stimulated insulin levels are clearly apparent within 15 minutes of food consumption and such effects decrease in a glucose dependent manner as the plasma glucose level drops.<sup>2</sup> Through this selective stimulation of early insulin release, nateglinide greatly reduces post-prandial glucose levels while minimizing the overall insulin exposure.

6

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Research has shown that improved glycemic control, as measured by a reduction of HbA<sub>1c</sub> levels, may lead to a dramatic lowering of deaths and complications from diabetes. Even a 1% reduction in HbA<sub>1c</sub> can correlate to a 21% decrease in deaths from diabetes and a 14% decrease in heart attacks.<sup>3</sup>

#### **About Starlix**

Starlix was approved in the United States in 2001 both as a monotherapy for drug-naïve patients with type 2 diabetes and also in combination with metformin, a leading oral antidiabetic agent. In December 2002, Novartis filed a supplemental new drug application (sNDA) for Starlix for use in combination with a thiazolidinedione (TZD). Starlix has an excellent safety and tolerability profile across all clinical trials. Starlix is also approved in many countries around the world for the treatment of type 2 diabetes. Nateglinide is licensed to Novartis Pharma AG from Ajinomoto Co., Inc.

This press 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 "would provide" and "would be managed" or similar expressions or by discussions of strategy, plans, intentions or potential outcomes. Such statements include descriptions of the Company's development programs and descriptions of new indications expected to be approved by the regulatory authorities and introduced by the Company and anticipated customer demand for such products as well as products in the Company's existing portfolio. Such statements reflect the current views of the Company with respect to future events and are subject to certain risks, uncertainties and assumptions. There can be no guarantee that any product or potential new indications for existing products will be commercialized in any market. Many factors could cause the actual results, performance or achievements of the Company to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. These factors include, among other things, unexpected regulatory delays, uncertainties relating to clinical trials and product development, the introduction of competing products, increased government pricing pressures, and the Company's ability to obtain or maintain patent and other proprietary intellectual property protection as well as other factors discussed in the Company's Form 20-F filed with the Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.

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#### **References:**

1. UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. (UKPDS 33). *Lancet* 1998; 352:837-853
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Horton E. *et al*, Nateglinide alone and in combination with metformin improves glycaemic control by reducing mealtime glucose spikes in type 2 diabetes. *Diabetes Care* 2000; 23:1660-1665

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7

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**Investor Relations Release**

**FDA approves Lescol® and Lescol® XL for secondary prevention of coronary events in patients with coronary heart disease**

Basel, Switzerland, 28 May 2003 Novartis announced today that the US Food and Drug Administration (FDA) has approved Lescol® (fluvastatin sodium) and Lescol® XL (fluvastatin sodium) 80 mg extended-release tablets to reduce the risk of undergoing coronary revascularization procedures in patients with coronary heart disease. The FDA approval is based on the positive findings of the landmark Lescol Intervention Prevention Study (LIPS) which was the first prospective statin trial in post-angioplasty patients. Lescol and Lescol XL 80 mg extended-release tablets have been approved for secondary prevention in several countries, including the United Kingdom, Germany and Mexico. Regulatory reviews are also ongoing in other key markets.

"The fact that nearly 2 million people world-wide require an angioplasty procedure each year underscores the importance of this new indication," said Thomas Ebeling, chief executive officer of Novartis Pharma AG. "The approval of Lescol to reduce the risk of revascularization procedures significantly broadens its scope in treating patients with coronary heart disease."

**About the LIPS Trial**

LIPS was designed to investigate whether cholesterol lowering with Lescol, initiated shortly after successful completion of a first PCI, with or without stent, would prolong cardiac disease-free survival. LIPS was the first prospective, randomized, placebo-controlled trial to examine a statin in this patient population and involved 1,677 patients in 57 centers in 10 countries. The data demonstrated that treatment with Lescol 80 mg (40 mg twice daily), routinely initiated within days after a first PCI procedure, significantly reduced the risk of major cardiac events (cardiac death, nonfatal MI, coronary revascularization) by 22 percent (p=0.013) versus placebo, even in patients with normal cholesterol levels with or without a history of myocardial infarction.<sup>1</sup>

The LIPS data further underscored the excellent safety profile of Lescol. In the study, there were no significant elevations of creatine phosphokinase (CPK) above 10 times the upper limits of normal (ULN) over the three to four years of follow up. Elevated CPK is an indication of muscle breakdown and is a potential side effect of statin therapies. These safety data match those from recent analyses finding that the rate of clinically relevant CPK elevations in patients receiving Lescol or Lescol XL as monotherapy or in combination with a fibrate was not significantly different from the rate seen in patients receiving placebo.<sup>2,3</sup>

**About Lescol**

Lescol and Lescol XL are statin drugs used in the treatment of atherosclerosis and vascular disease. Novartis introduced Lescol extended-release, once-daily 80 mg formulation in 2000 (Lescol XL), which has been shown in trials to provide effective lipid management, with reductions of 38% in LDL-cholesterol, up to 31% in triglycerides and increases of up to 21% in HDL-cholesterol.<sup>4</sup>

This release contains certain "forward-looking statements," relating to the business of Novartis, which can be identified by express or implied statements regarding the potential for additional sales of Lescol as a result of this new FDA approval. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantees that the new FDA approval will result in any additional sales of Lescol. Any such results can be affected by, amongst other things, uncertainties relating to clinical trial results and product development, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection and competition in general, as well as factors discussed in the Company's Form 20-F filed with the Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.

