

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 2002

Novartis AG  
(Name of Registrant)

Lichtstrasse 35  
4056 Basel  
Switzerland

\_\_\_\_\_  
(Address of Principal Executive Offices)

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

Yes  No

Enclosures:

1. Novartis Drug Glivec<sup>®</sup> (imatinib)\* Approved in European Union for Treatment of Life-Threatening GI Cancer (May 31, 2002)
2. Novartis Ophthalmics and QLT announce positive recommendation for Visudyne<sup>®</sup> approval in Europe from European Committee for Proprietary Medicinal Products (May 31, 2002)
3. Data demonstrating Zometa<sup>®</sup> as effective treatment for debilitating bone complications in prostate cancer patients presented at major urology meeting (May 27, 2002)
4. Geneva announces US District Court invalidates Augmentin<sup>®</sup> patents (May 23, 2002)

5. Data presented at APA meeting suggest Ritalin<sup>®</sup> LA (methylphenidate hydrochloride) extended-release capsules are an effective once-daily treatment for ADHD (May 22, 2002)
6. Two studies show Focalin<sup>™</sup> (dexmethylphenidate HCl) is an effective treatment for ADHD (May 22,2002)
7. Data demonstrating Zometa<sup>®</sup> as important advance in treating lung cancer-related bone complications presented at major oncology meeting (May 22, 2002)
8. Aromatase inhibitors in breast cancer assessed by ASCO Committee (May 21, 2002)
9. New head-to-head data show Glivec<sup>®</sup> is nearly three times more effective as first-line treatment for chronic myeloid leukemia patients than interferon combination therapy (May 21, 2002)
10. Glivec<sup>®</sup> maintains responses in patients with life-threatening gastrointestinal tumors after one year of treatment (May 21, 2002)
11. Head-to-head worldwide study of the two leading aromatase inhibitors shows more women respond to Femara<sup>®</sup> than Arimidex<sup>®</sup> in advanced breast cancer (May 21, 2002)
12. Novartis launches TARGET, largest world-wide arthritis clinical trial (May 21, 2002)
13. Gastrointestinal safety studies highlight benefits of investigational COX-2 inhibitor (May 21, 2002)
14. Elidel<sup>®</sup> cream offers new non-steroid approach to treating atopic eczema in babies and sensitive skin areas (May 16, 2002)
15. LOGIC, new 9,000-patient study, demonstrates patients switched to Lotrel<sup>®</sup> from Norvasc<sup>®</sup> experience better blood pressure control with less edema (May 14, 2002)
16. Starlix<sup>®</sup> enhances glucose control in people with impaired glucose tolerance (May 8, 2002)
17. Glivec<sup>®</sup> (imatinib)\* may be effective in rare blood disease according to new report in The Lancet (May 3, 2002)
18. Interim data from MO2ART study using Neoral<sup>®</sup> C<sub>2</sub> monitoring demonstrates impressive, low rates of kidney rejection (May 2, 2002)
19. Novartis broadens horizons in post-transplant immunosuppression:  
FTY720 plus Certican<sup>™</sup> shows efficacy and safety in a calcineurin inhibitor (CNI) - free regimen (May 2, 2002)

**- Investor Relations Release -**

## **Novartis Drug Glivec® (imatinib)\* Approved in European Union for Treatment of Life-Threatening GI Cancer**

*Glivec is approved to treat gastrointestinal stromal tumours (GISTs), the second indication in a record seven months*

*Basel, Switzerland, 31 May 2002 – Novartis announced today that, in record time, the European Commission (EC) has issued approval for the breakthrough drug Glivec® (imatinib)\* for the treatment of patients with Kit (CD 117)-positive unresectable (inoperable) and/or metastatic malignant gastrointestinal stromal tumours (GISTs). The approval follows a positive recommendation by the EU's Committee for Proprietary Medicine (CPMP) in February 2002. It is the second EC approval for Glivec in seven months: the first, on 7 November 2001, was as an oral therapy for the treatment of adult patients with Philadelphia (Bcr-Abl) chromosome-positive chronic myeloid leukemia (CML) in chronic phase after failure of interferon-alpha therapy, or in accelerated phase or blast crisis.*

*“Patients with GISTs have traditionally had very limited treatment options, so we are especially pleased that authorities are recognising the value of Glivec in treating this life-threatening cancer,” said Daniel Vasella, MD, Chairman and CEO of Novartis. “Glivec has already had a significant impact on the lives of people with CML and GISTs, and we are continuing to study it in other cancers to determine if it has the potential to help patients, either alone or in combination with other therapies.”*

GISTs are the most common malignant form of sarcoma that arise in the gastrointestinal tract. Worldwide, there are approximately 12 000 new cases each year. The incidence is highest in people 30-60 years of age. Historically, GISTs have been very difficult to treat due to their resistance to treatment with available chemotherapy and radiation therapy.

For patients with metastatic or unresectable disease, GISTs were an incurable malignancy with a median survival of 20 months and, with local recurrence, a median survival of 9-12 months. Until now, surgery has been the only treatment option, resulting essentially in palliation of the disease.

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\*In the US: Gleevec™ (imatinib mesylate); outside the US: Glivec® (imatinib)

### **About Glivec and GISTs**

The EC approval for the GIST indication is supported by data from an open-label, multinational study conducted in 147 patients with Kit (CD117) positive unresectable and/or metastatic malignant GISTs. Patients were randomised to receive either 400 mg or 600 mg of Glivec daily until remission. The overall response rate was 40%, based on confirmed partial responses and stable disease at the time of the data cut-off for the submission.

Data which have emerged since the submission for approval were presented in May 2002 at the 38<sup>th</sup> annual meeting of the American Society of Clinical Oncology (ASCO) in Orlando, Florida, USA. The data showed that in this study, more than 60% of patients with GIST achieved confirmed partial response to Glivec, and an additional 20% attained some degree of tumour shrinkage or stabilisation of their disease. The data also revealed that at a median follow-up of 15 months, 73% of patients remained on the study.

Glivec, a signal transduction inhibitor, is one of the first cancer drugs to be developed using rational drug design, based on an understanding of how some cancer cells are generated and exhibit unrestrained growth. Glivec targets the activity of specific enzymes called tyrosine kinases that play an important role within certain cancer cells. The activity of a tyrosine kinase known as Kit, a receptor that is the product of a gene called c-kit, is very often mutated and is known to drive the growth and division of most GISTs.

### **Glivec To Date**

The U.S. Food and Drug Administration (FDA) was the first to approve Glivec for the GIST indication, for which it was designated as an Orphan Drug, on 1 February 2002. Glivec also is approved for the GIST indication in Switzerland, where it was approved on 15 April 2002. To date, Novartis has received marketing clearance for Glivec for the CML indication worldwide.

### **Contraindications and Adverse Events**

Although the majority of patients had adverse events reported at least once during this trial, most events were mild to moderate in severity and included nausea, diarrhoea, periorbital oedema, muscle cramps, fatigue, headache and skin rash. About 23% of the patients had severe drug-related side effects that included low white blood cell counts, tumor haemorrhage and abdominal pain. In the GIST trial submitted for registration, drug was discontinued for adverse events in 13 patients (9% of patients). In this clinical trial, the most common adverse events were oedema, nausea, diarrhoea, abdominal pain, muscle cramps, fatigue and rash. In this trial, seven patients (5%) were reported to have gastrointestinal bleeds and/or intratumoral bleeds. Gastrointestinal tumor sites may have been the source of GI bleeds. 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.

In most countries where Glivec is approved, it is indicated for the treatment of patients with Philadelphia chromosome-positive CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy.

The foregoing release contains forward-looking statements that can be identified by terminology such as "shown the potential to help," "until now," "authorities are recognizing the value," or similar expressions. 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. In particular, management's ability to ensure satisfaction of the FDA's further requirements is not

guaranteed and management's expectations regarding further commercialisation of Glivec could be affected by, among other things, additional analysis of data; new data; unexpected clinical trial results for Glivec; 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 materialise, 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 healthcare with core businesses in pharmaceuticals, consumer health, generics, eye-care, and animal health. In 2001, the Group's businesses achieved sales of CHF 32.0 billion (USD 19.1 billion) and a net income of CHF 7.0 billion (USD 4.2 billion). The Group invested approximately CHF 4.2 billion (USD 2.5 billion) in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 72 600 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 can be found at [www.novartisoncologyvpo.com](http://www.novartisoncologyvpo.com) and at [www.novartisoncology.com](http://www.novartisoncology.com).

## **Novartis Ophthalmics and QLT announce positive recommendation for Visudyne® approval in Europe from European Committee for Proprietary Medicinal Products**

*This represents a major step in the marketing approval process in Europe for expanded use in patients with occult CNV secondary to age-related macular degeneration*

Basel, 31 May 2002 – Novartis Ophthalmics, the eye health unit of Novartis AG, and QLT Inc. today announced that the Committee for Proprietary Medicinal Products (CPMP) of the European Medicines Evaluation Agency (EMA), has adopted a positive opinion on Visudyne® (verteporfin) therapy to also include the treatment of patients with evidence of recent or ongoing disease progression in occult subfoveal choroidal neovascularization (CNV) secondary to age-related macular degeneration (AMD), a leading cause of blindness among people over the age of 50. The CPMP opinion will now be considered by the European Commission, which should make a final decision within three months regarding marketing authorization in the European Union.

Visudyne therapy is the only drug approved for the treatment of certain forms of wet AMD. AMD consists of two forms: wet and dry. Although only 15% of AMD patients suffer from the wet form of the disease this type is more aggressive and accounts for approximately 90% of severe vision loss. Approximately 500,000 new cases of the wet form of AMD occur each year worldwide, and this estimate is expected to grow dramatically as the population ages.

“We look forward to the European Commission’s final decision and to being able to provide Visudyne to the many patients for whom there is no approved drug treatment currently available,” said Paul Hastings, president and CEO of QLT.

This application was based on favorable two-year results from the Verteporfin in Photodynamic Study trial (VIP), a phase IIIb clinical trial, which included 258 patients with subfoveal occult without classic CNV, who had recent disease progression. The study showed that patients who received Visudyne therapy for 24 months had a significantly reduced risk of moderate and severe vision loss compared to the placebo group. The results were published in the May 2001 issue of the peer-reviewed *American Journal of Ophthalmology*.

“We are very pleased with the committee's recommendation for approval of Visudyne for occult wet AMD,” said Luzi von Bidder, head of Novartis Ophthalmics. “This positive recommendation is a very important milestone as occult CNV represents a considerable portion of the total wet

AMD population and if approved this indication could expand the current market for Visudyne to two-thirds of the total patient population in Europe.”

### **About AMD**

AMD is caused by a growth of abnormal blood vessels (CNV) under the central part of the retina or macula and occurs in two forms, dry and wet AMD. In the wet form, the vessels leak fluid and blood that lead to the development of scar tissue that destroys the central retina. This results in a deterioration of sight over a period of two months to three years. “Occult” and “classic” are terms used to describe the different patterns of CNV leakage as seen on fluorescein angiography.

### **About Visudyne**

Visudyne therapy, the only drug approved for the treatment of some forms of wet AMD, has treated approximately 150,000 patients worldwide. Visudyne is commercially available in 62 countries for the treatment of predominantly classic subfoveal CNV caused by AMD. It is also approved in 40 countries, including the EU, U.S. and Canada, for the treatment of subfoveal CNV due to pathologic myopia (severe near-sightedness). In the U.S., Visudyne has received an additional approval for CNV due to presumed ocular histoplasmosis.

Visudyne therapy, developed by Novartis Ophthalmics and QLT Inc., is a relatively painless two-step procedure performed in a doctor’s office. Visudyne is injected intravenously into the patient’s arm, and then a non-thermal laser light is shone into the patient’s eye to activate the treatment. Visudyne targets the abnormal blood vessels and does not affect normal/healthy blood vessels.

Visudyne is generally well tolerated and has an excellent safety profile. Potential side effects include injection site reactions, headaches, back pain, blurring, decreased sharpness and gaps in vision, and in 1-5% of patients a substantial decrease in vision with partial recovery in some patients. People should avoid direct sunlight for five days to avoid sunburn. People with porphyria should not be treated. For more information, visit [www.visudyne.com](http://www.visudyne.com).

