

NOVARTIS AG  
Form 6-K  
September 27, 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 September 24, 2010**

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

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**- Investor Relations Release -**

**Novartis drug Tasigna® recommended for approval in European Union to treat patients with newly diagnosed Ph+ chronic myeloid leukemia**

- *Positive CHMP opinion based on pivotal trial showing Tasigna superior to Glivec in achieving molecular and cytogenetic response, delaying cancer progression*
- *This recommendation follows Tasigna approval in the US and Switzerland in this setting; regulatory submissions under review in Japan and worldwide*

**Basel, September 24, 2010** Novartis has received a positive opinion recommending European Union approval of Tasigna® (nilotinib), a selective targeted therapy for adult patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase.

The Committee for Medicinal Products for Human Use (CHMP) recommended approval of Tasigna in the first-line indication based on a pivotal Phase III clinical trial in which Tasigna surpassed Glivec® (imatinib)\* in key measures of treatment efficacy. In the study, Tasigna was found superior to Glivec in achieving higher rates of both major molecular and complete cytogenetic response and in delaying cancer progression(1). The data were first published in the June 17 issue of *The New England Journal of Medicine* and were confirmed by 18-month median follow-up data presented at the 2010 annual meeting of the American Society of Clinical Oncology held in June(2).

We are glad that the development of Tasigna may result in a potential new treatment option for newly diagnosed CML patients seeking effective means of preventing disease progression, said Alessandro Riva, Global Head, Oncology Development & Medical Affairs, Novartis Oncology.

Following this positive opinion from CHMP, we look forward to working with regulatory authorities to bring Tasigna to clinical use in the first-line setting as soon as possible.

The European Commission generally follows the recommendations of the CHMP and delivers its final decision within three months. The decision will be applicable to all 27 European Union (EU) member states plus Iceland and Norway. In total, approximately 46,000 people in the EU are affected by CML, a life-threatening blood cancer(3).

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The US Food and Drug Administration (FDA) and Swiss health authority Swissmedic have already approved Tasigna for newly diagnosed Ph+ CML. Regulatory submissions are also under way in Japan and worldwide.

Tasigna is a potent and selective inhibitor of the Bcr-Abl protein that causes production of cancer cells in Ph+ CML(4),(5). It is also active against a broad spectrum of Bcr-Abl mutations associated with resistance to Glivec(6). The first clinical trials of Tasigna began only 21 months after its discovery, with the drug receiving its first regulatory approval as a second-line treatment in 2007.

Tasigna surpassed Glivec in key measures of treatment efficacy in the pivotal head-to-head trial, Evaluating Nilotinib Efficacy and Safety in Clinical Trials of Newly Diagnosed Ph+ CML Patients (ENESTnd). Tasigna reduced Bcr-Abl faster than Glivec, leading to lower rates of cancer progression even as early as 12 months(1). Deep reduction of Bcr-Abl, known as a major molecular response, is considered to be a critical therapeutic milestone associated with good long-term outcomes for patients with Ph+ CML(7)-(9). Treatment with Tasigna led to higher rates of both major molecular response and complete cytogenetic response (elimination of the Philadelphia chromosome that is the hallmark of the cancer) compared with Glivec(1).

The randomized, open-label, multicenter ENESTnd trial compared 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 in chronic phase.

Results showed that significantly fewer patients progressed to accelerated or blastic phase on Tasigna 300 mg twice daily than on Glivec 400 mg once daily (2 patients vs. 11 patients)(1) with 14 months of median follow-up. Fewer patients discontinued due to adverse events from the Tasigna 300 mg twice daily arm of the study compared to the Glivec 400 mg once daily arm(1).

Chronic myeloid leukemia is one of the four most common types of leukemia, responsible for about 15% of all leukemia cases worldwide(10).

#### **About Tasigna(4)**

Tasigna has been approved in more than 80 countries for the treatment of chronic phase (CP) 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 exceipients.

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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.

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 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(11)**

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 (SM), 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 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 recommended, recommendation, under review, recommending, look forward to, will, under way, potential or similar expressions, or by express or implied discussions regarding potential new indications or labeling for Tasigna or the timing of any approvals of such new indications or labeling, 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, or at any particular time. 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; the company's ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; unexpected clinical trial results, including unexpected new clinical data and unexpected additional analysis of existing clinical data; 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 102,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit <http://www.novartis.com>.



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**SIGNATURES**

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

**Novartis AG**

Date: September 24, 2010

By: /s/ MALCOLM B. CHEETHAM

Name: Malcolm B. Cheetham  
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