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- 1 Serruys PWJC, de Feyter P, Macaya C, et al. Fluvastatin for prevention of cardiac events following successful first percutaneous coronary intervention; a randomized controlled trial. *J Am Med Assoc* 2002;287:3215-3222.
- 2 Benghozi R, Bortolini M, Jia Y, Isaacsohn JL, Troendle AJ, Gonasun L. Frequency of creatine kinase elevation during treatment with fluvastatin. *Am J Cardiol* 2002;89:231-233.
- 3 Farnier M, Bortolini M, Salko T, et al. Frequency of creatine kinase elevation during treatment with fluvastatin in combination with fibrates (bezafibrate, fenofibrate, or gemfibrozil). *Am J Cardiol* 2003;91:238-240.
- 4 Ballantyne et al. Efficacy and tolerability of fluvastatin extended-release deliver system: a pooled analysis. *Clin Ther* 2001;23:177-192.

9

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**Investor Relations Release**

**New clinical research data on Glivec® in variety of cancers to be presented at  
American Society of Clinical Oncology meeting**

*Latest clinical research findings examine the potential of Glivec across a broad range of diseases*

Basel, 27 May 2003 New insights into the potential of Glivec® (imatinib®) in treating a variety of cancers will be the focus of more than 70 abstracts presented this week at the annual meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Illinois, USA. These data continue to show the promise of targeted therapies like Glivec in a wide range of clinical settings.

The diseases addressed in the research studies include prostate cancer, Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML), dermatofibrosarcoma protuberans (DFSP), Kit-positive gastrointestinal stromal tumors (GISTs), hypereosinophilia (HES), Kaposi's sarcoma and carcinoid tumors, among many others.

GIST and CML educational sessions will focus on the latest data in patients being treated with Glivec for these diseases.

Additionally, Brian Druker, MD, Oregon Health Sciences University, will be receiving the Karnofsky Memorial Award for his work with Novartis for the study of Glivec in patients with Ph+ CML.

"The latest data in Ph+ CML substantiate the promise that Glivec exhibited in clinical trials," said David Epstein, President, Novartis Oncology. "But even more important at this ASCO meeting are the data that demonstrate that this drug may have the potential to benefit patients in a number of other cancers."

***Data in CML***

More than 10 000 people have participated in Glivec trials in CML and thousands more have been taking the drug since it was approved for the treatment of Ph+ CML in all stages. Encouraging data from the largest number of Ph+ CML patients ever studied will be presented and compared with updated results from preceding Phase II registration studies (Abstract #2328).

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\*In the U.S.: Gleevec (imatinib mesylate)

Additionally, because results with longer-term follow-up have also been encouraging, researchers used data from the International Randomized Study of Interferon vs. STI571 (IRIS) and other previous CML studies to develop a new health economics model to predict life expectancy in Ph+ CML patients (Abstract #2368). IRIS was the first head-to-head study comparing Glivec to interferon-alpha and cytosine arabinoside (IFN/Ara-C) combination, a traditional treatment for CML. This health economics model will be presented at ASCO.

***Potential in Other Cancers***

Additional abstracts on Glivec, alone and in combination with chemotherapy for the treatment of a variety of diseases including other cancers will also be presented. Studies examining the potential of Glivec include:

Glivec in patients with prostate cancer (Abstract #1645, 1648)

Glivec in patients with DFSP (Abstract #781)

Glivec in patients with HES (Abstract #2264)

Glivec in patients with Kaposi's sarcoma (Abstract #782)

Glivec in patients with carcinoid tumors (Abstract #1491)



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Additionally, data highlighting improved quality of life in newly diagnosed chronic phase CML patients taking Glivec (from the IRIS study) will be presented (Abstract #2367).

Throughout the course of the ASCO meeting, daily updates will be provided on [www.novartisoncologyvpo.com](http://www.novartisoncologyvpo.com). This Novartis site, which includes information for journalists, provides a platform with the latest information and data relating to Glivec and the other Novartis cancer drugs including the full text of the abstract after it has been officially presented.