*Visudyne® is a trademark of Novartis AG.*

The foregoing press release contains forward-looking statements, that can be identified by terminology such as “should make” or “could expand”, or by discussions regarding potential new indications for existing products. Such forward-looking statements involve known and unknown risks, uncertainties and other factors, which may cause the actual results and assumptions to be materially different from any future results, performance or achievements expressed or implied by such statements. There are no guarantees that any of the potential potential new indications will be commercialized in any market. Any such commercialization can be affected by, among other things, the risk that the CPMP opinion may be rejected by the European Commission, uncertainty regarding the market size of the occult wet AMD population in Europe and the effect of the CPMP opinion and pending decision of the European Commission on Visudyne sales, other risks associated with the development and commercialization of the treatment, including uncertainties relating to manufacturing, clinical trials, registration, pricing and reimbursement; patient and physician demand for the treatment; competition; any uncertainty regarding patents and proprietary rights; and additional factors as described in detail in QLT Inc.’s Annual Information Form on Form 10-K and recent and forthcoming quarterly reports on Form 10Q, and Novartis AG’s Form 20-F, and other filings with the US Securities and Exchange Commission and Canadian Securities Regulatory authorities.

### **Background on Novartis Ophthalmics and QLT**

Novartis Ophthalmics: With worldwide headquarters in Bulach, Switzerland, Novartis Ophthalmics is a global leader in research, development and manufacturing of leading ophthalmic pharmaceuticals that assist in the treatment of glaucoma, age-related macular degeneration, eye inflammation, ocular allergies and other diseases and disorders of the eye. Novartis Ophthalmics products are available in more than 110 different countries. The North American headquarters is based in Atlanta, Georgia. Novartis Ophthalmics has production sites in Switzerland, France and Canada. For more information, visit [www.novartisophthalmics.com](http://www.novartisophthalmics.com) or [www.novartisophthalmics.com/us](http://www.novartisophthalmics.com/us).

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QLT Inc. (NASDAQ: QLTI; TSE:QLT) is a global biopharmaceutical company dedicated to the discovery, development, and commercialization of innovative therapies to treat cancer, eye diseases and immune disorders. Combining expertise in ophthalmology, oncology and photodynamic therapy, QLT has commercialized two products to date, including Visudyne therapy which is the largest selling ophthalmology product ever launched. For more information, visit our web site at [www.qltinc.com](http://www.qltinc.com).

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## **Data demonstrating Zometa® as effective treatment for debilitating bone complications in prostate cancer patients presented at major urology meeting**

Basel, Switzerland, 27 May 2002 – The Novartis drug Zometa® (zoledronic acid) is effective for the treatment of potentially debilitating skeletal related events from bone metastases in prostate cancer patients according to the data presented at the 97<sup>th</sup> annual meeting of the American Urological Association (AUA) in Orlando, Florida, USA. Patients with advanced prostate cancer are at high risk for developing bone complications—or skeletal related events (SREs)—which include bone pain, pathologic fractures, need for radiation or surgery to bone, spinal cord compression and hypercalcaemia. This study marks the first time a bisphosphonate has demonstrated efficacy in treating bone metastases in this patient population. Further, Zometa offers patients, nurses and clinicians a convenient 4 mg (in 100 ml of solution), 15-minute infusion time.

“Bone metastases can result in debilitating pain, fractures and compression of the spine and are a significant problem for patients with advanced prostate cancer. Until now, there were few effective therapies available for these patients,” said Fred Saad, MD, Associate Professor of Urology and Director of Urologic Oncology at the Montreal Cancer Institute, University of Montreal. “Zometa represents a significant advance in the overall treatment of advanced prostate cancer patients and should be a welcome addition for urologists and oncologists in the care of their patients.”

### **Study Design**

The study was designed to investigate the efficacy of Zometa in patients with bone complications resulting from prostate cancer, particularly with respect to reducing the proportion of patients with SREs and delaying the time to first SRE. A total of 643 patients with at least one bone metastasis participated in the multicentre, randomized, placebo-controlled trial. The final analysis was based on evaluating Zometa 4 mg (in 100 ml of solution) compared to placebo at an infusion rate of 15 minutes, given every three weeks for 15 months. Initially, a third arm of the study evaluated an 8 mg dose of Zometa; however, that dose offered no efficacy advantage compared to the recommended dose (4 mg/15 minute infusion), but was associated with a higher incidence of adverse events, including increased serum creatinine levels. Therefore, dosing on this arm was changed to 4 mg and was not included in this efficacy analysis.

### **Clinical Data**

The data demonstrated that 25% fewer patients taking Zometa 4 mg experienced any SRE compared to those patients taking placebo (Zometa 33% vs. placebo 44%,  $p=0.021$ ). The 15-month data also demonstrated that fewer patients taking Zometa 4 mg had a pathologic fracture compared to those patients taking placebo (Zometa 13% versus placebo 22%,  $p=0.015$ ). Patients taking Zometa 4 mg also showed a slower rate of progression of pain compared with placebo. All

patients experienced a mean increase from baseline in composite Brief Pain Inventory (BPI) pain scores over time; however, the increases were lower at every time point for patients treated with Zometa 4 mg compared with placebo (statistically significant at months three and nine).

### **About Prostate Cancer and Bone Metastases**

Bone metastases are the spread of cancerous cells from the original tumor to bones. Bone metastases/lesions are common in prostate cancer and research indicates bone metastases occur in 65-75% of all advanced prostate cancer patients and often bone is the only site of metastases. Some studies have shown that complications of metastases are the primary cause of death among patients with prostate cancer; therefore, treating the bone metastases may successfully improve clinical outcome. Prior to Zometa, current therapeutic options for complications of bone metastases included hormonal therapy, surgery, radiotherapy, chemotherapy and analgesics for pain management.

### **About Zometa**

Zometa received U.S. FDA approval on 22 February 2002 for the treatment of patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. These solid tumors studied include prostate cancer, breast cancer and other solid tumor types including renal, colorectal and lung. In prostate cancer, patients should have progressed after treatment with at least one hormonal therapy. Zometa also received a positive opinion for this indication from the Committee for Proprietary Medicinal Products (CPMP) in the European Union (EU). The EU Commission usually grants approval of products four months after a CPMP positive opinion.

### **Contraindications and Adverse Events**

In clinical trials in patients with bone metastases, Zometa was generally well tolerated, with 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, anaemia, weakness, cough, dyspnoea and oedema. 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.

Zometa and other bisphosphonates 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 administered with 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.

This release may contain forward-looking statements regarding the potential launch of Zometa in markets in which it currently is not approved, or regarding potential new indications for Zometa in existing markets. 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 are no guarantees that Zometa or any potential new indications for Zometa will be commercialized in any market. Any such commercialization can be affected by, among other things, uncertainties relating to product development and clinical trials, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection and competition in general, as well as factors discussed in Novartis AG's Form 20-F filed 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 described herein as anticipated, believed, estimated or expected.

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MEDIA RELEASE · COMMUNIQUE AUX MEDIAS · MEDIENMITTEILUNG

## Geneva announces US District Court invalidates Augmentin® patents

Plainsboro, New Jersey, 23 May 2002 – Geneva Pharmaceuticals, Inc. ("Geneva") announced today that the US District Court for the Eastern District of Virginia rendered a decision in Geneva Pharmaceuticals, Inc., et al. v. GlaxoSmithKline PLC, et al. (Civ. Act. Nos. 2:01-CV-391; 2:01-CV-677; and 2:01-CV-925) invalidating the three remaining patents claiming GlaxoSmithKline PLC's ("Glaxo's") antibiotic Augmentin® (amoxicillin/clavulanate potassium).

The Court ruled that US Patent Nos. 4,525,352; 4,529,720; and 4,560,552, which are otherwise due to expire on June 25, July 16 and December 24, 2002, respectively, are invalid for double-patenting. The Court had previously granted motions for summary judgment invalidating a number of other patents claiming Augmentin which were due to expire in 2017 and 2018. Geneva has received final approval from the US Food and Drug Administration for its generic version of Augmentin, in several strengths and dosage forms.

Geneva Pharmaceuticals, Inc. is one of the largest prescription generic drug companies in the US. Geneva produces more than 200 products each year, with an annual manufacturing capability exceeding 10 billion tablets and capsules. Geneva products range across many therapeutic drug categories including anti-infectives, anti-arthritics, cardiovasculars, gastrointestinal agents and psychotherapeutics. Geneva is an affiliate of the Novartis AG (NYSE: NVS) is a world leader in healthcare with core businesses in pharmaceuticals, consumer health, generics, eye-care, and animal health. In 2001, the Group's businesses achieved sales of CHF 32.0 billion (USD 19.1 billion) and a net income of CHF 7.0 billion (USD 4.2 billion). The Group invested approximately CHF 4.2 billion (USD 2.5 billion) in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 72 600 people and operate in over 140 countries around the world. For more information about Geneva, please see our website at [www.genevarx.com](http://www.genevarx.com). For more information on Novartis, [www.pharma.us.novartis.com](http://www.pharma.us.novartis.com) or [www.novartis.com](http://www.novartis.com).

The foregoing press release contains forward-looking statements that can be identified by terminology such as "will evaluate," "will examine," "will assess," "will be assessed" or similar expressions. 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 are no guarantees that the aforementioned clinical trials will result in the commercialization of any product in any

market. Any such commercialization can be affected by, amongst other things, uncertainties relating to product development, including the results of clinical trials, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection and competition in general, as well as factors discussed in Novartis' Form 20F 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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## **Data presented at APA meeting suggest Ritalin® LA (methylphenidate hydrochloride) extended-release capsules are an effective once-daily treatment for ADHD**

**Philadelphia, PA, 22 May 2002** – Data presented at the 155th Annual Meeting of the American Psychiatric Association (APA), suggest that Ritalin® LA (methylphenidate HCl) extended-release capsules, are an effective and well-tolerated, once-daily formulation of Ritalin® (methylphenidate HCl), designed to last the school day and eliminate the need for the midday dose of Ritalin. Results from a double-blind, randomized, placebo-controlled study found that a once-daily morning dose of Ritalin LA was effective in reducing Attention-Deficit/Hyperactivity Disorder (ADHD) symptoms in both home and school settings. Ritalin LA uses SODAS™ technology\*, a proprietary drug delivery technology of Elan Corporation, plc.

“The data presented suggest Ritalin LA is an effective and safe once-daily formulation of Ritalin,” said Joseph Biederman, MD, Chief, Joint Program in Pediatric Psychopharmacology, Massachusetts General Hospital, Professor of Psychiatry, Harvard Medical School, and lead author of the study. “This formulation would have the significant benefit of eliminating the need to take medication during school hours.”

One hundred and sixty ADHD patients, aged 6 – 12, were enrolled in a multi-center study to compare the safety and efficacy of Ritalin LA to placebo. After an initial single-blind screening and titration period, the patients were randomized to receive either a once-daily, morning dose of Ritalin LA or placebo. Efficacy was evaluated by examining the presence of ADHD symptoms in the school and home environment. In this analysis, the primary outcome was measured by the change from baseline in the Conners ADHD/DSM-IV total subscale for teachers (CADS-T), a validated tool for the assessment of ADHD symptoms by teachers. Ritalin LA was found to be clinically and statistically superior to placebo in managing ADHD symptoms in all primary and secondary efficacy variables.

Ritalin LA was also shown to be safe and well tolerated. The incidence of adverse events was similar for Ritalin LA and placebo (24.6% vs. 23.9%). In this study, Ritalin LA exhibited a low rate of discontinuation due to adverse events versus placebo, (1.5% vs. 0.0%).

Ritalin LA is designed to deliver an immediate release of Ritalin and a second equal release of approximately 4 hours after administration, mimicking the pharmacokinetic profile of twice-daily Ritalin. The bimodal release formulation of Ritalin LA provides two peak concentrations of medication, mimicking twice-daily Ritalin but with less fluctuation. Ritalin LA provides the same rapid onset as Ritalin and its efficacy lasts throughout the school day. Ritalin LA may be swallowed whole with capsules, or, for children who have difficulty swallowing, it may be administered by sprinkling the beaded contents on applesauce.

Ritalin LA was developed by Elan's drug delivery division and will be supplied to Novartis under an exclusive worldwide royalty and manufacturing agreement between the companies. Novartis Pharmaceuticals Corporation has commercialization rights to Ritalin LA in the U.S.

ADHD is the most studied childhood psychiatric disorder and is supported by a substantial body of scientific evidence. Its symptoms have been described in the medical literature since 1902. Scientific research indicates that ADHD may be related to disturbances in certain neurotransmitters in the brain. Novartis supports only the proper diagnosis and treatment of ADHD.

The Novartis ADHD product portfolio includes Ritalin, Ritalin SR, and Focalin™ (dexamethylphenidate), a refined formulation of Ritalin. Celgene Corporation (Nasdaq: CELG) of Warren, New Jersey granted Novartis Pharma AG an exclusive worldwide (excluding Canada) license covering its intellectual property rights associated with Ritalin LA as well as Focalin. Pursuant to an agreement between Novartis Pharma AG and Novartis Pharmaceuticals Corporation, Novartis Pharmaceuticals Corporation markets Focalin in the U.S.

