

NOVARTIS AG  
Form 6-K  
December 06, 2010

# 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 December 6, 2010

(Commission File No. 1-15024)

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**- Investor Relations Release -**

**Longer-term Phase III data show Novartis drug Tasigna® continues to surpass Glivec® in slowing disease progression in patients with newly diagnosed CML**

- *Fewer patients taking Tasigna for Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase progressed to advanced stages of the disease*
- *24-month analysis confirms Tasigna induces deeper and more durable cytogenetic and molecular responses*
- *Tasigna now approved in the US and Switzerland for this indication; regulatory submissions under review in EU, Japan and other countries worldwide*

**Basel, December 6, 2010** Novartis announced today 24-month data showing that Tasigna® (nilotinib) continues to surpass Glivec® (imatinib)\* in the treatment of adult patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase(1). These new data, from the first Phase III comparison of the two oral therapies as initial treatment for this blood cancer, were presented at the 52nd Annual Meeting and Exposition of the American Society of Hematology (ASH) in Orlando, Florida.

With this longer-term follow-up at 24 months, first-line treatment with Tasigna at 300 mg twice daily was found to result in a lower incidence of progression to accelerated phase and blast crisis, compared to the standard approved dose of Glivec 400 mg once daily. Patients receiving Tasigna also had a lower incidence of suboptimal response and treatment failure as defined by study criteria(1).

These data also showed that Tasigna induced deeper and more durable complete cytogenetic response (CCyR) and major molecular response (MMR) compared to Glivec, as well as a significantly higher rate of an even deeper response – a trace amount of 0.0032% or less of the Bcr-Abl protein that causes Ph+ CML, which is considered a complete molecular response (CMR)(1). Fewer patients taking Tasigna in the study discontinued treatment due to adverse events compared to Glivec(1). Tasigna and Glivec were generally well tolerated.

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These 24-month Phase III data extend the evidence of clinical benefit for newly diagnosed patients with chronic phase Ph+ CML treated with Tasigna, compared to Glivec, said Timothy P. Hughes, MD, ENESTnd study investigator and Clinical Professor at the University of Adelaide, Australia. Now we can begin to evaluate the long-term treatment outcomes of patients who achieve and maintain deep reductions in Bcr-Abl on Tasigna.

Rates of MMR and CCyR remain statistically higher for Tasigna versus Glivec at the 24-month minimum follow-up. MMR was achieved by 71% of patients taking Tasigna 300 mg twice daily and 67% of patients taking Tasigna 400 mg twice daily, compared to 44% of patients taking Glivec by 24 months. Durable MMR rates were statistically significantly higher in the Tasigna 300

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mg twice daily and Tasigna 400 mg twice daily arms compared to Glivec 400 mg once daily (42%, 39% and 21% respectively). Significantly more patients achieved CCyR in the Tasigna 300 mg and 400 mg arms compared to the Glivec arm at 87% and 85% vs. 77% respectively by 24 months.

The US Food and Drug Administration (FDA) and Swissmedic have approved Tasigna in this first-line indication. In September, Novartis received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) recommending European Commission approval for Tasigna for this indication. Regulatory submissions are under review in the European Union, Japan and other countries worldwide.

This year, Novartis also began a collaboration with molecular diagnostics company Cepheid to develop a new FDA cleared/approved Bcr-Abl test, which adheres to the International Scale. The goal of the collaboration is to help doctors more reliably monitor Ph+ CML patients. Cepheid and Novartis also will develop a next generation test, which is expected to enable even more sensitive testing, indicating the depth of a patient's response to tyrosine kinase inhibitors, including Tasigna and Glivec. Currently there are no FDA cleared/approved tests to monitor for Bcr-Abl.

The creation and introduction of Glivec revolutionized the treatment of Ph+ CML by substantially improving overall survival rates for patients, said Hervé Hoppenot, President, Novartis Oncology. We are encouraged by the ongoing clinical development of Tasigna as a new treatment showing that at 24 months it continues to surpass Glivec in slowing disease progression in patients with newly diagnosed chronic phase Ph+ CML.

Another study will be presented at this year's annual ASH meeting which provides further support for the use of Tasigna in patients with newly diagnosed Ph+ CML. The Gruppo Italiano Malattie Ematologiche dell'Adulto (GIMEMA) study, an ongoing, open-label, single-stage, multicenter Phase II clinical trial, will be presented on Monday, December 6, 2010(2).

### **ENESTnd Study Details**

The clinical trial, ENESTnd (Evaluating Nilotinib Efficacy and Safety in Clinical Trials of Newly Diagnosed Ph+ CML Patients), is a Phase III randomized, open-label, multicenter trial comparing the efficacy and safety of Tasigna versus Glivec in adult patients with newly diagnosed Ph+ CML in chronic phase(1). It is the largest global randomized comparison of two oral therapies ever conducted in newly diagnosed Ph+ CML patients.

ENESTnd is being conducted at 217 global sites with 846 patients enrolled. Patients were randomized to receive Tasigna 300 mg twice daily (n = 282), Tasigna 400 mg twice daily (n = 281) or Glivec 400 mg once daily (n = 283). The primary endpoint was MMR at 12 months; the key secondary endpoint was durable MMR at 24 months (patients having MMR when evaluated at both 12 and 24 months)(1). MMR was defined in the study as reduction in the level of the abnormal Bcr-Abl gene to less than or equal to 0.1% of the pretreatment level based on an internationally agreed standard(1). Planned follow-up is for five years. Patients on the Glivec treatment arm who had suboptimal response or treatment failure were allowed to escalate dose and/or switch to Tasigna via a protocol extension. These data, presented at ASH, were the 24-month minimum follow-up.