### **About Glivec**

Glivec is indicated for the treatment of newly diagnosed adult and pediatric patients with Ph+ CML in the EU, Switzerland, and a number of other markets. Glivec is approved in the U.S. for newly diagnosed adult patients with Ph+ chronic phase CML and pediatric patients with Ph+ chronic phase CML whose disease has recurred after stem cell transplant or who are resistant to interferon-alpha therapy. In addition, Glivec is already approved in over 80 countries for the treatment of adult patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.

Glivec is also approved in the EU, US and more than 45 other countries for the treatment of patients with Kit (CD 117)-positive unresectable (inoperable) and/or metastatic malignant GISTs.

### **Contraindications, Warnings and Adverse Events**

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

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

11

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

The foregoing release contains forward-looking statements that can be identified by terminology such as "to be," "will," "may have," "predict," or similar expressions, or by discussions regarding potential new indications for Glivec or potential future revenue from Glivec, or regarding the long-term impact of a patient's use of Glivec. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Glivec to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Glivec will be approved for any additional indications in any market or will achieve any particular revenue levels in the future. Neither can there be any guarantee regarding the long-term impact of a patient's use of Glivec. In particular, management's expectations regarding Glivec could be affected by, among other things, additional analysis of Glivec clinical data; new clinical data; unexpected clinical trial results; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; 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.

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Additional information on Novartis Oncology and Glivec can be found at [www.novartisoncology.com](http://www.novartisoncology.com) or [www.glivec.com](http://www.glivec.com). Additional media information can be found at [www.novartisoncologyvpo.com](http://www.novartisoncologyvpo.com).

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**MEDIA RELEASE COMMUNIQUE AUX MEDIAS MEDIENMITTEILUNG**

**Zometa® significantly increased bone mineral density in men receiving hormonal therapy for non-metastatic prostate cancer, study showed**

*Data in Journal of Urology show benefits of Zometa treatment in preventing cancer treatment-induced bone loss*

Basel, 23 May 2003 Treatment with Zometa® (zoledronic acid) significantly increased bone-mineral density (BMD) in the spines and hips of men receiving hormonal therapy for prostate cancer, according to a study published in this month's *Journal of Urology*.

Cancer treatment-induced bone loss is a side effect of androgen deprivation, a hormone-based treatment approach that is commonly used in prostate cancer. The condition has been associated with hip and other serious skeletal fractures. The published results in *Journal of Urology* demonstrated that Zometa treatment not only prevented treatment-related bone loss, but in one year of treatment it led to a mean 5.6% increase in lumbar spine bone mineral density, compared with a 2.2% loss in men receiving placebo.

Androgen deprivation therapy, a standard treatment approach for metastatic prostate cancer, is being used with increasing frequency and success to treat non-metastatic prostate cancer as well. More than 350,000 men worldwide are diagnosed with prostate cancer every year.

"The data indicating that Zometa increases bone density in prostate cancer patients being treated with androgen deprivation therapy are very encouraging," said lead author Matthew R. Smith, M.D., Ph.D., Massachusetts General Hospital, Boston, Massachusetts, USA, Assistant Professor of Medicine, Harvard Medical School. "Many patients and physicians don't recognize the seriousness of cancer treatment-induced bone loss. This study demonstrates that Zometa not only prevents bone loss, but also increases bone density."

**Study Details**

The multicenter, randomized, placebo-controlled trial enrolled 106 men who were beginning initial androgen deprivation therapy with a gonadotropin-releasing hormone agonist (GnRH) with or without an antiandrogen. Patients had no evidence of distant metastases. After randomization to Zometa 4 mg or placebo, the men received a 15-minute infusion every three months for one year. Participants were instructed to take a daily calcium supplement (500 mg) and a daily multivitamin containing 400 IU of vitamin D. The majority of men in the Zometa group (47, or 86%) and in the placebo group (42, or 82%) received all five injections.

After a year, the lumbar spine BMD was increased by 5.6% from baseline for the Zometa group ( $p < 0.001$ ) while the BMD in the placebo group decreased by 2.2% ( $p = 0.012$ ). The difference between the groups was 7.8% (95% CI 5.6%-10.0%,  $p = 0.001$ ).

For Zometa patients, BMD also increased significantly from baseline vs. placebo in the total hip, femoral neck, and trochanteric region ( $p < 0.001$ ).

The rate of severe adverse events (grade 3 or 4) was 24% for those in the Zometa group and 39% for men receiving placebo. Two men receiving Zometa and three men receiving placebo withdrew from the study because of an adverse event.

**Prostate Cancer, Androgen Deprivation Therapy/Breast Cancer, Aromatase Inhibitor Therapy and Bone Loss**

Cancer treatment-induced bone loss is a condition that is prevalent in many types of cancer, particularly prostate cancer treated with androgen deprivation therapy and breast cancer treated with aromatase inhibitor therapy. This condition causes the bones to weaken, often leading to serious complications, which may include fractures. There has been an increasing and earlier use of androgen deprivation therapy in men with prostate cancer and of aromatase inhibitor therapy in women with breast cancer. As a result, there is also a need for an effective treatment to prevent bone loss and restore bone integrity in these populations, reducing the risk of serious complications.