In addition, Ritalin LA, a once-daily form of Ritalin, is currently under review at the Food and Drug Administration (FDA). Novartis Pharmaceuticals Corporation received an approvable letter from the FDA for Ritalin LA in October 2001.

The foregoing press release contains forward-looking statements that can be identified by forward-looking terminology such as "suggest", "is designed to", "will be" or similar expressions. Such forward looking statements involve known and unknown risks, uncertainties and other factors that may cause the actual results to be materially different from any future results, performance, or achievements expressed or implied by such statements. In particular, management's expectation regarding the commercialization of Ritalin LA could be affected by amongst other things, results of future clinical trials, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection and competition in general, as well as factors discussed in the Company's Form 20F 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 anticipated, believed, estimated or expected.

Novartis Pharmaceuticals Corporation researches, develops, manufacturers and markets leading innovative prescription drugs used to treat a number of diseases and conditions, including central nervous system disorders, organ transplantation, cardiovascular diseases, dermatological diseases, respiratory disorders, cancer and arthritis. The company's mission is to improve people's lives by pioneering novel healthcare solutions.

Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG (NYSE: NVS), a world leader in healthcare with core businesses in pharmaceuticals, consumer health, generics, eye-care, and animal health. In 2001, the Group's businesses achieved sales of CHF 32.0 billion (USD 19.1 billion) and a net income of CHF 7.0 billion (USD 4.2 billion). The Group invested approximately CHF 4.2 billion (USD 2.5 billion) in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ about 72 600 people and operate in over 140 countries around the world. For further information please consult <http://www.novartis.com>

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\*SODAS Technology is a trademark of Elan Corporation, plc.

## **Two studies show Focalin® (dexamethylphenidate HCl) is an effective treatment for ADHD**

Philadelphia, PA, 22 May 2002 – Data from two double-blind, randomized, placebo-controlled studies presented today at the 155th Annual Meeting of the American Psychiatric Association (APA) demonstrate that Focalin™ (dexamethylphenidate HCl) is effective in the management of the symptoms of Attention-Deficit/Hyperactivity Disorder (ADHD) at half the dose of Ritalin® (d,l methylphenidate HCl). Focalin, a refined formulation of Ritalin, contains only the effective, or d-isomer of d,l methylphenidate HCl.

The first study consisted of 132 ADHD patients, 6 – 17 years of age, randomized to receive Focalin, d,l methylphenidate (Ritalin), or placebo. In this study, the primary rating scale to assess efficacy was the teacher SNAP-ADHD (Swanson, Nolan, and Pelham) rating scale, a standard behavioral assessment tool used in clinical trials. Secondary efficacy measures included change from baseline on the parent-completed SNAP-ADHD Rating Scale (Parent SNAP), Clinical Global Impression-Improvement (CGI-I) scale score, and Math Test performance.

Results of the study showed the treatment effects of Focalin can be obtained at half the milligram dose of d,l methylphenidate. Both Focalin and d,l methylphenidate demonstrated a substantial reduction of ADHD symptoms on primary and secondary efficacy measures across multiple settings including teachers, parents, clinicians and patients. In addition, Focalin, but not d,l methylphenidate showed significant improvements in Parent SNAP (P=.0085) and Math Test (P=.0169) scores at 6 hours post dosing compared with placebo.

The second study was conducted with 89 patients (6 – 17 years of age, all meeting criteria for ADHD) and consisted of three phases: a 6-week, open-label dose-titration (Part A), in which all children received Focalin in doses of 2.5 mg to 10 mg twice daily; a double-blind, placebo-controlled, 2-week withdrawal (Part B), in which half the children previously responding to Focalin received placebo, while half remained on Focalin; and a 44-week open-label extension (Part C) to assess long-term efficacy and safety.

Results from the study showed that patients treated with Focalin demonstrated a substantial reduction of ADHD symptoms on primary and secondary efficacy measures across multiple settings, followed by a significant worsening of symptoms upon withdrawal of the treatment as compared to placebo. The primary efficacy variable was the percentage of Treatment Failures as assessed by the CGI-I scale at the end of the withdrawal phase (Part B). Secondary efficacy variables were included the Teacher SNAP-ADHD, the SNAP-ADHD rated by parents (Parent SNAP-ADHD) at 3 PM and 6 PM, and a Math Test administered at the clinic/office and at home.

Data reported a duration of action of up to 6 hours for Focalin after the second dose, as supported by significant improvements in both the 6-hour post dose (6 PM) Parent SNAP-ADHD scores.

“The results presented today signify that dexamethylphenidate HCl, which contains only the active d-isomer, is a safe and effective treatment for ADHD at half the dose of Ritalin,” said Keith Conners, Ph.D., Professor Emeritus of Psychiatry and Behavioral Sciences, Duke University Medical Center and lead author of the study.

Both studies demonstrated that Focalin was safe and well tolerated with no serious adverse events reported. In addition, no patients needed to discontinue therapy due to adverse events or intolerability in the double blind phase in each of the studies.

Focalin received marketing clearance from the Food and Drug Administration (FDA) in November 2001 for the treatment of ADHD. Focalin is administered twice daily, at least four hours apart. Overall, there was a low incidence of adverse events with the majority being of mild severity. In double-blind, placebo-controlled trials there were no discontinuations due to adverse events. In long-term extension studies, only 7 %, or 50 of 684, of children and adults treated with Focalin experienced an adverse event that resulted in discontinuation. Like most drugs approved for the treatment of ADHD, and like Ritalin, Focalin is contraindicated in patients known to be hypersensitive to the drug or to Ritalin, in patients with glaucoma, and in patients with motor tics or with a family history or diagnosis of Tourette’s syndrome. It is also contraindicated during treatment with monoamine oxidase inhibitors and also within a minimum of 14 days following discontinuation of a monoamine oxidase inhibitor (hypertensive crises may result). In addition, like most drugs approved for the treatment of ADHD, Focalin is a schedule II drug.

ADHD is the most studied childhood psychiatric disorder and is supported by a substantial body of scientific evidence. Its symptoms have been described in the medical literature since 1902. Scientific research indicates that ADHD may be related to disturbances in certain neurotransmitters in the brain. Novartis supports only the proper diagnosis and treatment of ADHD.

The Novartis ADHD product portfolio includes Ritalin, Ritalin SR, and Focalin™, a refined formulation of Ritalin. Celgene Corporation (Nasdaq: CELG) of Warren, New Jersey granted Novartis Pharma AG an exclusive worldwide (excluding Canada) license covering its intellectual property rights associated with Focalin as well as Ritalin LA, a once-daily form of Ritalin that is currently under review at the FDA. Pursuant to an agreement between Novartis Pharma AG and Novartis Pharmaceuticals Corporation, Novartis Pharmaceuticals Corporation markets Focalin in the U.S.

In addition, Novartis Pharmaceuticals Corporation received an approvable letter from the FDA for Ritalin LA in October 2001. Ritalin LA was developed by Elan Corporation, plc’s drug delivery division and will be supplied to Novartis under an exclusive worldwide royalty and manufacturing agreement between the companies. Novartis Pharmaceuticals Corporation has commercialization rights for Ritalin LA in the U.S.

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commercialization of Ritalin LA could be affected by amongst other things, results from future clinical trials, 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 20F 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 anticipated, believed, estimated or expected.

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Celgene Corporation, headquartered in Warren, New Jersey, is an independent biopharmaceutical company engaged primarily in the discovery, development and commercialization of orally administered small molecule drugs for the treatment of cancer and inflammatory diseases through gene regulation. Please feel free to visit the Company's Web site at <http://www.celgene.com>.

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**- Investor Relations Release -**

## **Data demonstrating Zometa® as important advance in treating lung cancer-related bone complications presented at major oncology meeting**

*Onset of debilitating bone complications delayed for patients; Zometa is first bisphosphonate demonstrating efficacy across a broad range of solid tumors; Data presented at American Society of Clinical Oncology*

Basel, 22 May 2002 – Study results demonstrating that Zometa® (zoledronic acid) delays the initial onset of bone complications by more than two months in patients with non-small cell lung cancer and other solid tumors were presented at the 38<sup>th</sup> annual meeting of the American Society of Clinical Oncology (ASCO) in Orlando, Florida, USA. Bone complications – or skeletal related events (SREs) – represent a significant problem for cancer patients in advanced stages of disease; they include bone pain, pathologic fractures, need for radiation or surgery to bone, spinal cord compression and hypercalcaemia. For this patient population Zometa represents the first and only bisphosphonate proven effective in delaying the onset of SREs. Further, Zometa at 4 mg offers patients, nurses and clinicians a more convenient 15-minute infusion time.

Zometa received U.S. FDA approval on 22 February 2002 for the treatment of patients with multiple myeloma and patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. These solid tumors include prostate cancer, lung cancer, breast cancer and other solid tumor types studied in the clinical trials including renal, bladder and colorectal cancer. Zometa also received a positive opinion for this indication from the Committee for Proprietary Medicinal Products (CPMP) in the European Union (EU). The EU Commission usually grants approval of products four months after a CPMP positive opinion.

“Zometa offers a tremendous benefit for cancer patients,” said Lee S. Rosen, MD, Assistant Professor of Medicine, UCLA Jonsson Comprehensive Cancer Center and lead study investigator. “Since bone complications can be devastating, delaying the time when a patient experiences them – by even two months – is a significant advance.”

### **Study Design**

The study was designed to investigate the efficacy of Zometa in the prevention of SREs across a broad range of solid tumors, other than breast cancer or prostate cancer. A total of 773 patients were randomised to the study; 52% of the patients had lung cancer (primarily non-small cell lung cancer) and the remainder had other solid tumors (renal, colorectal and bladder). The final analysis

was based on evaluating Zometa 4 mg compared to placebo at an infusion rate of 15 minutes, given every three weeks for nine months. Measurements of SREs were the endpoints and included delay in onset of SREs, proportion of patients experiencing any SRE, and the reduction in risk of individual patients experiencing multiple SREs (thus contributing more significantly to morbidity).

### **Clinical Data**

In regards to multiple SREs, the data in patients with bone metastases from lung cancer and other solid tumors demonstrate that there was a 26% reduction in the rate at which patients experienced skeletal-related events, including multiple SREs ( $p=0.006$ ). Overall, findings demonstrate that patients receiving Zometa 4 mg at an infusion rate of 15 minutes experienced a significant delay in the onset of SREs (230 days for Zometa vs. 155 days for placebo [ $p=0.007$ ]). As the median survival of patients with advanced cancers may be approximately six months, a delay of more than two months provides a significant clinical benefit to physicians and patients. Also, after nine months, patients on Zometa experienced fewer SREs overall (38% of patients receiving Zometa vs. 47% receiving placebo [ $p=0.039$ ]).

### **About Zometa**

Zometa is a new generation intravenous (IV) bisphosphonate. The approval for Zometa was based on data from three large international clinical trials evaluating more than 3,000 patients with prostate cancer, lung cancer and other solid tumors (renal, bladder and colorectal), breast cancer and multiple myeloma. This is the largest set of clinical trials ever conducted to evaluate the efficacy and tolerability of a bisphosphonate in treating the complications associated with cancerous bone lesions.

Novartis initially received marketing clearance for Zometa in the treatment of hypercalcaemia of malignancy (HCM), also known as tumor-induced hypercalcaemia (TIH). It has obtained approval for HCM in countries throughout the world.

### **Contraindications and Adverse Events**

In clinical trials in patients with bone metastases, Zometa was generally well tolerated, with a safety profile similar to other bisphosphonates. The most commonly reported adverse events included flu-like syndrome (fever, arthralgias, myalgias, skeletal pain), fatigue, gastrointestinal reactions, anaemia, weakness, cough, dyspnoea and oedema. 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.

Zometa and other bisphosphonates 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 administered with other potentially nephrotoxic drugs. Due to the risk of clinically significant deterioration in renal function, which may progress to renal failure, single doses of Zometa should not exceed 4 mg and the duration of infusion should be no less than 15 minutes.

This release may contain forward-looking statements regarding the potential launch of Zometa in markets in which it currently is not approved, or regarding potential new indications for Zometa in existing markets. 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 are no

guarantees that Zometa or any potential new indications for Zometa will be commercialized in any market. Any such commercialization can be affected by, among other things, uncertainties relating to product development and clinical trials, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection and competition in general, as well as factors discussed in Novartis AG's Form 20-F filed 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 described herein as anticipated, believed, estimated or expected.

