

NOVARTIS AG  
Form 6-K  
November 06, 2007

## **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 dated November 5, 2007**

**(Commission File No. 1-15024)**

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**Novartis AG**

**(Name of Registrant)**

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**(Address of Principal Executive Offices)**

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

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Yes:  No:

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**- Investor Relations Release -**

**Tasigna® receives US approval providing new hope to chronic myeloid leukemia patients with resistance or intolerance to existing therapies**

*Tasigna produced responses in 40% of patients with Philadelphia chromosome-positive chronic myeloid leukemia resistant or intolerant to prior treatment*

*Approval and availability in US means Novartis can offer physicians and patients a comprehensive treatment approach for this disease*

**Basel, October 29, 2007** Tasigna® (nilotinib) has been approved in the US as a new anti-cancer therapy for certain patients with a life-threatening form of leukemia who are resistant or intolerant to prior treatment including Glivec® (imatinib)<sup>(1)</sup>, an established treatment standard and a leading Novartis medicine.

Novartis will make Tasigna available throughout the US within days following this approval by the Food and Drug Administration (FDA) to meet the treatment needs of these patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML).

CML is one of the four most common types of leukemia, a form of blood cancer, and affects around 4,500 people in the US each year <sup>(1)</sup>.

Tasigna represents an important advance for the small number of patients who are resistant or intolerant to prior therapy, said David Epstein, President and CEO of Novartis Oncology. This approval means we can offer physicians a comprehensive treatment approach with effective medicines to treat their Ph+ CML patients.

Taken twice daily, Tasigna works by inhibiting the proliferation of cells containing an abnormal chromosome. It does this by targeting the production of the Bcr-Abl protein, which is produced only by cells containing the abnormal Philadelphia chromosome. This protein is recognized as the key cause and driver of the overproduction of cancer-causing white blood cells in patients with Ph+ CML.

Tasigna was specifically designed to target the Bcr-Abl protein more preferentially than Glivec without adding new mechanisms of action. At six months follow-up, Tasigna reduced or eliminated cells carrying the abnormal Philadelphia chromosome in 40% of patients in chronic phase of the disease.

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(1) Known as Gleevec<sup>®</sup> (imatinib mesylate) in the US, Canada and Israel.

Applying experience gained from the development of Glivec, which remains the most frequently prescribed treatment for patients with CML, a team of Novartis scientists created Tasigna in August 2002, just a year after the launch of Glivec. In preclinical studies, the medicine was able to overcome resistance resulting from Bcr-Abl kinase mutations in 32 of 33 cell lines commonly associated with Ph+ CML. Patients with a variety of these mutations also responded to treatment with Tasigna.

The first worldwide approval for Tasigna came in Switzerland in July 2007. European Union approval is expected by the end of this year after the Committee for Medicinal Products for Human Use (CHMP), which reviews medicines in Europe, issued a positive opinion in September. Tasigna was also submitted for approval in Japan in June.

Without treatment, CML typically progresses over three to five years from the initial (chronic) phase through a transition period (accelerated phase) to a rapidly fatal form (blast crisis)<sup>(2)</sup>. Recent landmark clinical trial results for Glivec show that nearly 90% of newly diagnosed chronic-phase Ph+ CML adult patients treated with Glivec were alive after five years<sup>(3)</sup>, but some develop resistance or cannot tolerate this therapy.

The FDA approved Tasigna for treatment of chronic-phase and accelerated-phase Ph+ CML in adult patients resistant or intolerant to prior treatment, that included Glivec. This approval is based on an open-label multicenter clinical trial evaluating the drug's safety and rates of cytogenetic response (i.e. reduction or elimination of the Philadelphia chromosome) and hematologic response (i.e. normalization of white blood cell counts) in Glivec-resistant or -intolerant patients with Ph+ CML in chronic phase (n=280) and accelerated phase (n=105).

In clinical trials, the primary endpoint for patients in chronic phase was unconfirmed major cytogenetic response (MCyR). After a minimum follow-up of six months (median treatment duration 8.7 months), Tasigna produced MCyR in 40% of 232 chronic phase patients evaluated for efficacy. The complete cytogenetic response in these patients was 28%.

For patients in accelerated phase, the primary endpoint was confirmed hematological response (HR). Complete HR was reported in 18% of patients in accelerated phase. (Accelerated phase patients had a minimum follow-up of four months and a median treatment duration of 6.4 months).

The highest prior Glivec dose was at least 600 mg/day in 77% of patients, with 44% of patients receiving doses of 800 mg/day or higher. In addition, 24 different mutations in Bcr-Abl were noted in 19% of chronic phase and 25% of accelerated phase CML patients who were evaluated for mutations.

#### **Tasigna safety information**

Because taking Tasigna with food may increase the amount of drug in the blood, Tasigna should not be taken with food and patients should wait at least two hours after a meal before taking Tasigna. In addition, no food should be consumed for at least one hour after the dose is taken.

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In countries where it is approved, Tasigna is indicated for the treatment of chronic phase and accelerated phase Philadelphia chromosome-positive chronic myelogenous leukemia in adult patients resistant or intolerant to at least one prior therapy including Glivec. The effectiveness of Tasigna is based on hematologic and cytogenetic response rates. There are no controlled trials demonstrating a clinical benefit, such as improvement in disease-related symptoms or increased survival.

The most frequent Grade 3 or 4 adverse events for Tasigna were primarily hematological in nature and included neutropenia and thrombocytopenia. Elevations were seen in bilirubin, liver function tests, lipase enzymes and blood sugar, which were mostly transient and resolved over time. These cases were easily managed and rarely led to discontinuation. Pancreatitis was reported in less than 1% of cases. The most frequent non-hematologic drug-related adverse events were rash, pruritus, nausea, fatigue, headache, constipation, and diarrhea. Most of these adverse events were mild to moderate in severity.