#### **About Zometa**

Novartis has received marketing authorisation for Zometa in more than 60 countries, including the member states of the European Union and the United States, for the prevention of skeletal related events in patients with advanced malignancies metastatic to bone. These malignancies include multiple myeloma, prostate cancer, breast cancer, lung cancer, renal cancer and other solid tumors. Novartis also has received marketing clearance for Zometa in the treatment of tumor-induced hypercalcemia (TIH), also known as hypercalcemia of malignancy (HCM), in more than 80 countries throughout the world. The proven safety and efficacy profile of this treatment has resulted in more than 300,000 patients worldwide receiving Zometa to date.

#### **Contraindications and Adverse Events**

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.

In this study, the safety profile with Zometa was similar to that of other intravenous bisphosphonates. Zometa and other IV bisphosphonates, such as pamidronate, have 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 asthma 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.

The foregoing release contains forward-looking statements that can be identified by terminology such as "encouraging," "may reduce," or similar expressions, or by express or implied discussions regarding potential new indications for Zometa, or regarding potential future sales of Zometa. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Zometa to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Zometa will be approved for any additional indications in any market. Neither can there be any guarantee regarding potential future sales of Zometa. In particular, management's expectations regarding Zometa could be affected by, among other things, additional analysis of 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; and other risks and factors referred to in the Company's current Form 20-F on file with the Securities and Exchange Commission of the United States. 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.

#### **About Novartis**

Novartis AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2002, the Group's businesses achieved sales of USD 20.9 billion and a net income of USD 4.7 billion. The Group invested approximately USD 2.8 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 77 200 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

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Additional information on Novartis Oncology and Zometa can be found at [www.us.novartisoncology.com](http://www.us.novartisoncology.com) or [www.zometa.com](http://www.zometa.com). Additional media information can be found at [www.novartisoncologyvpo.com](http://www.novartisoncologyvpo.com).

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**MEDIA RELEASE COMMUNIQUE AUX MEDIAS MEDIENMITTEILUNG**

**New data confirm Zelmac® is effective, safe and well tolerated in treating IBS**

*Data from patients around the world presented at largest gastroenterology conference*

Basel, 21 May 2003 New data presented this week at the 2003 Digestive Disease Week (DDW) meeting in Orlando demonstrates Zelmac® (tegaserod) is effective, safe and well tolerated in the treatment of patients suffering from Irritable Bowel Syndrome (IBS). Data presented from China, Latin America, Pakistan, Germany and the Nordic region shows Zelmac significantly relieves the abdominal discomfort/pain, bloating and constipation experienced by patients with IBS.

**Placebo Controlled Studies**

**China:** In a 4-week study conducted in China, Zelmac-treated patients experienced a significant reduction of IBS symptoms including abdominal pain, bloating and constipation, versus placebo-treated patients ( $p < 0.0001$ ).

**Nordic region:** In a similar 12-week study conducted in the Nordic region, Zelmac-treated patients had significantly greater overall relief of their IBS symptoms ( $p < 0.05$ , 2-sided 5% test) than placebo-treated patients at weeks two and three and for each week from weeks five to twelve. Zelmac also increased the number of days patients experienced  $> 3$  bowel movements for weeks 1-4 ( $p < 0.0001$ ).

"These data are key in reinforcing the efficacy and safety profile of Zelmac in both controlled clinical trials and in normal clinical practice settings for patients with IBS," said Dr. Joerg Reinhardt, Head of Development, Novartis Pharma AG. "Zelmac offers a real option for physicians and patients around the world who have struggled to manage this devastating condition."

**Open-label Studies**

**Germany:** The aim of this study was to determine if retreatment with Zelmac is as effective and safe as an initial course of therapy. 436 patients responded to Zelmac (85%) during the initial treatment phase of 12 weeks. 88 percent of patients who entered the re-treatment phase of the trial, responded to treatment.

**Latin America:** The results from an open-label study conducted in Latin America found that 82 percent of patients were responsive to Zelmac treatment over a one-month initial treatment period. Patients who were maintained on the therapy were less likely to relapse compared with patients who were in the withdrawal arm (10% vs. 67%, respectively).

"These re-treatment studies point to the potential benefit of continuous treatment to delay symptom relapse in patients with IBS," said Dr. Reinhardt.

**Pakistan:** In a small 6-week study in Pakistan, treatment with Zelmac significantly decreased the number of patients experiencing abdominal pain/discomfort, bloating, sense of incomplete evacuation and straining at defecation ( $p = 0.001$  for all variables). Further, results show Zelmac was equally effective in males and females in relieving the symptoms of abdominal pain, bloating and straining.