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## **Aromatase inhibitors in breast cancer assessed by ASCO Committee**

*Recent studies of aromatase inhibitors – a new generation of hormone therapy – prompt ASCO evaluation*

Basel, 21 May 2002 – Data from recent studies on the use of aromatase inhibitors in the treatment of postmenopausal women with breast cancer have generated significant interest from the medical oncology community and have prompted organizations to evaluate current treatment regimens. Following data presented in December at a major breast cancer conference, the American Society of Clinical Oncology (ASCO) convened a blue ribbon panel to review the use of aromatase inhibitors.

### **Adjuvant Setting**

Specific to the adjuvant breast cancer setting, the Committee reviewed the ATAC (Arimidex [anastrozole], Tamoxifen Alone or in Combination) data and declined to recommend the use of aromatase inhibitors at this time because of the lack of compelling and mature data. However, Novartis is encouraged that the Committee recognizes the importance of this category; and the Company is looking forward to the results of its ongoing Femara<sup>®</sup> (letrozole) adjuvant studies that should provide data sufficiently robust to enable the Committee to move forward with its recommendations. Currently, the largest set of adjuvant studies evaluating aromatase inhibitors – with more than 10,000 women participating – is evaluating the use of Femara. One study compares Femara to placebo in women who have remained disease free for five years of tamoxifen therapy; the other study compares Femara to tamoxifen in various treatment sequences over a period of five years. Results are expected in 2004.

### **Advanced Setting**

Specific to the advanced breast cancer setting, data on aromatase inhibitors have been presented both at this year's ASCO meeting and at the December San Antonio Breast Cancer Symposium (SABCS 2001). At ASCO, data comparing the two leading aromatase inhibitors Femara and Arimidex were presented and demonstrated that 50% more women responded to Femara than Arimidex in the second-line treatment setting. This means that Femara is more likely than is Arimidex to shrink breast cancer tumours even in patients who had progressed after prior anti-estrogen therapy. There were no statistically significant differences in time to disease progression (primary endpoint) or other endpoints.

Data presented at the SABCS 2001 meeting showed that in the first-line advanced breast cancer setting, Femara offered a statistically significant greater early survival advantage throughout the first two years of therapy compared to tamoxifen. In addition, approximately five years after initiation of the study (November, 1996), more women who had begun therapy with Femara were

still alive and free of tumor progression compared to those who started on tamoxifen. No differences were seen in duration of tumor response or overall survival.

Additional data from another study presented at the SABCs 2001 meeting demonstrated that Femara may be more effective than tamoxifen in treating postmenopausal women with ER and HER-2 positive breast cancer. The results are important because HER-2 positive breast cancers in postmenopausal women are especially difficult to treat.

Furthermore, results of the largest neo-adjuvant (pre-operative) trial evaluating endocrine agents demonstrated that Femara is a more effective therapy for postmenopausal women with hormone receptor positive tumours than tamoxifen. In 324 postmenopausal women with hormone-sensitive breast cancer, the number of clinical responses was significantly higher for Femara than for tamoxifen and significantly more women on Femara underwent breast-conserving surgery compared to tamoxifen.

### **About Femara**

Femara, an aromatase inhibitor, is an oral once-a-day 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 women with disease progression after prior antiestrogen therapy. Femara is currently available in more than 75 countries worldwide. Not all indications are available in each country.

Femara is contraindicated in patients with known hypersensitivity to Femara or any of its excipients. Femara is generally well tolerated and adverse reactions rates in the first-line study in which Femara was compared to tamoxifen were similar with those seen in second-line studies. The most commonly reported adverse events for Femara vs. tamoxifen were bone pain (20% vs. 18%), hot flushes (18% vs. 15%), back pain (17% vs. 17%), nausea (15% vs. 16%), dyspnea or labored breathing (14% vs. 15%), arthralgia (14% vs. 13%), fatigue (11% vs. 11%), coughing (11% vs. 10%), constipation (9% vs. 9%), chest pain (8% vs. 8%) and headache (8% vs. 7%). 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  $\leq 2\%$ .

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 “looking forward to,” “should provide data,” “may be more effective” or similar expressions, or by discussions of potential new treatments or indications for Femara. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that any new treatments or indications for Femara 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. Some of these are uncertainties relating to unexpected regulatory delays; unexpected clinical trial results with Femara; additional analysis of clinical data; new data; government regulation or competition in general; as well as factors discussed in the Company’s Form 20F 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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**- Investor Relations Release -**

## **New head-to-head data show Glivec® is nearly three times more effective as first-line treatment for chronic myeloid leukemia patients than interferon combination therapy**

*Data Comparing Efficacy of Glivec to Interferon/Chemotherapy Combination Presented at American Society of Clinical Oncology Meeting*

Basel, 21 May 2002 – Data from the first ever head-to-head study of the Novartis drug Glivec® (imatinib)\* demonstrate that Glivec is nearly three times more effective in achieving a cytogenetic response in the first-line treatment of newly diagnosed chronic myeloid leukemia (CML) patients than the combination of interferon-alpha and cytarabine arabinoside, a form of chemotherapy (IFN/Ara-C). In addition, Glivec significantly delayed the time to progression to the more advanced stages of CML compared to IFN/Ara-C. These new data were presented at the 2002 meeting of the American Society of Clinical Oncology (ASCO) in Orlando, Florida, USA. Glivec is a novel therapy that offers new hope to patients suffering from a disease that previously had very limited treatment options, and that has provided researchers with new insights into the biological mechanisms of cancer.

“The results clearly show that the earlier Glivec is used in treating CML, the better the response,” said lead investigator Brian Druker, MD, Professor of Medicine, Oregon Health Sciences University. “These data are so supportive of using Glivec in patients newly-diagnosed with CML that physicians need to strongly reconsider the current treatment options for CML patients.”

### **Clinical Data**

The International Randomised Study of Interferon vs. STI571 (IRIS) is an open-label Phase III trial that enrolled 1106 patients in 177 centres across 16 countries. There were two arms to the study: one arm received Glivec at 400 mg/day, the other arm received IFN at a target dose of 5 MIU/M<sup>2</sup>/day with Ara-C 20 mg/M<sup>2</sup>/day. The results presented were based on data collected up to 12 months after the last patient was randomised; the median follow-up was 14 months. The results showed that patients had achieved major and complete cytogenetic responses of 84% and 69% (Ph<35%), compared with patients in the IFN/Ara-C arm, who experienced major and complete cytogenetic responses of 30% and 11.5%. The complete haematologic response rates were 96% for the Glivec arm and 67% for the IFN/Ara-C arm.

Last January, based on a review of the six-month positive results for Glivec, an Independent Data Monitoring Board (IDMB) requested a change in the study protocol that enabled patients receiving

IFN/Ara-C to switch to Glivec if they had not achieved a major cytogenetic response after one year of the combination therapy.

At the time of this analysis, fewer than 1% of Glivec-treated patients crossed over to the IFN/Ara-C therapy, compared with 39% of IFN/Ara-C-treated patients who crossed over to Glivec due to insufficient efficacy or intolerance.

In the study, patients taking Glivec had an improved overall progression-free survival compared to those taking IFN/Ara-C. The estimated rate of progression-free survival at 12 months was 97.2% in the Glivec arm as compared with 80.3% in the patients randomised to IFN+Ara-C ( $P < 0.001$ ). Progression was defined as progression to accelerated phase or blast crisis, rapid increase in white blood cell count; loss of either complete haematologic response or major cytogenetic response; or death during treatment. In particular, the estimated probability of being free of progression to accelerated phase or blast crisis at 12 months was also significantly superior in the Glivec arm (98.5%) as compared to the control group (93.1%), regardless of crossover.

The safety profile with Glivec was similar to that of previous Phase II studies, and was superior to that of the IFN/Ara-C combination regimen. The most frequent adverse events with Glivec were mild to moderate superficial oedemas, muscle cramps, skin rash and nausea. The most frequent adverse events with IFN/Ara-C were nausea, fatigue, headache and diarrhoea. In the Glivec arm, only 2% and 0.7% of patients discontinued from the study or crossed over the control arm for safety reasons. In contrast, in the IFN/Ara-C arm, 6% and 23% of patients discontinued from the study or crossed over for safety reasons, respectively.

The Philadelphia chromosome (Ph) is the genetic abnormality that characterises most cases of CML; it is the result of the transfer of DNA between chromosomes 9 and 22. Cytogenetic response, regarded as the ultimate goal of CML treatment, is the disappearance or reduction of the number of cells containing the Philadelphia chromosome. In CML, therefore, a “complete cytogenetic response” indicates that there are no longer any Ph+ cells detected.

“Novartis is extremely pleased with the performance of Glivec in the IRIS study,” said David Parkinson, MD, Vice President, Clinical Research, Novartis Oncology. “Based upon these results, we will shortly submit to health authorities globally an application for use of Glivec as first line-treatment in CML.”

This study was one of several posters and presentations about Glivec and CML at the ASCO meeting. Topics covered by these studies include data in newly diagnosed Philadelphia-chromosome positive chronic phase CML patients; preliminary data from a dosing study and cost effectiveness data.

### **Contraindications and Adverse Events**

The majority of patients treated with Glivec experience 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, fluid retention, vomiting, diarrhoea, haemorrhage, muscle cramps, skin rash, fatigue, headache, dyspepsia and dyspnoea, as well as neutropenia and thrombocytopenia.

In most countries where Glivec is approved, it is indicated for the treatment of patients with Philadelphia chromosome-positive CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy. The effectiveness of Glivec is based on overall haematologic and cytogenetic response rates.

The foregoing release contains forward-looking statements that can be identified by discussions of potential new indications for Glivec. 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 aforementioned clinical trials will result in the commercialisation of any new indication for Glivec in any market. Any such commercialisation can be affected by, among other things, additional analysis of data; new 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.

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**- Investor Relations Release -****Glivec® maintains responses in patients with life-threatening gastrointestinal tumors after one year of treatment**

*New data on gastrointestinal stromal tumors (GISTs) presented at American Society of Clinical Oncology annual meeting*

Basel, 21 May 2002 – New data demonstrate that more than 60% of patients with an inoperable and life-threatening form of gastrointestinal cancer are continuing to respond to the Novartis drug Glivec® (imatinib)\* or maintain stable disease after one year of treatment. The data also show that more than 80% of patients overall experienced significant tumor shrinkage or stabilization of tumor growth. The data were presented at the 38<sup>th</sup> annual meeting of the American Society of Clinical Oncology (ASCO) in Orlando, Florida, USA.

“These results are quite impressive, especially when you contrast them with current treatment alternatives, which are very limited,” said Margaret von Mehren, MD, Associate Member of the Fox Chase Cancer Centre in Philadelphia, PA, USA, and a lead investigator on the study. “GISTs are an extremely difficult cancer to treat, so the fact that a convenient, oral, once daily therapy, like Glivec, can offer this type of response is very welcome news to patients and oncologists.”

GISTs are the most common malignant form of sarcoma that arises in the gastrointestinal tract. Historically, they have been very difficult to treat due to their high levels of resistance to treatment with traditional chemotherapy and radiation therapy. For patients with metastatic or unresectable (inoperable) disease, GISTs represented an incurable malignancy with a median survival of approximately 10 to 12 months. Until now, surgery has been the only effective treatment option for most GISTs, resulting essentially in palliation of the disease.

**Clinical Data**

In this randomised Phase II study, 147 patients with inoperable and/or metastatic GISTs were treated with either 400 or 600 mg of Glivec orally per day, and patients were monitored beginning one month after initial treatment. With a median follow-up of 15 months, the overall rate of partial response was >60% based on Southwest Oncology Group (SWOG) criteria. At the 15 months follow-up, approximately 70% of the patients remained free of treatment failure (had not progressed, discontinued treatment or died). More than 60% of patients had tumors that shrank by at least half; 20% had tumors that shrank by one-quarter to one-half, or stabilised. Only 12% of patients did not respond to treatment. Results did not differ substantially between the two dosages used in the study. To date, the median survival time has not been established.

This study was one of approximately 15 posters and presentations about Glivec and GIST at the ASCO meeting. Topics covered by these studies include the possibility of predicting potential response to Glivec based on the presence of specific genetic mutations, preliminary data from a large dosing study and an overview of effective screening techniques for measuring the response of GIST to treatment.

“Glivec continues to provide new insights into the molecular pathways driving certain cancers, such as GIST,” said David Parkinson, MD, Vice President, Clinical Research, Novartis Oncology. “The understanding it has afforded should allow us to identify approaches that may further enhance the patient benefit of Glivec in GIST, as well as potentially in other cancers and conditions.”

