

NOVARTIS AG  
Form 6-K  
October 09, 2008

## **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 October 8, 2008**

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

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**Novartis AG**

**(Name of Registrant)**

**Lichtstrasse 35**

**4056 Basel**

**Switzerland**

**(Address of Principal Executive Offices)**

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

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Yes:  No:

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**- Investor Relations Release -**

**Early data show potential for imatinib to treat life-threatening form of pulmonary artery disease**

- *Exploratory study shows clinical improvement in patients with pulmonary arterial hypertension (PAH)*
- *Current treatment options have limited benefit for this debilitating, rapidly progressive and incurable blood vessel disease*
- *Imatinib, available as Glivec<sup>®</sup> for treatment of certain cancers, known to inhibit protein associated with PAH*
- *Novartis to further explore potential of imatinib in PAH in 2009*

**Basel, October 8, 2008** An early proof-of-concept study presented today shows promising results for imatinib in the treatment of pulmonary arterial hypertension (PAH), a severe, incurable blood vessel disorder.

Preliminary findings from a 59-patient, multi-center Phase II clinical trial suggest imatinib provides a treatment benefit, as demonstrated by a significant improvement in pulmonary vascular resistance and a numerical increase in cardiac output, key hemodynamic measures used to monitor the progression of the disease. Improvements in the six-minute walk test, the primary endpoint of the study, approached, but did not reach, statistical significance.

These initial data were presented today at the European Respiratory Society (ERS) congress in Berlin, Germany, and further details on the study are expected to be published later this year. Imatinib is available for oncology indications in many countries as Glivec<sup>®</sup> (imatinib), and as Gleevec<sup>®</sup> (imatinib mesylate) tablets in the US, Canada and Israel.

The outcomes of this trial are clinically important given the rapid progression of PAH and the poor prognosis for these patients, said Professor Ardeschir Ghofrani, MD, Head of Pulmonary Hypertension Division, University Hospital Giessen und Marburg, Germany. Our observations suggest that imatinib holds promise in treating PAH.

PAH is a debilitating disease that is characterized by a marked and sustained elevation in pulmonary artery pressure(1). The disease is rapidly progressive and can result in heart failure and death(1). There is no known cure for PAH and the goal of current treatments is to control symptoms of the disease(2). The prognosis for many PAH patients is similar to that of some advanced cancers, and with current treatment options, the five-year survival rate is 50%(3).

Imatinib is an orally administered targeted therapy that has successfully treated many patients with certain rare cancers. It works by inhibiting the activity of several proteins called tyrosine kinases, such as Bcr-Abl, c-KIT and platelet-derived growth factor receptor (PDGFR), which is also thought to be involved in the progression of PAH3. In patients with PAH, PDGFR may cause smooth muscle cells in the pulmonary arteries to multiply, resulting in the constriction of these arteries(4).

Plans for research to further explore the potential of imatinib in PAH are ongoing and will be announced at a later date.

The double blind, placebo-controlled trial presented at ERS enrolled 59 patients with PAH to evaluate the effectiveness and safety of imatinib 400 mg. The study participants had previously failed to improve after receiving standard therapy with prostanoids, endothelin antagonists or PDE-5 inhibitors.

There is a high unmet need for new treatments that address the underlying mechanisms of PAH, said David Epstein, President and CEO of Novartis Oncology. These early findings support exploring the potential of imatinib in PAH in a larger randomized clinical trial.

It is estimated that approximately 130,000 to 260,000 people worldwide have PAH(5). The mean age at diagnosis is 35 years, and most patients present with moderate-to-severe disease. PAH occurs most often in otherwise healthy people, and more often in women than in men(4).

The exact process by which PAH develops is not known. However, it appears to be associated with a variety of disease processes, including chronic thromboembolic disease (blood clots), connective tissue diseases, congenital heart disease and exposure to external factors including appetite suppressants or infectious diseases such as HIV(3).

Novartis has also conducted early stage research with imatinib in another non-oncology disease called idiopathic pulmonary fibrosis (IPF), a condition in which the lungs become scarred over time, making it more and more difficult to breathe(6). Early clinical trial results in IPF did not show a significant treatment benefit over placebo, and clinical trials have therefore been halted.

### **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. Glivec is not currently approved in any markets for PAH.

Not all indications are available in every country.

### **Glivec contraindications, warnings and adverse events in approved oncology indications**

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 of 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 potential, to further explore, promising, suggest, expected, promise, can, goal, prognosis, will, plans, estimated, or similar expressions, or by express or implied discussion of potential new indications or labelling for Glivec, regarding potential future revenues from Glivec, or regarding the long-term impact of a patient's use of Glivec. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of the Company regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with Glivec to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Glivec will be approved for any additional indications or labelling in any market. Nor can there be any guarantee that Glivec will achieve any particular levels of revenue in the future. Neither can there be any guarantee regarding the long-term impact of a patient's use of Glivec. In particular, management's expectations regarding Glivec could be affected by, among other things, unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical trial data; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry and general public pricing pressures; the impact that the foregoing factors could have on the values attributed to the Novartis Group's assets and liabilities as recorded in the Group's consolidated balance sheet, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and

Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

#### **About Novartis**

Novartis AG provides healthcare solutions that address the evolving needs of patients and societies. Focused solely on healthcare, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic pharmaceuticals, preventive vaccines, diagnostic tools and consumer health products. Novartis is the only company with leading positions in these areas. In 2007, the Group's continuing operations (excluding divestments in 2007) achieved net sales of USD 38.1 billion and net income of USD 6.5 billion. Approximately USD 6.4 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 98,000 full-time 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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**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: October 8, 2008

By: /s/ MALCOLM B. CHEETHAM

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