Previous studies have demonstrated Zelmac to be safe and well tolerated in European and North American patients with IBS with constipation. The abstracts presented at DDW 2003 extend this safety profile to patients from China, Pakistan, Latin America with IBS with Constipation, and in patients from the Nordic region with IBS whose primary bowel symptom was not diarrhea. The overall frequency of adverse events was similar among studies. The most common adverse event was diarrhea in the Zelmac groups, and was generally mild, transient and typically resolved with continued treatment. The overall discontinuation rate due to side effects was small. In addition, the safety profile was shown to be the same for initial treatment and retreatment with Zelmac in patients with IBS with Constipation.

### **About Irritable Bowel Syndrome (IBS)**

IBS is characterized by abdominal pain and discomfort, bloating, and altered bowel function (constipation and/or diarrhea). Until recently, the cause of IBS has been poorly understood and under appreciated. However, in recent years, new research has yielded a better understanding of IBS and its causes. People who have abdominal pain and discomfort, bloating and constipation associated with IBS may have altered sensitivity, motility and impaired secretory functions of their GI tract. This may be due to the way their lower GI tract reacts to changes in 5HT (serotonin), a naturally occurring substance, in their body that regulates motility and perception of pain and discomfort in the intestinal system.

### **About Zelmac**

Zelmac is the first in a new class of medicines, known as 5HT<sub>4</sub> agonists (serotonin type 4 agonists) developed especially for the treatment of the multiple symptoms associated with IBS with constipation. By activating 5HT<sub>4</sub> receptors in the gastrointestinal tract, Zelmac normalizes impaired motility and reduces sensitivity of the intestinal tract. In clinical studies, significantly more patients experienced a general relief of symptoms when treated with Zelmac, such as a decrease in abdominal pain, bloating and constipation. In most patients who responded to Zelmac, the onset of relief occurred within just one week. The medicine was well tolerated and showed a profile of side effects similar to that of placebo.

Zelmac was discovered and developed by Novartis. Zelmac, known in the United States, Canada, the Philippines and South Africa as Zelnorm®, is approved in more than 45 countries including Switzerland, Canada, the United States, Mexico and Brazil. In the Asian Pacific region, Zelmac is also approved for use in Australia, Thailand, Singapore, Vietnam and Indonesia.

Digestive Disease Week (DDW) is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA), the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW takes place May 17-22, 2003 in Orlando, Florida. The meeting showcases approximately 5,000 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology.

The foregoing press release contains certain forward-looking statements related to the business of Novartis, which can be identified by express or implied discussions regarding potential new indications or approvals for Zelmac, or potential future sales of Zelmac. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantees that Zelmac will be approved for any additional indications or in any additional markets. Nor can there be any guarantee that Zelmac will achieve any particular sales levels. Management's expectation regarding the commercial potential of tegaserod in any market could

be affected by, amongst other things, uncertainties relating to product development, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection and competition in general, as well as factors discussed in the Company's Form 20-F filed with the Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.

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Date May 20, 2003

**MEDIA RELEASE   MEDIENMITTEILUNG   COMMUNIQUÉ AUX MÉDIAS**

**Return of a traditional name:  
Novartis Generics rebranded as Sandoz**

*Novartis Generics companies worldwide adopting the Sandoz name*

*New biotechnology facilities coming on stream in Kundl*

*Since 2000 EUR 260 million investment in Austria*

**Vienna, 20 May 2003.** From 21 May 2003, Novartis, one of the world's leading pharmaceutical groups, will be conducting its generics operations hitherto Novartis Generics under a single brand name, Sandoz. Austria's flagship pharmaceutical company, Biochemie GmbH (Kundl/Tyrol), will likewise be operating under the new name.

Christian Seiwald, Head of Novartis Generics and henceforth CEO of Sandoz, commented: "Over the last few years, Novartis Generics has grown extremely dynamically and undertaken a series of strategic acquisitions. While we are currently the world's second-biggest generics group, we are not recognized as such due to the large number of different brand names. The establishment of a uniform brand and identity represents a milestone in our strategy for strengthening and harmonizing our international business."

In Seiwald's view, the Sandoz name reinforces the company's reputation for high quality and innovation and provides the additional bonus of a company tradition going back more than a century: "We want Sandoz to become the undisputed no. 1 global brand for generic pharmaceutical products."

Sandoz, which was established in Basel in 1886, was a pharmaceutical market player up until its merger with Ciba-Geigy in 1996 to form Novartis. The rebranding of Novartis Generics now marks the return of this time-honored name. For the time being, our affiliate Lek will keep its name as agreed between the management of the two companies at the time of Lek's acquisition.

Since February 2003, Sandoz's global headquarters have been located in Vienna, further strengthening the company's traditionally close ties with Austria; the company had previously had a strong Austrian presence in the shape of Biochemie GmbH.