### **About Glivec**

Glivec, a signal transduction inhibitor, is one of the first cancer drugs to be developed using rational drug design, based on an understanding of how some cancer cells work. Glivec targets the activity of a type of enzymes called tyrosine kinases that play an important role within certain cancer cells. Studies have shown the effectiveness of Glivec in treating Philadelphia chromosome-positive chronic myeloid leukemia (CML) and in gastrointestinal stromal tumors GIST, driven by the cancer-causing proteins Bcr-Abl and Kit respectively. Glivec was approved by the US Food and Drug Administration (FDA) in February 2002 for the treatment of patients with Kit (CD 117) positive unresectable (inoperable) and/or metastatic malignant GISTs. Prior to the availability of Glivec, patients with GIST had no effective treatment options beyond surgery. In the EU, the Committee for Proprietary Medicinal Products (CPMP) issued a positive opinion for the GIST indication in February 2002, and approval is anticipated shortly.

### **Contraindications and Adverse Events**

Although the majority of patients had adverse events reported at least once during this trial, most events were mild to moderate in severity and included nausea, diarrhoea, periorbital oedema, muscle cramps, fatigue, headache and skin rash. About 23% of the patients had severe drug-related side effects that included low white blood cell counts, tumor haemorrhage and abdominal pain. In the GIST trial submitted for registration, drug was discontinued for adverse events in 13 patients (9% of patients). In this clinical trial, the most common adverse events were oedema, nausea, diarrhoea, abdominal pain, muscle cramps, fatigue and rash. In this trial, seven patients (5%) were reported to have gastrointestinal bleeds and/or intratumoral bleeds. Gastrointestinal tumor sites may have been the source of GI bleeds. 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.

In most countries where Glivec is approved, it is indicated for the treatment of patients with Philadelphia chromosome-positive CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy. The effectiveness of Glivec in CML is based on overall haematologic and cytogenetic response rates.

The foregoing release contains forward-looking statements that can be identified by terminology such as “is anticipated,” “should allow,” “potentially” and “further enhance,” or similar expressions. 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. In particular, management’s ability to ensure satisfaction of the FDA’s further requirements is not guaranteed and management’s expectations regarding further commercialization of Glivec could be affected by, among other things, additional analysis of data; new 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 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**

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**- Investor Relations Release -**

## Head-to-head worldwide study of the two leading aromatase inhibitors shows more women respond to Femara® than Arimidex® in advanced breast cancer

*Study in second-line breast cancer setting presented at American Society of Clinical Oncology meeting shows significantly greater objective response rate with Femara*

Basel, 21 May 2002 – In a head-to-head worldwide study of the two leading aromatase inhibitors, data demonstrate that 50% more women respond to Femara® (letrozole) than to Arimidex® (anastrozole) in advanced breast cancer. This means that more women treated with Femara had at least a 50% reduction in the size of their tumour. The data from this multicentre, international study of 713 postmenopausal women with ER+ and/or PgR+ or ER/PgR status unknown receiving second-line treatment for advanced disease were presented at the 38<sup>th</sup> annual meeting of the American Society of Clinical Oncology (ASCO).

“It is becoming increasingly evident that aromatase inhibitors are challenging and are likely to replace tamoxifen in the treatment of postmenopausal women with endocrine-dependent breast cancer. Studies like this are critical because they provide evidence to identify the aromatase inhibitor most likely to work best,” said Carsten Rose, M.D., Director, Department of Oncology, Universitetkliniken, Onkologiska Klinik, Lund, Sweden, and lead investigator in the study. “The data in this trial show that more women respond to Femara than to Arimidex, which is important information for physicians to consider when treating advanced breast cancer patients.”

### Study Design

The data are from a randomised, open-label study of 713 postmenopausal women who were either oestrogen and/or progesterone receptor positive (ER+ and/or PgR+) or ER/PgR status unknown. The study was conducted in 19 countries and compared the efficacy of Femara vs. Arimidex in women with metastatic breast cancer following failure of anti-oestrogen therapy (e.g., tamoxifen).

The primary and secondary endpoints of the study were time to disease progression, objective response rate, duration of objective response, overall clinical benefit, time to treatment failure, and survival. Patients were randomly allocated Femara 2.5 mg once-daily or Arimidex 1 mg once-daily.

The data show that 50% more women responded to Femara than to Arimidex (based on objective response rate) [Femara group 19% vs. Arimidex group 12%,  $P=0.013$ ]. Complete response rate

was 7% for Femara vs. 4% for Arimidex. No statistically significant differences were seen in time to disease progression (primary endpoint) or other endpoints.

The data also show that overall response rate in patients with soft tissue disease (i.e. soft tissue dominant, no bone or visceral involvement) was two-times higher for women receiving Femara compared to women receiving Arimidex (Femara 37% vs. Arimidex 19%). In viscera dominant disease (viscera +/- bone +/- soft tissue) overall response rate to Femara was also higher than to Arimidex (Femara 14% vs. Arimidex 10%). There were no statistically significant differences in any other endpoints.

Both Femara and Arimidex were generally well-tolerated and there were no statistically significant differences between treatment arms in reported frequencies of adverse events, including serious adverse events.

“The use of aromatase inhibitors is increasing and physicians need compelling data by which they can make the right choice for the treatment of breast cancer,” said David Parkinson, M.D., Vice President, Clinical Research, Novartis Oncology. “The consistent efficacy and overall performance of Femara in the various clinical settings is extremely encouraging, and Novartis is looking forward to the results of the ongoing Femara adjuvant studies.”

### **Data Demonstrates Consistent Performance of Femara**

#### *Femara Offers Enhanced Inhibition of Oestrogen and Total Body Aromatization Compared to Arimidex*

The head-to-head results represent the most recent data in a series of studies, which have compared the third generation aromatase inhibitors Femara and Arimidex. In pre-clinical studies, it had been shown that in human and animal cell systems, letrozole was consistently at least 10-fold more potent than anastrozole in inhibiting intracellular aromatase.

These pre-clinical studies were followed by a study comparing the ability of Femara and Arimidex to inhibit total body aromatisation and suppress plasma oestrogen levels in 12 postmenopausal women with metastatic breast cancer. Hormone sensitive breast cancers rely on oestrogen for growth. In this study, Femara was shown to be a more effective inhibitor of total body aromatisation and suppressor of plasma oestrogen levels than Arimidex (that is, two out of three oestrogen components were more significantly suppressed by Femara). The differences between the two drugs were statistically significant in favour of Femara; however, the clinical relevance of this finding is yet to be determined.

The data from the head-to-head study of Femara versus Arimidex presented at ASCO are the most recent in a series of pre-clinical and clinical studies that demonstrate that Femara is a more effective aromatase inhibitor than Arimidex at inhibiting aromatase and achieving a greater objective response rate.

#### *Femara versus tamoxifen --Survival Data in First-Line Setting*

These new data add to the growing body of medical and scientific knowledge regarding Femara. Reported at the San Antonio Breast Cancer Conference in December 2001 were the results of a study of 907 postmenopausal women comparing Femara to tamoxifen as first-line therapy in women with locally advanced or metastatic breast cancer. The results demonstrated that Femara had a statistically significant survival advantage compared to tamoxifen throughout the first two years of therapy. No other aromatase inhibitor has shown a survival advantage vs. tamoxifen to date. The data also demonstrated that, approximately five years after initiation of the study

(November, 1996), more women who had begun their therapy on Femara were still alive and free of tumour progression compared to those who started on tamoxifen (minimum treatment duration in patients still on first-line treatment at the cut-off date for analysis was three years). In addition, patients taking Femara had a 78% greater chance of responding to treatment than patients treated with tamoxifen, and the chance that their tumours would progress was 28% less with Femara than with tamoxifen.

#### *Femara Efficacy in the Neo-Adjuvant Setting*

The results of the largest neo-adjuvant (pre-operative) trial evaluating endocrine agents demonstrated that Femara is a more effective therapy for postmenopausal women with hormone receptor positive tumours than tamoxifen. In the Phase III, randomised, controlled trial, Femara or tamoxifen was administered for four months prior to surgery to reduce tumour size. In 324 postmenopausal women with hormone-sensitive (ER+ and/or PgR+), large localised or locally advanced breast cancers not amenable to breast-conserving surgery, the number of clinical responses was significantly higher for Femara than for tamoxifen (55% versus 36%,  $P<0.001$ ). Significantly more women on Femara underwent breast-conserving surgery compared to tamoxifen (45% versus 35%,  $P=0.022$ ).

In addition, after adjustment for tumour size, nodal involvement and age, the odds of undergoing breast-conserving surgery were increased by more than 65% for Femara compared with the odds for tamoxifen ( $P=0.0508$ ). Both Femara and tamoxifen were equally well-tolerated.

#### **About Femara**

Femara, an aromatase inhibitor, is an oral once-a-day 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 antioestrogen therapy, and as neo-adjuvant (pre-operative) therapy. Femara is currently available in more than 75 countries worldwide. Not all indications are available in each country.

In postmenopausal women, the primary source of oestrogen is from fat, liver, muscle, and breast tissue through a process that turns adrenal androgens into oestrogen, which stimulates the growth of certain hormone-dependent cancer cells. A breast tumour itself also may generate oestrogen. Femara works by binding to the enzyme aromatase and blocking it from converting adrenal androgens to oestrogen in these tissues.

Femara is contraindicated in patients with known hypersensitivity to Femara or any of its excipients. Femara is generally well tolerated and adverse reactions rates in the first-line study in which Femara was compared to tamoxifen were similar with those seen in second-line studies. The most commonly reported adverse events for Femara vs. tamoxifen were bone pain (20% vs. 18%), hot flushes (18% vs. 15%), back pain (17% vs. 17%), nausea (15% vs. 16%), dyspnoea or labored breathing (14% vs. 15%), arthralgia (14% vs. 13%), fatigue (11% vs. 11%), coughing (11% vs. 10%), constipation (9% vs. 9%), chest pain (8% vs. 8%) and headache (8% vs. 7%). 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 2%.

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 “becoming

increasingly,” “are likely to,” “most likely to” or similar expressions, or by discussions of strategy, plans or intentions. 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. 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. Some of these are uncertainties relating to unexpected regulatory delays; unexpected clinical trial results with Femara; additional analysis of clinical data; new data; government regulation or competition in general; as well as factors discussed in the Company’s Form 20F 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.

### **About Novartis**

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# # #

## **Novartis launches TARGET, largest world-wide arthritis clinical trial**

Basel, 21 May 2002 – Novartis' investigational drug Prexige™ (lumiracoxib/COX189) is the focus of the world's largest arthritis clinical trial, TARGET (Therapeutic Arthritis Research & Gastrointestinal Event Trial) to date. Prexige is an innovative COX-2 inhibitor currently being studied for the treatment of symptoms of arthritis and pain. Sponsored by Novartis, TARGET will evaluate the safety, tolerability and efficacy of Prexige compared with the non-steroidal anti-inflammatory drugs (NSAIDs) ibuprofen and naproxen over 12 months.

TARGET will examine, as a primary objective, the gastrointestinal safety of Prexige compared with the NSAIDs, as well as cardiovascular safety as a pre-specified secondary endpoint. "TARGET is the first COX-2 inhibitor gastrointestinal safety trial where cardiovascular safety will be assessed as one of the pre-specified endpoints," said Thomas Schnitzer, MD, Director of the Office of Clinical Research and Training at Northwestern University and a lead investigator for the study. The trial will evaluate the incidence of complicated gastrointestinal ulcers and cardiovascular events in patients taking and not taking low-dose aspirin for cardioprotection in combination with arthritis medication.

"With the increasing use of COX-2 inhibitors, it is essential to provide data showing that Prexige is a safe therapeutic option for the treatment of osteoarthritis," said Joerg Reinhardt, Head of Development, Novartis Pharma AG. "The launch of TARGET confirms Novartis' strong commitment to the development of new treatment alternatives for the millions who suffer with arthritis and pain and still have unmet needs."

This study will evaluate more than 18 000 patients worldwide. Participants will be men and women aged 50 years or older who are symptomatic sufferers of osteoarthritis. TARGET is an international, multicenter, stratified, randomized, double-blind, double-dummy active-controlled, parallel-group trial. The TARGET protocol has been reviewed by the US Food and Drug Administration.

Osteoarthritis, the most common form of arthritis, is characterized by the breakdown of cartilage in joints, causing affected bones to rub against each other. This often leads to inflammation, pain and loss of function. Globally, osteoarthritis accounts for half of all chronic conditions in people aged 65 and above. It is estimated that more than 25 million Europeans and more than 20 million people in the US are affected by osteoarthritis, most of them women.