Results showed that fewer patients progressed to accelerated phase or blast crisis while on treatment with Tasigna at 300 mg twice daily (n = 2) and 400 mg twice daily (n = 3) versus Glivec at 400 mg once daily (n = 12)(1) with 24 months of minimum follow-up demonstrating a significant improvement in disease control.

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These data also showed that nearly three times more patients taking Tasigna 300 mg twice daily achieved CMR defined as a trace amount of 0.0032% or less of the Bcr-Abl protein that causes Ph+ CML with Tasigna 300 mg twice daily (n = 70) than with Glivec (n = 25) by 24-months(1).

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All patients had a minimum of 24 months of treatment or discontinued early; the median follow-up was 25 months. Overall, 75%, 78% and 68% of patients remained in the study on Tasigna 300 mg twice daily, Tasigna 400 mg twice daily and Glivec 400 mg once daily, respectively(1).

Both Tasigna and Glivec were generally well tolerated overall. Rates of discontinuation due to adverse events or laboratory abnormalities were 9% for Tasigna 300 mg twice daily, 13% for Tasigna 400 mg twice daily and 11% for Glivec 400 mg once daily(1). No patients treated with Tasigna in the study had prolongation of QT interval >500 milliseconds(1). No sudden deaths occurred in any of the treatment arms(1).

#### **About Philadelphia Chromosome-Positive Chronic Myeloid Leukemia (Ph+ CML)**

Chronic myeloid leukemia is a disease in which the body produces cancerous white blood cells. Almost all patients with CML have an abnormality known as the Philadelphia chromosome, which produces a protein called Bcr-Abl. Bcr-Abl causes malignant white blood cells to proliferate(3). Worldwide, CML is responsible for approximately 10% to 15% of all adult cases of leukemia(4), with an incidence of one to two cases per 100,000 people per year(5).

#### **About Tasigna(6)**

Tasigna has been approved in over 85 countries for the treatment of chronic phase and accelerated phase Ph+ CML in adult patients resistant or intolerant to at least one prior therapy, including Glivec. The effectiveness of Tasigna for this indication is based on confirmed hematologic and unconfirmed cytogenetic response rates. There are no controlled trials demonstrating a clinical benefit, such as improvement in disease-related symptoms or increased survival.

Tasigna is not approved in the EU for the treatment of newly diagnosed Ph+ CML-CP.

#### **Tasigna Important Safety Information**

Tasigna should be taken twice daily at an interval of approximately 12 hours apart and must not be taken with food. No food should be consumed for two hours before the dose and for at least one hour after the dose. Avoid grapefruit juice and other foods that are known to inhibit CYP3A4.

Tasigna should not be used in patients who are hypersensitive to nilotinib or any of the excipients.

Treatment with Tasigna has been associated with hematological side effects, such as thrombocytopenia, neutropenia and anemia which was generally reversible and usually managed by withholding Tasigna temporarily or dose reduction. Complete blood counts should be performed every two weeks for the first two months and then monthly thereafter as clinically indicated.

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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. Close monitoring for an effect on the QTc interval is advisable and a baseline electrocardiography is recommended prior to initiating therapy with Tasigna and as clinically indicated. Uncommon cases (0.1 to 1%) of sudden death have been reported in clinical studies in patients with significant risk factors.

Tasigna should be used with caution in patients with liver impairment, in patients with a history of pancreatitis and in patients with total gastrectomy. Patients with rare hereditary problems of galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption should not

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use Tasigna. Tasigna should not be used during pregnancy unless clearly necessary and breast feeding is not recommended during treatment.

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

#### **About Glivec(7)**

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 US, EU 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 the US and EU, Glivec is now approved for the post-surgery treatment of adult patients following complete surgical removal of Kit (CD117)-positive gastrointestinal stromal tumors. 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 hematological and cytogenetic response rates and progression-free survival in CML, on hematological and cytogenetic response rates in Ph+ ALL, MDS/MPD, on hematological response rates in systemic mastocytosis, HES/CEL, on objective response rates and progression-free survival in unresectable and/or metastatic GIST, on recurrence free survival in adjuvant GIST and on objective response rates in DFSP. Increased survival in controlled trials has been demonstrated only in newly diagnosed chronic phase CML and GIST.

Not all indications are available in every country.

#### **Glivec Important Safety Information**

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 and 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

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gastrointestinal tract), diverticulitis, gastrointestinal perforation, tumor hemorrhage/necrosis and 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 under review, expected, goal, or similar expressions, or by express or implied discussions regarding potential new indications or labeling for Tasigna or regarding potential future revenues from Tasigna or Glivec. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results with Tasigna or Glivec to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Tasigna will be approved for any additional indications or labeling in any market. Nor can there be any guarantee that Tasigna or Glivec will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Tasigna and Glivec 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; 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 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 2009, the Group's continuing operations achieved net sales of USD 44.3 billion, while approximately USD 7.5 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 100,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit <http://www.novartis.com>.

Novartis is on Twitter. Sign up to follow @Novartis at <http://twitter.com/novartis>.

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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: December 6, 2010

By: /s/ MALCOLM B. CHEETHAM

Name: Malcolm B. Cheetham  
Title: Head Group Financial  
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