#### **New high-tech facilities and major investments in Austria**

Today (Tuesday, 20 May), coinciding with Biochemie GmbH's adoption of the new Sandoz GmbH name, two new high-tech facilities for the production of active biopharmaceutical ingredients have officially come on stream in Kundl/Tyrol. In addition, a new office complex for the management of the global Industrial Business Franchise has been officially inaugurated. Investments in these facilities amount to EUR 100 million. Since the year 2000 the company has invested around EUR 260 million in Austria.

Dr. Heinrich Scherfler, Chairman of the Board of Sandoz GmbH, Austria, commented: "With the adoption of the Sandoz name and our latest program of investments in state-of-the-art active ingredients, we are pleased to be setting a new, double milestone in our company's history."

The new facilities comprise a number of research laboratories, technical installations and equipment for the production of recombinant biopharmaceuticals, i.e. potent pharmaceutical agents produced using the latest biotechnological methods. Biopharmaceuticals including various hormones, interferons and other substances that occur naturally in humans are playing an increasingly important role in modern medicine.

With over 20 years' experience in the development and manufacture of biotechnologically produced active ingredients, entry into this sector was a logical step for the company now rebranded as Sandoz. This Business Franchise currently employs more than 350 staff and has accounted for more than half of the striking increase in headcount (more than 500 new jobs) that has occurred over the past four years. The company now employs a total of 2,500 people in Austria.

According to Christian Seiwald, "The decision to move into the biopharmaceutical sector is a decision to secure the future of our Kundl and Schaftebau locations in Tyrol. Over the next decade, biopharmaceuticals will be one of our key growth drivers. However, we are also investing heavily in our pharmaceutical finished products business and in active pharmaceutical and biotechnological ingredients."

In addition to this capital investment program, expenditure on R&D has risen continuously in recent years, reaching the record level of EUR 84 million in 2002. More than 400 staff around 16% of the company's Austrian workforce is working in this area alone. A substantial proportion of recent expenditure has been committed to development activities for biopharmaceuticals. As Dr. Scherfler pointed out, "In contrast to earlier research projects, this initiative received support from government agencies. We see this as a sign of the state's support for Austria as a business location, and I would also like to thank the funding agencies for their assistance."

The opening of the company's new administrative center is also a signal for the importance of the Tyrol site. The modern office complex for the management of the global Industrial Business Franchise is a state-of-the-art building, accommodating more than 70 staff.

#### **Company Information**

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 profound know-how make Sandoz a renowned partner in the Franchises Pharmaceuticals, Biopharmaceuticals and Industrial Products. Altogether, Sandoz employs around 11,500 people worldwide and posted sales of USD 1.8 billion in 2002.

Novartis AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2002, the Group's businesses achieved sales of USD 20.9 billion and a net income of USD 4.7 billion. The Group invested approximately USD 2.8 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 77,200 people and operate in over 140 countries around the world. For further

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

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 "coming on stream", "will be", "to become", or similar expressions, or by express or implied discussions regarding strategies, plans and expectations. Such statements reflect the current plans or views of the Group with respect to future events and are subject to certain risks, uncertainties and assumptions. Management's expectations could be affected by, among other things, competition in general, and other risks referred to in Novartis AG's 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.

21

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**Investor Relations Release**

**New study shows Zelmac® is effective and well tolerated for chronic constipation**

Basel, 20 May 2003 New data from a large pivotal US trial demonstrates Zelmac®(tegaserod) was significantly more effective than placebo in providing rapid and sustained relief from chronic constipation based on a trial of more than 1,300 patients. Furthermore, Zelmac provided relief of several chronic constipation symptoms including bowel movement frequency, straining, stool consistency, abdominal discomfort or pain, bloating or distension.

These new data, including findings that further support the safety and tolerability profile of Zelmac, were presented at the 34<sup>th</sup> Annual Digestive Disease Week Meeting. A supplemental submission to the US Food and Drug Administration (FDA) for the drug's use in patients with chronic constipation is planned for the fourth quarter of 2003.

"If approved for use in chronic constipation, tegaserod would be the first treatment not only to improve bowel frequency but also to provide relief of multiple symptoms to patients," said John Johanson, MD, MSC, lead investigator and Clinical Associate Professor of Medicine at the University of Illinois College of Medicine in Rockford. "This advance would be welcomed by the medical community because there is a need for additional therapies that are effective and well tolerated."