The economic impact of musculoskeletal diseases, including osteoarthritis, is substantial, and costs the US nearly USD 65 billion per year in direct expenses, lost wages and production. Risk factors associated with osteoarthritis include accidents, age, joint injuries due to sports, obesity, or work-related activity.

The foregoing press release contains forward-looking statements that can be identified by terminology such as “will” or similar expressions or by discussions regarding the potential outcome of the COX189-TARGET clinical trial. 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 are no guarantees that the aforementioned clinical trials will have any particular result, or that the COX189-TARGET clinical trial will result in the commercialization of any product in any market. Any such commercialization can be affected by, amongst other things, uncertainties relating to product development, including the actual outcome of the COX189-TARGET clinical trial itself, 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 20F 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.

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- Investor Relations Release -

## Gastrointestinal safety studies highlight benefits of investigational COX-2 inhibitor

*First data on Prexige™ demonstrate strong gastrointestinal safety profile compared to Celecoxib, Ibuprofen and Naproxen*

Basel, 21 May 2002 – Clinical results from three studies to be presented at Digestive Disease Week showed that gastrointestinal injuries in patients taking Prexige™ (lumiracoxib/COX189), an investigational COX-2 inhibitor, were comparable to celecoxib and significantly lower than commonly-used nonsteroidal anti-inflammatory drugs (NSAIDs). These data support the strong gastrointestinal safety of Prexige, an innovative COX-2 inhibitor being developed by Novartis for the treatment of symptoms of arthritis and pain.

Traditional NSAIDs, such as ibuprofen and naproxen, have been proven effective in relieving arthritis and pain but are known to cause ulcers in the lower stomach, or gastroduodenum in some patients.

Findings from one 13-week study of 1 042 osteoarthritis patients showed that use of therapeutic doses of Prexige (200 mg and 400 mg once a day) resulted in a significantly ( $p < 0.01$ ) lower gastroduodenal ulcer rate than ibuprofen (three times a day at 800 mg) at an anti-inflammatory dose and a rate similar to celecoxib (once a day at 200 mg).

A second 7-day study evaluated the gastroduodenal effects of Prexige (200 mg twice a day) compared to naproxen (500 mg twice a day) and placebo, showing that in 60 healthy male subjects Prexige was well tolerated and effects on the gastroduodenum were similar to that of placebo. No erosions were detected in participants in either the Prexige group or the placebo group. Duodenal erosions were detected in sixty-five percent of patients taking naproxen.

Results of a third 8-day study in 25 healthy volunteers demonstrated that Prexige once a day at 800 mg (twice the anticipated maximum dose for Prexige) is a COX-2 inhibitor that causes little or no injury to the lining of the gastrointestinal tract when compared to naproxen (500 mg twice a day) which caused gastric erosions in seventy-five percent of patients.

## **About Prexige**

Prexige is an innovative COX-2 inhibitor being developed for the treatment of symptoms of arthritis and pain.

Additional safety studies are currently underway to evaluate the safety and efficacy of Prexige, including TARGET (Therapeutic Arthritis Research & Gastrointestinal Event Trial). TARGET will examine, as a primary objective, the gastrointestinal safety of Prexige compared with the NSAIDs ibuprofen and naproxen, as well as cardiovascular safety as a pre-specified secondary endpoint. The study will evaluate more than 18 000 patients world-wide making it the largest arthritis clinical study undertaken to date. TARGET will compare the safety and efficacy of Prexige to commonly used NSAIDs, ibuprofen and naproxen, over 12 months.

The foregoing press release contains forward-looking statements that can be identified by terminology such as “will examine”, “will evaluate”, “will compare” or similar expressions, or by discussions of potential new products. 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 are no guarantees that the aforementioned clinical trials will result in the commercialisation of any product in any market. Any such commercialisation can be affected by, amongst other things, uncertainties relating to product development, including the results of clinical trials, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection and competition in general, as well as factors discussed in the Company’s Form 20F filed with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialise, 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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**- Investor Relations Release -****Elidel® cream offers new non-steroid approach to treating atopic eczema in babies and sensitive skin areas**

*Elidel is also proven effective in treating atopic eczema in adults*

Basel, 16 May 2002 – Atopic eczema affecting babies and sensitive skin areas such as the face has been successfully treated with the new non-steroid cream Elidel® (pimecrolimus), according to data presented at the Society for Investigative Dermatology congress in Los Angeles, USA, today. Studies<sup>1</sup> in patients aged 3 months to 18 years showed that on the face and neck, where treatment with topical corticosteroids is often restricted because of potential side effects such as skin thinning, Elidel reduced the severity of the eczema by an average of 64% over 6 weeks. This compared with only a 12% reduction on average for patients treated with a vehicle cream. In a long-term management study<sup>2</sup>, 64% of 204 infants aged 3 to 23 months with the itching, red skin condition were managed without any topical corticosteroids over 12 months by using moisturisers for dry skin and starting Elidel treatment at the first signs or symptoms. This compared with only 35% of infants in the control group.

"Since their introduction 50 years ago, topical corticosteroids have been the mainstay of treatment for atopic eczema or atopic dermatitis, as it is otherwise called," said Professor Alexander Kapp, Chairman and Director of the Department of Dermatology and Allergology at the Hannover Medical University, Germany. "However, for infants and sensitive skin areas such as the face, topical steroids are either not recommended or only the mildest should be used because of concerns over side effects. As eczema typically begins in childhood and commonly occurs on the face, I am sure physicians will welcome a therapy that can be safely used on all skin surfaces."

A further study<sup>3</sup> in adults with moderate to severe eczema showed that itching – considered the most bothersome symptom of eczema – was significantly relieved after 3 days of treatment with Elidel compared with those receiving a vehicle cream.

A prescription-only medicine, Elidel was first launched in the USA in February this year for the treatment of mild to moderate atopic eczema in patients aged two years and older. The manufacturers of Elidel – Novartis - plan to hold further discussions with the Food and Drug Administration in the USA this year regarding the use of Elidel in infants under 2 years of age.

In March, Elidel gained its first European approval, in Denmark, where it is indicated for the short term treatment of the signs and symptoms of atopic eczema and intermittent long-term treatment to prevent progression to flares in patients 3 months of age and above. Elidel is expected to be available in Denmark around mid-year. Novartis is seeking approvals in other countries in Europe and elsewhere worldwide.

More than 4 000 patients have now been treated with Elidel in clinical trials. The incidence of adverse events has been low, the most common reported side effect being a mild-to-moderate temporary feeling of warmth or burning on the skin where the cream was applied. This occurred in 8% of children aged two to 17 years and in 10% of adults.

### ***About Elidel***

Discovered by the Novartis Research Institute in Vienna, Austria, Elidel contains the active ingredient pimecrolimus, which is derived from ascomycin, a natural substance produced by the fungus *Streptomyces hygroscopicus* var. *ascomyceticus*. Pimecrolimus selectively blocks the production and release of cytokines from T-cells in the skin. It is these cytokines which trigger processes leading to the inflammation, redness and itching associated with eczema.

This press release contains forward looking statements which can be identified by the use of forward-looking terminology such as "plan", "is expected," or similar expressions, or by discussions regarding potential new indications for Elidel, or the potential approval of Elidel in additional markets. 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 are no guarantees that the aforementioned data, clinical trials and regulatory approvals will result in new indications for Elidel in any market, or that Elidel cream will be commercialized in any additional market. Any such results can 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 Novartis AG's Form 20-F filed with the US Securities and Exchange Commission. Any of these and other factors can cause the actual results to differ materially from the expected or predicted results.

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References: (All of the following abstracts are accepted for presentation at the Society for Investigative Dermatology, Los Angeles, USA, 15 – 17 May 2002)

1. Pariser D et al. Efficacy and local tolerability of pimecrolimus cream 1% in the treatment of atopic dermatitis in the face/neck region of pediatric subjects
2. Kapp A et al. Treatment with pimecrolimus cream 1% is corticosteroid sparing in infants with atopic dermatitis
3. Meurer M et al. Pimecrolimus cream 1% provides significant and rapid relief of pruritus and improves disease control and quality of life in atopic dermatitis in adults

- Investor Relations Release -

## **LOGIC, new 9,000-patient study, demonstrates patients switched to Lotrel® from Norvasc<sup>®</sup> experience better blood pressure control with less edema**

*Two other studies, ALERT and SHIELD, evaluate Lotrel efficacy in diabetic hypertension, arterial compliance, left ventricular hypertrophy*

Basel, 14 May 2002 – Novartis today announced that three new studies evaluating the efficacy and safety of Lotrel<sup>®</sup> (amlodipine/benazepril HCl) in a broad range of hypertensive patients will be presented this week during the 17<sup>th</sup> annual meeting of the American Society of Hypertension (ASH). Lotrel is a single-capsule combination of two antihypertensive medications: amlodipine, the calcium channel blocker (CCB) found in Norvasc<sup>®</sup> and the angiotensin converting enzyme (ACE) inhibitor Lotensin<sup>®</sup> (benazepril).

The studies – LOtrel: Gauging Improved Control (LOGIC), Study of HypertensIon and the Efficacy of Lotrel in Hypertensive Diabetics (SHIELD) and A Lotrel Evaluation of Hypertensive Patients with ARterial Stiffness and Left Ventricular HyperTrophy (ALERT) –demonstrate Lotrel's effects in treating a broad range of hypertensive patients, including those with diabetes or arterial stiffness and left ventricular hypertrophy. The LOGIC study also demonstrated that Lotrel alleviated a common side effect of Norvasc monotherapy known as pedal edema (swelling of the feet and legs). More than 9,500 patients were involved in these studies.

Lotrel is available in the US only, where it is one of the fastest growing branded high blood pressure therapies on the market. Lotrel is indicated for hypertension, but not for initial therapy, and was approved for marketing in the U.S. in 1995.

“Physicians are embracing the value of combination therapy with an ACE inhibitor and calcium channel blocker for tough-to-treat hypertensive patients because the combination provides superior blood pressure control with excellent tolerability. The new data will make physicians more confident in prescribing Lotrel for a wide array of hypertensive patients,” said William Daley, MD, MPH, Executive Director, Cardiovascular & Metabolism, US Medical Affairs, Novartis Pharmaceuticals Corporation. “Novartis will continue to research ACE/CCB combination therapy. We are currently conducting studies to evaluate the efficacy of Lotrel in African-Americans, patients with diabetes and hypertension and in those with isolated systolic hypertension.”

## **Lotrel Studies Presented at American Society of Hypertension Meeting**

### **LOGIC (LOtrel: Gauging Improved Control)**

***Patients switched from amlodipine to Lotrel in a practice-based setting experienced better blood pressure control with less pedal edema.***

LOGIC is a four-week, multi-center, practice-based, open-label study that evaluated the antihypertensive efficacy and tolerability of once-daily Lotrel versus amlodipine in 9,208 patients with mild-to-moderate hypertension. The patients were divided into two groups: patients who did not achieve blood pressure control with amlodipine (Group I) and patients whose blood pressure was controlled, but who experienced unacceptable edema with amlodipine (Group II).

The 7,468 patients in Group I whose blood pressures were not adequately controlled with either 5 mg or 10 mg of amlodipine (mean sitting diastolic blood pressures (MSDBP) of  $\geq 90$  mmHg but  $\leq 110$  mmHg) were switched to either 5 mg/10 mg or 5 mg/20 mg of Lotrel. The decision to switch patients to Lotrel 5 mg/10 mg or 5 mg/20 mg was based on the treating physicians' clinical judgment. An additional 1,739 patients taking amlodipine (Group II) who had controlled blood pressure ( $\leq 90$  mmHg) but who experienced unacceptable amlodipine-induced pedal edema were also switched to Lotrel.

After four weeks of treatment, Group I patients experienced significant reductions in MSDBP of 11.5 mmHg and in mean sitting systolic pressure (MSSBP) of 15.6 mmHg when they were switched from amlodipine to Lotrel ( $p < 0.001$ ). Amlodipine-induced pedal edema improved in 85% of patients in Group II when they were switched to Lotrel ( $p < 0.001$ ).

**Lotrel was well tolerated. The most commonly occurring side effects were cough (3.66%), dizziness (1.50%), edema (1.46%) and headache (1.23%).**

The full results of this study will be published in the June edition of the *American Journal of Hypertension*.

LOGIC presented by: Franz Messerli, MD, Alton Ochsner Medical Foundation, Tulane University, New Orleans, LA, Friday, May 17, 2002.