Tasigna should be used with caution in patients with uncontrolled or significant cardiac disease (e.g. recent heart attack, congestive heart failure, unstable angina or clinically significant bradycardia), as well as in patients who have or may develop prolongation of QTc. These include patients with abnormally low potassium or magnesium levels, patients with congenital long QT syndrome, patients taking anti-arrhythmic medicines or other drugs that may lead to QT prolongation. Low levels of potassium or magnesium must be corrected prior to Tasigna administration.

Studies have also shown virtually no non-hematologic cross-intolerance between Glivec and Tasigna. (Cross-intolerance occurs when patients cannot tolerate two different drugs because of the same side effects). Causes of non-hematologic intolerance to Glivec included Grade 3 or 4 rash/skin toxicity, fluid retention, gastrointestinal intolerance, liver toxicity, and myalgia/arthralgia.

#### **About Glivec**

Glivec is approved in more than 90 countries including the US, EU and Japan for the treatment of all phases of Ph+ CML. Glivec is also approved in the EU, US and other countries for the treatment of patients with Kit (CD117)-positive gastrointestinal tumors (GIST), which cannot be surgically removed and/or have already spread to other parts of the body (metastasized). In Japan, Glivec is approved for the treatment of patients with Kit (CD117)-positive GIST. In the EU, Glivec is also approved for the treatment of adult patients with newly diagnosed Ph+ acute lymphoblastic leukemia (Ph+ ALL) in combination with chemotherapy and as a single agent for patients with relapsed or refractory Ph+ ALL. Glivec is also approved for the treatment of adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP) who are not eligible for surgery. Glivec is also approved for the treatment of patients with myelodysplastic/myeloproliferative diseases (MDS/MPD). Glivec is also approved for hypereosinophilic syndrome and/or chronic eosinophilic leukemia (HES/CEL).

The effectiveness of Glivec is based on overall hematologic and cytogenetic response rates and progression-free survival in CML, on hematological and cytogenetic response rates in Ph+ ALL, and on objective response rates in GIST and DFSP. There are no controlled trials demonstrating increased survival. Not all indications are available in every country.

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

The majority of patients treated with Glivec in clinical trials experienced adverse events at some time. Most events were of mild to moderate grade and treatment discontinuation was not necessary in the majority of cases.

The safety profile of Glivec was similar in all indications. The most common side effects included nausea, superficial edema, muscle cramps, skin rash, vomiting, diarrhea, abdominal pain, myalgia, arthralgia, hemorrhage, fatigue, headache, joint pain, cough, dizziness, dyspepsia and dyspnea, dermatitis, eczema, fluid retention, as well as neutropenia, thrombocytopenia and anemia. Glivec was generally well-tolerated in all the

studies that were performed, either as monotherapy or in combination with chemotherapy, with the exception of a transient liver toxicity in the form of



transaminase elevation and hyperbilirubinemia observed when Glivec was combined with high-dose chemotherapy.

Rare/serious adverse reactions include: sepsis, pneumonia, depression, convulsions, cardiac failure, thrombosis/embolism, ileus, pancreatitis, hepatic failure, exfoliative dermatitis, angioedema, Stevens-Johnson syndrome, renal failure, fluid retention, edema (including brain, eye, pericardium, abdomen and lung), hemorrhage (including brain, eye, kidney and gastrointestinal tract), diverticulitis, gastrointestinal perforation, tumor hemorrhage/ necrosis, hip osteonecrosis/avascular necrosis.

Patients with cardiac disease or risk factors for cardiac failure should be monitored carefully and any patient with signs or symptoms consistent with cardiac failure should be evaluated and treated. Cardiac screening should be considered in patients with HES/CEL, and patients with MDS/MPD with high level of eosinophils (echocardiogram, serum troponin level).

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.

#### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as will, should, can, expected, may or similar expressions, or by express or implied discussions regarding potential regulatory approvals, new indications or labeling for, or potential future sales of, Glivec or Tassigna. Such forward-looking statements reflect the current views of Novartis regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with Glivec or Tassigna to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Tassigna will be approved in the EU, Japan or any additional market; that that Glivec or Tassigna will be approved for any additional indications or labelling in any market; or that Glivec or Tassigna will reach any particular level of sales. In particular, management's expectations regarding Glivec or Tassigna could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; Novartis' ability to obtain or maintain patent or other proprietary intellectual property protection; unexpected delays due to manufacturing; competition in general; government, industry and general public pricing pressures, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the U.S. Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

#### **About Novartis**

Novartis AG (NYSE: NVS) is a world leader in offering medicines to protect health, cure disease and improve well-being. Our goal is to discover, develop and successfully market innovative products to treat patients, ease suffering and enhance the quality of life. We are strengthening our medicine-based portfolio, which is focused on strategic growth platforms in innovation-driven pharmaceuticals, high-quality and low-cost generics, human vaccines and leading self-medication OTC brands. Novartis is the only company with leadership positions in these areas. In 2006, the Group's businesses achieved net sales of USD 37.0 billion and net income of USD 7.2 billion. Approximately USD 5.4 billion was invested in R&D. Headquartered in Basel, Switzerland, Novartis



Group companies employ approximately 100,000 associates and operate in over 140 countries around the world. For more information, please visit <http://www.novartis.com>.

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**References**

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- (3) Druker, B. et al. Five-Year Follow-up of Patients Receiving Imatinib for Chronic Myeloid Leukemia. N Engl J Med 2006;355:2408-17.

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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: November 5, 2007

By: /s/ MALCOLM B. CHEETHAM

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