**Zelmac provides rapid and sustained response over three months**

The study found that the response rate for Zelmac (2 mg b.i.d."twice a day" or 6 mg b.i.d.) was superior to placebo (p<0.0001) in increasing the number of complete spontaneous bowel movements (CSBM). After four weeks, the 2 mg treated group had a 41.4 percent response rate, similar to the 6 mg treated group (43.2%), both of which were significantly better than the placebo group (24.9%) at four weeks. At 12 weeks the response rate for the 2 mg treated group was 40.3%, while 44.8% of those receiving 6 mg responded, again both treatments were significantly better than the placebo group (26.9%). In addition, satisfaction with bowel habits improved and overall bothersomeness of symptoms decreased in patients receiving Zelmac. Once the 12-week treatment period with Zelmac was over, patients' symptoms returned within two weeks.

The study also showed that Zelmac was well tolerated in female and male patients over the duration of the study. While the most frequent adverse events reported during the study were headache and cold-like symptoms (nasopharyngitis), they occurred more often in placebo-treated



patients. Diarrhea was also reported as an adverse event and was generally mild or moderate in severity, of short duration (median <2 days), occurred only once in the majority of patients, and had a low discontinuation rate (<1%). No clinically significant ECG changes were noted, including QTc interval (duration). Clinical and laboratory parameters examined showed no alterations in electrolytes or

vitamin absorption. Overall, this study with more than 1300 patients supports the safety and tolerability profile of this potential new therapeutic option for patients with chronic constipation.

#### **About the study**

This US multicenter, double-blind, placebo-controlled study included patients randomly assigned to 2 mg b.i.d. (n=450) or 6 mg b.i.d. (n=451) doses of Zelmac taken orally or placebo (n=447) for a period of 12 weeks. Successful response was defined as a an increase of at least one CSBM per week compared to baseline and a minimum of seven days of treatment. Stool frequency and bowel habits for all participants were established during the two-week baseline period. The primary efficacy variable was the response during the first month of treatment. Secondary endpoints included response over three months and intensity of specific symptoms (bloating/distention, abdominal discomfort/pain, straining, stool consistency). Satisfaction with bowel habits and bothersomeness of overall symptoms were also assessed.

This study defined chronic constipation as symptoms for at least six months duration with less than three CSBMs per week and straining, incomplete evacuation and/or hard stools. Ninety percent of the patients in the study were women who had constipation symptoms for an average of 19 years.

#### **About constipation**

There are approximately 2.5 million constipation related visits to physicians each year in the United States. It is estimated that patients spend approximately \$350-400 million annually on over-the-counter laxatives to help alleviate their constipation. Chronic constipation is a prevalent and bothersome disorder that can negatively impact patient's lives. Women are affected two to three times more often than men, and there are approximately four million people in the United States with chronic constipation.

#### **About Zelmac**

Zelmac is the first in a new class of medicines, known as 5HT<sub>4</sub> agonists (serotonin type 4 agonists) developed especially for the treatment of the multiple symptoms associated with Irritable Bowel Syndrome (IBS) with constipation. By activating 5HT<sub>4</sub> receptors in the gastrointestinal tract, Zelmac normalizes impaired motility and reduces sensitivity of the intestinal tract. In clinical studies, significantly more patients experienced a general relief of symptoms when treated with Zelmac, such as a decrease in abdominal pain, bloating and constipation. In most patients who responded to Zelmac, the onset of relief occurred within just one week. The medicine was well tolerated and showed a profile of side effects similar to that of placebo.

Zelmac was discovered and developed by Novartis. Zelmac, known in the United States, Canada, Philippines and South Africa as Zelnorm®, is approved in more than 45 countries including Australia, Switzerland, Canada, the United State, Mexico and Brazil. In the Asian Pacific region, Zelmac is also approved for use in Thailand, Singapore, Vietnam and Indonesia.

#### **About DDW**

Digestive Disease Week (DDW) is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA), the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW takes place May 17-22, 2003 in Orlando, Florida. The meeting showcases approximately 5,000 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology.

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regarding potential new indications for Zelmec, or potential future sales of Zelmec. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results with Zelmec to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantees that the data described above will result in any new indications for Zelmec, or that Zelmec will reach any particular sales levels. Any such success can be affected by, among other things, uncertainties relating to product development, future clinical trial results, adverse regulatory actions or delays, government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection, competition in general and other risks and factors referred to in the Company's current Form 20-F on file with the Securities and Exchange Commission of the United States.

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### Investor Relations Release

#### **FDA advisory committee unanimously recommends approval of Xolair**

*Potential first biologic treatment for allergic asthma targets underlying cause of disease*

Basel, 16 May 2003 Novartis announced today that the US Food and Drug Administration's (FDA) Pulmonary-Allergy Drugs Advisory Committee (PADAC) voted unanimously that Xolair (omalizumab) for injection be approved based on a favourable risk benefit profile for the treatment of moderate-to-severe allergic asthma in adults and adolescents. Xolair represents a novel treatment approach and is the first humanized monoclonal antibody developed for the treatment of allergic asthma; it is the only allergic asthma treatment designed to block the IgE antibody, specifically targeting an underlying cause of allergic asthma. Based on the outcome of the Advisory Committee meeting, the sponsors will conduct further discussions with the FDA regarding product labeling and post-marketing commitments.