**ALERT (A Lotrel Evaluation of Hypertensive Patients with ARterial Stiffness and Left Ventricular HyperTrophy)**

***Low doses of Lotrel showed greater improvements in arterial compliance and greater regression of left ventricular mass than higher doses of amlodipine and benazepril monotherapy.***

ALERT is a 26-week, prospective, open-label, blinded endpoint, parallel group study involving 106 patients with mild to moderate hypertension (DBP of 95-114 mmHg). The study compared the effects of low-dose Lotrel (5 mg/20 mg) versus high-dose amlodipine (10 mg) and benazepril (40 mg) monotherapy on arterial stiffness and left ventricular mass.

Patients taking Lotrel experienced significantly greater improvements in arterial stiffness versus amlodipine and benazepril-treated patients ( $0.71 \pm 0.51\%$  mL/mmHg vs.  $0.28 \pm 0.69\%$  mL/mmHg and  $0.39 \pm 0.62\%$  mL/mmHg, respectively  $p=0.008$ ,  $p=0.03$ ). Moreover, patients taking Lotrel had significantly greater regressions in left ventricular mass index as measured by echocardiography than amlodipine-treated patients ( $-29.9 \pm 25.5$  g/m<sup>2</sup> vs.  $-14.1 \pm 22.1$  g/m<sup>2</sup> respectively;  $p=0.01$ ).

Left ventricular mass index reductions were numerically greater in Lotrel than in benazepril-treated patients ( $-19.3 \pm 20.3 \text{ g/m}^2$ ).

These improvements were seen despite the fact that patients on all three medications achieved similar reductions in systolic and diastolic blood pressure.

Lotrel was well tolerated. The most commonly occurring side effects were GI complaints (11.4%), peripheral edema (8.6%), cough (5.7%) and headache (2.8%). Lotrel is not indicated for the treatment of arterial stiffness or left ventricular hypertrophy.

ALERT presented by: Joel Neutel, MD, Orange County Heart Institute and Research Center, Orange County, CA, Saturday, May 18, 2002.

**SHIELD** (Study of Hypertension and the Efficacy of Lotrel in Hypertensive Diabetics)

***Patients with diabetes and hypertension taking Lotrel reached their target blood pressure goal (<135/80 mmHg) 22% faster than those on Vasotec® (enalapril) monotherapy.***

SHIELD is a 12-week, randomized, multi-center, double-blind, parallel group study that evaluated the safety and efficacy of Lotrel versus enalapril monotherapy in 214 patients with hypertension and type 2 diabetes. ACE inhibitor treatment with an agent like enalapril is the standard of care for patients with diabetes. This study was conducted to determine if Lotrel would provide superior blood pressure control while providing the recommended ACE inhibitor therapy.

Patients in the study with average diastolic blood pressures (DBP) between 90 and 109 mmHg were randomized to either Lotrel 5 mg/10 mg or enalapril 10 mg. If patients did not reach the target blood pressure of <130/85 mmHg after four weeks, they were titrated to either Lotrel 5 mg/20 mg or enalapril 20 mg. Patients not reaching goal after eight weeks received 12.5 mg of hydrochlorothiazide on top of their treatment regimen.

At the conclusion of the study, patients taking Lotrel reached their target blood pressure approximately 22% faster than those taking enalapril (5.3 weeks versus 6.4 weeks respectively,  $p=0.0001$ ). Moreover, Lotrel-treated patients experienced significantly greater reductions in systolic blood pressure (SBP) and DBP than those taking enalapril ( $-20.5/-13.9 \text{ mmHg}$  versus  $-14.5/-9.6 \text{ mmHg}$  respectively,  $p = 0.002$ ,  $p = 0.001$ ). A statistically significant difference in reduction in triglyceride levels favoring the Lotrel regimen was also observed ( $p=0.039$ ). Lotrel-treated patients experienced a mean decrease in triglycerides of 21.7 mg/dL, compared with a mean increase of 14.8 mg/dL among enalapril-treated patients. The changes from baseline in all other lipid levels were comparable across the treatment groups. There was no negative impact on glycemic control with either Lotrel or enalapril.

Additionally, a sub-study of 20 SHIELD patients found that Lotrel combination therapy offered a statistically significant improvement in vascular compliance (a measure of the arteries' ability to expand and contract with changes in pressure), over enalapril monotherapy ( $p<0.05$ ). This improvement occurred despite the absence of a significant difference in blood pressure between the groups.

Both Lotrel and enalapril were well tolerated. There were a few reported incidents of bronchitis, dyspnea, congestive heart failure, angina and foot ulcers, but none of these was considered to be the result of the study medication.

SHIELD presented by: George Bakris, MD, Rush University Hypertension Center, Rush Presbyterian/St. Luke's Medical Center, Chicago, IL, Thursday, May 16, 2002.

SHIELD sub-study presented by: Nathaniel Winer, MD, SUNY Downstate Medical Center, Brooklyn, NY, Saturday, May 18, 2002.

### Ongoing Lotrel Studies

Novartis is conducting clinical studies to further explore the clinical potential of Lotrel. The **LEAAD** (Lotrel and Enalapril in African-Americans with Hypertension and Diabetes) trial is examining the efficacy of Lotrel versus the ACE inhibitor enalapril on blood pressure reduction and kidney function in African-Americans with diabetes. Another trial, called SELECT (Systolic Evaluation of Lotrel Efficacy and Comparative Therapies), is comparing the effects of Lotrel to amlodipine and benazepril monotherapy on systolic blood pressure, a critical indicator of cardiovascular risk.

Due to its ACE inhibitor component, Lotrel should be discontinued as soon as pregnancy is detected because of concerns over its effect on the unborn child. Also, angioedema, a potentially dangerous swelling of the mouth and throat, has been reported in patients receiving Lotrel. In clinical trials, the most common side effects were cough and headache. For full prescribing information, please consult [www.pharma.us.novartis.com](http://www.pharma.us.novartis.com).

This release contains certain "forward-looking statements," relating to the Company's business, which can be identified by the use of forward-looking terminology such as "will be," "will make," "will continue," or similar expressions, or by discussions regarding potential new indications for existing products, or the potential outcome of clinical trials. Such forward looking statements reflect the current views of the Company with respect to future events and are subject to certain risks, uncertainties and assumptions. There are no guarantees that any of the potential new indications will be commercialized in any market, that any additional sales of existing products will occur as a result of any clinical trial results, or that any of the aforementioned clinical trials will have any particular result. Any commercialization of any new indication and any additional sales of existing products can be affected by, among other things, uncertainties relating to product development and clinical trials, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection and competition in general, as well as factors discussed in Novartis AG's Form 20-F filed 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 described herein as anticipated, believed, estimated or expected.

Vasotec<sup>®</sup> is a registered trademark of Merck & Co. Norvasc<sup>®</sup> is a registered trademark of Pfizer Inc. The amlodipine active ingredient found in Lotrel is supplied to Novartis Pharmaceuticals Corporation by Pfizer Inc.

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## **Starlix® enhances glucose control in people with impaired glucose tolerance**

*New supporting study underlines the rationale for using Starlix in NAVIGATOR, the largest diabetes prevention trial to date*

Basel, 8 May 2002 – New research presented at the World Congress of Cardiology describes results from the first study to show that Starlix® (nateglinide) enhances early insulin secretion and controls post-prandial blood glucose in people with impaired glucose tolerance (IGT). This suggests that Starlix may be a useful agent for controlling post-prandial hyperglycaemia in this pre-diabetic patient group.

It is estimated that as many as 150 million people may have IGT. People with IGT show abnormalities in both insulin secretion and response to insulin (insulin sensitivity), and are at high risk of progressing to type 2 diabetes, with a 40-50% chance of developing the disease within ten years. IGT is an intermediate state between normal blood glucose control and type 2 diabetes and is characterised by an excessive rise in blood glucose following an oral glucose tolerance test. IGT is also a major risk factor for cardiovascular disease.

Dr Leif Groop of the University of Lund in Sweden, one of the study's lead investigators, commented, "Loss of early insulin secretion is one of the first pathophysiological signs of progression to type 2 diabetes. By restoring the normal, physiological pattern of insulin secretion, nateglinide essentially normalised glucose tolerance in these patients".

The study, which took place at centres in six European countries, involved 288 people with IGT (plasma glucose two hours after consuming 75 g glucose 7.8mmol/l but <11.1 mmol/l and fasting plasma glucose < 7 mmol/l). Subjects were randomly allocated to take 30 mg, 60 mg, or 120 mg of Starlix (nateglinide), or a placebo, before main meals for eight weeks. At the start and end of the study, blood glucose and insulin levels were measured at intervals for three hours after a standard meal.

The results showed that Starlix (nateglinide) enhanced early insulin secretion and reduced both the size of the blood glucose peak and the total increase in blood glucose over the three hours following the meal. Fasting glucose levels were not affected.

Confirmed hypoglycaemia (plasma glucose levels 3.7 mmol/l) occurred in five (6.6%) subjects receiving 60 mg nateglinide and 23 (26.7%) of subjects taking the 120 mg dose. All symptoms were mild and quickly resolved.

“60 mg nateglinide was extremely well tolerated in these IGT patients,” remarks Dr Groop. “The fast-on, fast-off, and glucose-dependent action of nateglinide means that the risk of hypoglycaemia is minimal, even in these patients who do not yet have diabetes.”

People with IGT are the ideal population to be involved in diabetes prevention trials. The mode of action of nateglinide and its excellent safety profile have led to its inclusion in the NAVIGATOR trial launched in November 2001. NAVIGATOR will be the largest diabetes prevention trial to date, involving 7,500 subjects in 40 countries, and will determine whether long-term administration of Starlix (nateglinide) (60 mg before main meals) or the angiotensin II receptor blocker Diovan<sup>®</sup> (valsartan) (160 mg a day) prevents or delays type 2 diabetes and cardiovascular disease in people who have IGT and are at high cardiovascular risk.

Dr Richard Pratley, Medical Director for the NAVIGATOR trial at Novartis Pharma Corp, East Hanover, USA, explained: “With type 2 diabetes increasing rapidly all over the world, it is now vital that we explore prevention strategies. This study demonstrates the clear rationale for including Starlix in the NAVIGATOR trial. NAVIGATOR will show us whether restoring early insulin secretion with Starlix can slow decline to type 2 diabetes and prevent cardiovascular disease in this high-risk group.”

### **Forward-looking statement**

The forgoing press release contains forward-looking statements which can be identified by terminology such as “may be useful”, “will be”, “will show”, or similar expressions, or by discussions regarding the potential outcome of the NAVIGATOR clinical trial, or regarding potential new indications for existing products. 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 are no guarantees that the aforementioned clinical trials will result in the commercialisation of any product in any market. Any such commercialisation can be affected by, amongst other things, uncertainties relating to product development, including the actual outcome of the NAVIGATOR clinical trial itself, 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 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.

### **About Novartis**

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## **Glivec® (imatinib)\* may be effective in rare blood disease according to new report in *The Lancet***

*Case report provides additional clinical insight into Hypereosinophilic Syndrome (HES)*

Basel, Switzerland, 3 May 2002 – The Novartis drug Glivec® (imatinib)\* may have efficacy in certain patients with hypereosinophilic syndrome (HES), according to a case report from researchers at the Mayo Clinic and Foundation in Rochester, Minnesota; and the University of Utah in Salt Lake City, Utah, USA. The report is published in the 4 May 2002 issue of *The Lancet*<sup>1</sup>.

HES is a very rare group of myeloproliferative disorders of unknown origin, characterised by the persistent overproduction of eosinophils (a type of white blood cell that is involved in a variety of functions, including defense against parasitic infection and allergic responses). HES is most commonly diagnosed in male patients aged 20-50 years. The symptoms can appear suddenly and dramatically, and can involve virtually any organ system, but more often they are insidious. Typically, patients with HES have no detectable chromosomal abnormality. Notoriously difficult to manage, HES is often treated with the same therapies used to treat chronic myeloid leukemia (CML). This led the researchers to hypothesise that HES patients might respond to Glivec, a novel agent that has demonstrated unprecedented cytogenetic response rates in CML.

"Glivec is a targeted signal transduction inhibitor. Although the mechanism by which the drug exerts its effects on HES is unclear, Novartis is encouraged by the preliminary data which suggest that Glivec may play a role in treating these patients," said David Parkinson, M.D., Vice President, Novartis Oncology. "Novartis will monitor and investigate potential activity in this area."

### **Case Report**

In the case report, Gleich and colleagues describe five patients, four male and one female, with clinical manifestations of HES. Glivec was initially administered to the patients at daily doses of 100 mg--considerably lower than those dosages required for the treatment of CML and GIST. These findings, however, do not impact dosing for CML and GIST patients (400 mg to 600 mg/day). By day seven of treatment with Glivec, four of the five patients had responded.