In clinical trials of moderate to severe patients, Xolair was found to reduce asthma exacerbations (allergic asthma attacks) and enabled many patients to reduce or eliminate usage of inhaled corticosteroids. Novartis and its partners are seeking approval to market Xolair in the US as a potential maintenance therapy for the prophylaxis of asthma exacerbations and control of asthma symptoms in adults and adolescents (12 years and older) with moderate-to-severe allergic asthma that is inadequately controlled, despite the use of inhaled corticosteroids.

"We are very pleased that the advisory committee has recognized the significant benefits that Xolair could offer to people with allergic asthma whose needs are unmet by the existing range of therapies," said Joerg Reinhardt, Head of Development for Novartis Pharma AG. "We look forward to working closely with the FDA to secure approval, so that this unique therapy can be made available to patients at the earliest possible opportunity."

Xolair is being jointly developed under an agreement among Novartis Pharma AG, Genentech, Inc. and Tanox, Inc. The Biologics License Application for Xolair was filed in June 2000 and a supplemental data amendment was submitted in December 2002. The FDA generally

follows the advice of its advisory committees, although the agency is not bound by its recommendations. A decision by the FDA is expected in late June 2003.

If approved by the FDA, Xolair would be the first IgE blocker in the US and the first biologic therapy for the treatment of moderate to severe allergic asthma. Furthermore, it is potentially the first asthma product to be administered every two or four weeks. Xolair is designed specifically to block the IgE antibody, a key underlying cause of allergic asthma. When an allergen (e.g. dust, mold, pollen) interacts with (cross-links) IgE bound to mast cells in the human immune system, these cells release inflammatory chemicals such as histamine and leukotrienes that lead to the inflammation and bronchial

25

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constriction of allergic asthma. Decreasing the amount of IgE bound to mast cells can disrupt the release of these chemical mediators that cause the clinical symptoms of allergic asthma.

### **Xolair Clinical Trial Results**

The Advisory Committee's discussions focused on data from two 52-week pivotal Phase III clinical trials with 1 071 allergic asthma patients, as well as data from several supportive safety and efficacy studies. The pivotal trials were designed to investigate a dual benefit of reduction in asthma exacerbations and reduction in inhaled corticosteroid dose. Patients treated with Xolair showed significant improvements in asthma exacerbations and symptoms, and most patients reduced their use of steroids and rescue bronchodilators.

In clinical trials, when used as an add-on therapy to inhaled corticosteroids, Xolair was found to reduce exacerbations (allergic asthma attacks) by approximately 50%. Additionally, the average dose of inhaled corticosteroids in patients taking Xolair in the two pivotal trials was reduced by 83% and 75% respectively, compared with 50% in the placebo groups. Steroid use was discontinued in 40-43% of patients in the Xolair groups compared with 19% in the placebo groups.

The expanded safety database submitted to the FDA includes clinical data from more than 6 000 patients, of which approximately 4 200 patients have been treated with Xolair. In clinical trials, Xolair treatment was generally well tolerated and the frequency of reported adverse events was comparable between the Xolair-treated and control groups. The most frequently observed adverse events included viral infections, sinusitis, upper respiratory infection and headache. Serious adverse events were infrequent and of similar incidence in both the Xolair and control groups. The final labeled efficacy and safety profile description in the product labeling will be determined by the FDA.

### **About Allergic Asthma**

Allergic asthma is the most common form of asthma, a chronic inflammatory disorder of the airways characterized by recurrent episodes of wheezing, breathlessness, chest tightness and coughing that affects approximately 54 million world-wide. In allergic asthma, exposure to an allergen (such as dust, mold or pollen) triggers an allergic cascade, which results in airway obstruction. According to the World Health Organization (WHO) an estimated 180 000 people die from asthma each year worldwide.

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", "will be", "look forward", "is expected", "if approved... would be", "potentially", or similar expressions, or express or implied discussions regarding the potential approval of Xolair or potential future sales Xolair. 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 Xolair will be approved, or, if approved, will reach any particular sales levels. In particular, management's expectations could be affected by, among other things, new clinical data; unexpected clinical trial results; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; and other risks and factors referred to in the Company's current Form 20-F on file with the 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 AG (NYSE: NVS) is a world leader in pharmaceuticals and consumer health. In 2002, the Group's businesses achieved sales of USD 20.9 billion and a net income of USD 4.7 billion. The Group invested approximately USD 2.8 billion in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 77 200 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>.

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**SIGNATURES**

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

NOVARTIS AG

Date: June 2, 2003

By: /s/ MALCOLM B. CHEETHAM

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Name: Malcolm B. Cheetham

Title: *Head Group Financial Reporting and Accounting*

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