The fifth patient did not respond to Glivec. However, unlike the other patients, she had abnormally elevated levels of serum interleukin-5 (IL-5), a cytokine, or protein, involved in mediating certain immune interactions. The authors suggest that this finding may help discriminate among patients with HES. The authors also observed a sixth patient with elevated IL-5 who did not respond to treatment with Glivec, but they did not report on this patient in detail.

Based on their preliminary findings in this small group of patients, the authors conclude that Glivec may be effective in male patients with HES and normal concentrations of IL-5. They also suggest that a tyrosine kinase, similar to those which Glivec has shown to inhibit, but more sensitive to low doses of the drug, may be the target that accounts for the observed activity of Glivec in these patients.

### **About Glivec**

Glivec is a signal transduction inhibitor which inhibits the activity of certain enzymes, called tyrosine kinases, which play an important role within certain cancer cells. In CML, for example, it inhibits BCR-ABL, a by-product of the specific chromosomal abnormality, the Philadelphia chromosome, which characterises the disease in most patients. In gastrointestinal stromal tumours (GISTs), Glivec has been shown to inhibit the c-kit tyrosine kinase, and *In vitro*, Glivec has also been shown to inhibit PDGF-R (platelet derived growth factor receptors). Novartis is investigating the efficacy of Glivec, alone and in combination with other therapies, in a range of diseases in which these tyrosine kinases play a role.

In most countries where it is approved, Glivec is indicated for the treatment of patients with Philadelphia chromosome-positive CML in the blast crisis, accelerated phase or in chronic phase after failure of interferon-alpha therapy. The effectiveness of Glivec is based on overall haematological and cytogenetic response rates.

Glivec has been approved for the CML indication in the United States, the European Union and more than 60 countries. In the U.S. and in Switzerland, it is approved for the treatment of patients with Kit (CD 117) positive unresectable (inoperable) and/or metastatic malignant gastrointestinal stromal tumours (GISTs). The Committee for Proprietary Medicinal Products (CPMP) in the EU issued a positive opinion for the GIST indication in February 2002, and approval is expected shortly.

### **Contraindications and Adverse Events**

The majority of patients treated with Glivec experience adverse events at some time. Most events are of mild to moderate grade, but in clinical trials for CML the drug was discontinued for adverse events in 2% of patients in chronic phase, 3% in accelerated phase and 5% in blast crisis. Women of childbearing potential should be advised to avoid becoming pregnant while taking Glivec. The most common side effects included nausea, fluid retention, vomiting, diarrhoea, haemorrhage, muscle cramps, skin rash, fatigue, headache, dyspepsia and dyspnoea, as well as neutropenia and thrombocytopenia. Serious and severe side effects, such as hepatotoxicity (1% to 4%), fluid retention syndrome (3% to 12%), neutropenia (8% to 48%) and thrombocytopenia (less than 1% to 33%) have also been reported in some patients. There are no long-term safety data on Glivec treatment available up to now.

The foregoing release contains forward-looking statements that can be identified by terminology such as "encouraged," "may be the target," "may play a role" and "may be effective," or similar expressions. 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. In particular, management's ability to ensure satisfaction of the Health Authorities' further requirements is not guaranteed and management's expectations regarding further commercialisation of Glivec could be affected by, among other things, additional analysis of data; new 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 materialise, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected.

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## **Interim data from MO2ART study using Neoral® C<sub>2</sub> monitoring demonstrates impressive, low rates of kidney rejection**

Basel, 2 May 2002 – Neoral® C<sub>2</sub> monitoring results in acute organ rejection rates of only 10% in kidney transplant patients, according to interim data of the MO2ART study. The findings were presented at the third joint annual meeting of the American Society of Transplant Surgeons and the American Society of Transplantation as part of the American Transplant Congress (ATC) held in Washington, DC.

“This is the lowest rate of acute rejection ever demonstrated with cyclosporin-based triple therapy in a multicentre international trial” said Dr. Paul Keown, University of British Columbia. “These data underscore my belief that individualizing patient immunosuppression will be the future in organ transplantation management.”

MO2ART (Monitoring Of 2-hour Neoral Absorption in Renal Transplantation), sponsored by Novartis, is the first prospective, randomized, international study designed to evaluate the clinical benefit of Neoral C<sub>2</sub> patient management in kidney transplantation. The MO2ART study will also help to determine the optimum Neoral C<sub>2</sub> levels for maintenance therapy. This open label 12-month trial is being conducted in 30 centers in 10 countries. All transplant patients received triple immunosuppression - Neoral (cyclosporin for microemulsion), steroids, mycophenolate mofetil (MMF) / azathioprine. Interim analyses were performed when 117 of the 290 patients completed three months on the study.

“Today, organ transplantation is very successful, yet we can still do more in terms of reducing acute rejection following transplantation,” said Tony Rosenberg, Global Head of Transplant and Immunology Business Unit, Novartis Pharma AG. “These primary results suggest that Neoral C<sub>2</sub> monitoring is a cutting edge patient management technique that may assist clinicians in individualizing therapy to optimize patient outcomes.”

Interim results of the MO2ART study demonstrate impressive, low levels of acute rejection both in patients with immediate graft function (IGF) and in those experiencing delayed graft function (DGF). Specifically:

- The Acute Rejection (AR) rate\* within the current trial population (n=117) was 10%
- The AR rate\* within the IGF group (n=70) was 6%
- The AR rate\* within the DGF group (n=47), who are at increased risk of AR\*, was also very low at 16%

(\*AR was measured as BPAR – Biopsy Proven Acute Rejection)

“I think that these results demonstrate that monitoring of Neoral therapy using C<sub>2</sub> is an effective, safe and simple tool for optimizing patient therapy and achieving low levels of acute organ rejection,” said Professor Björn Nashan at the Clinic for Visceral and Transplantation surgery in Hannover, Germany. “We will continue to watch the MO2ART study evolve with great interest.”

In this interim analysis, safety and tolerability were excellent. The proportion of patients experiencing cyclosporin-related acute renal dysfunction was 5%. Median serum creatinine at month 3 was 129  $\mu\text{mol/L}$  for IGF and 133  $\mu\text{mol/L}$  for DGF patients, demonstrating excellent renal function even in the DGF population. Also, there were only seven serious adverse events related to cyclosporin.

These results, based on a three-month interim analysis, provide support that:

- $C_2$  monitoring is an effective, safe and simple tool for optimizing Neoral therapy, achieving low levels of acute rejection in renal transplantation.
- Achieving early target  $C_2$  exposure is associated with very low incidence of acute rejection with excellent renal tolerability.

### **What is Neoral $C_2$ monitoring?**

Neoral  $C_2$  monitoring is a patient management tool which involves making Neoral dose adjustments based on a measurement of the concentration of cyclosporin in a patient's blood two hours ( $C_2$ ) post-dose as opposed to the traditional practice of trough level ( $C_0$ ) monitoring - immediately before drug intake. This allows clinicians to individualize therapy according to drug absorption characteristics of each patient, which may then reduce the risks for acute rejection and cyclosporin toxicity. Ultimately, this may result in marked improvements in the efficacy and safety of Neoral.

Neoral, introduced in 1995, is indicated for the prophylaxis of organ rejection in kidney, liver and heart allogeneic transplants, and continues to be a cornerstone of immunosuppressive therapy. Neoral is contraindicated in patients with a hypersensitivity to cyclosporin or any ingredients in its formulation. Only physicians experienced in the management of systemic immunosuppressive therapy for the indicated disease should prescribe Neoral. Neoral may be administered with other immunosuppressant agents.

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 "demonstrates," "determines," "cutting-edge," "support," "may" or similar expressions, or by discussions of strategy, plans or intentions. Such statements include descriptions of the potential benefit of Neoral as evidenced by the results of clinical studies. Those statements reflect the current views of the Company with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could cause the actual results, performance or achievements of the Company and Neoral to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. There are no guarantees that the aforementioned study will result in the increased sales of Neoral in any market. Any such commercialisation can be affected by, among other things, additional analysis of data, new data, 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, competition in general and other risks and factors referred to in the Company's current Form of 20-F on file with the Securities and Exchange commission of the United States.

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## **Novartis broadens horizons in post-transplant immunosuppression: FTY720 plus Certican™ shows efficacy and safety in a calcineurin inhibitor (CNI) - free regimen**

Basel, 2 May 2002 – Organ transplant patients may soon be able to benefit from a promising alternative to standard calcineurin inhibitor (CNI) based immunosuppressive regimens<sup>1</sup>, according to a new study presented at this year's American Transplant Congress (ATC).

The multicentre, prospective Phase II study of 52 kidney transplant patients at high risk of delayed graft function (DGF) showed that a combination of the Novartis investigational agents FTY720 (a lymphocyte-homing agent which reversibly redirects lymphocytes away from the graft) and Certican™ (a proliferation inhibitor which targets primary causes of chronic rejection), together with standard corticosteroids, achieved immunosuppressive efficacy comparable to that seen with CNI-based regimens, without the risk of nephrotoxicity often associated with CNI use.

Lead investigator Dr Marc I. Lorber, Professor of Surgery and Chief, Section of Organ Transplantation and Immunology at the Yale University School of Medicine, commented: “The patients in this study were all at high risk of experiencing delayed graft function<sup>2</sup>, a situation associated with a deleterious effect on ultimate graft survival<sup>3</sup>. To that end, they represented a particularly vulnerable group. Nonetheless, the incidence of graft loss and acute rejection seen to date compared favourably with the rates usually seen with more conventional CNI-based regimens in this difficult patient population. Importantly, the FTY720 / Certican™ regimen resulted in good renal function in these high risk patients, with serum creatinine levels comparable to those expected in a low risk group. This approach may offer a viable alternative to CNI-based immunosuppression among patients at risk of DGF, possibly representing an important immunosuppression strategy for these high risk patients.”

FTY720 is a completely novel therapeutic agent with a highly selective mode of action. Through its targeted lymphocyte homing activity, FTY720 is expected to protect the graft from T-cell mediated damage, while leaving other aspects of the immune response unimpaired and thus still able to ward off systemic infections. Pre-clinical studies have shown that the host's response to infectious challenge is not impaired by FTY720.

Furthermore, in clinical trials, treatment with FTY720 was associated with a low incidence of regimen-related adverse events. A negative chronotropic effect (bradycardia<sup>4</sup>) has been observed previously in patients being treated with FTY720, and in this study was reported in 10% of patients. Bradycardia associated with FTY720 treatment is generally transient, mild, and recovers spontaneously in the majority of patients.

In a second FTY720 clinical study presented at this year's ATC, it was demonstrated that, in contrast to most other immunosuppressants, therapeutic drug monitoring is not required during FTY720 administration, potentially increasing ease of use for the patient and the physician.

Novartis is currently exploring further the possibility of CNI-free regimens in animal models. A study of the combination of FTY720 with *Myfortic*<sup>TM</sup> – a gastroprotective formulation of the immunosuppressant mycophenolic acid – was shown to be promising and to merit further investigation.

“FTY720 is being actively investigated in renal transplant patients and accumulating results suggest this agent may represent an important advance in our efforts to provide more effective, better tolerated and safer immunosuppression”, Dr Lorber said.

With its broad portfolio of developmental products, Novartis is continuing to shape the future of transplantation.

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 “to broaden horizons”, “may soon be able to benefit from a promising alternative”, “potentially increasing”, “may represent an important advance”, or similar expressions, or by or by discussions regarding the potential development of new products. Such statements include descriptions of Novartis' transplantation products either on the market or under development by the Company. Such statements reflect the current views of the Company with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could cause the actual results to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. There are no guarantees that any new products will be commercialized in any market. Any such commercialization can be affected by, among other things, uncertainties relating to product development and clinical trials, regulatory actions or delays or government regulation generally, the ability to obtain or maintain patent or other proprietary intellectual property protection and competition in general, 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 materialise, 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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## NOTES TO EDITORS

1. Calcineurin inhibitor (CNI) based regimens are those based on cyclosporin or tacrolimus. Neoral<sup>®</sup> (cyclosporin microemulsion) is the most widely prescribed immunosuppressant in the world and the cornerstone of treatment in transplant recipients.
2. Patients were selected on the basis of having a DGF probability of 50% or more using a DGF risk index developed specifically for this study.
3. In kidney transplant patients with good early graft function, graft survival six months post-transplant is typically 96% but this falls to 82% in those with delayed graft function (DGF).
4. Bradycardia = slowing of the heart rate

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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 6, 2002

By: /s/ MALCOLM B. CHEETHAM

Name: Malcolm B. Cheetham

Title: Head Group Financer  
Group Fin. Reporting and Accounting