

NOVARTIS AG  
Form 6-K  
June 04, 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 June 4, 2010**

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**- Investor Relations Release -**

**New data at ASCO show Novartis drug Tasigna® surpasses Glivec® in slowing disease progression for newly diagnosed CML patients**

- *18-month median follow-up from the first head-to-head comparison of these two oral therapies to be presented Monday, June 7 at ASCO*
- *In this study, Tasigna produced deeper molecular responses and significantly reduced progression to advanced disease, resulting in fewer deaths due to CML*
- *Three times more patients achieved undetectable disease at the molecular level with Tasigna than with Glivec*
- *Tasigna registration data further confirmed by this new data; filing received FDA priority review and also submitted in EU, Switzerland, Japan*

**Basel, June 4, 2010** Novartis announced today 18-month results (median follow-up) showing that Tasigna® (nilotinib) significantly surpasses Glivec® (imatinib)\* in slowing disease progression in adult patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase(1).

This 18-month median follow-up is from the first head-to-head comparison of these two oral therapies as initial treatment for this life-threatening blood cancer and will be presented on June 7 at the 46th American Society of Clinical Oncology (ASCO) annual meeting in Chicago.

Tasigna produced deeper levels of molecular response than Glivec in front-line Ph+ CML and significantly reduced progression to accelerated phase and blast crisis, resulting in fewer deaths due to CML(1). Notably, three times more patients achieved undetectable disease at the molecular level with Tasigna than with Glivec(1). Further, Tazigna surpassed Glivec in other key measures of treatment efficacy.

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Tasigna demonstrates that by more selectively inhibiting BCR-ABL, the key driver of Ph+ CML, we can reduce progression to advanced disease even further than with the current gold standard Glivec, said Richard Larson, MD, ENESTnd study investigator and Director of the Hematologic Malignancies Program at the University of Chicago. The efficacy and safety findings achieved by Tasigna in this study provide patients and physicians with an important new treatment option.

In February 2010 the US Food & Drug Administration (FDA) granted Tasigna priority review status for newly diagnosed Ph+ CML patients. Regulatory submissions have been filed in the EU, Switzerland and Japan. The new ENESTnd data to be presented at ASCO will further confirm the findings in those filings, all of which were based on 13.8-month median follow-up data from the study.

## Study details

The clinical trial, Evaluating Nilotinib Efficacy and Safety in Clinical Trials of Newly Diagnosed Ph+ CML Patients (ENESTnd), 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 major molecular response (MMR) at 12 months; a secondary endpoint was complete cytogenetic response (CCyR) by 12 months(1). Planned follow-up is for five years(2). 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. The data to be presented at ASCO is the 18-month median follow-up.

Results showed that fewer patients progressed to accelerated phase or blast crisis on Tasigna at 300 mg twice daily (n = 2) and 400 mg twice daily (n = 1) versus Glivec at 400 mg once daily (n = 12)(1) with 18 months of median follow-up, demonstrating a significant improvement in disease control. The data also showed fewer deaths due to CML on Tasigna at 300 mg twice daily (n = 2) and 400 mg twice daily (n = 1) versus Glivec at 400 mg once daily (n = 8). Rate of MMR and CCyR remain superior for Tasigna versus Glivec at the 18-month median follow-up.

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(2). Notably, three times more patients in the ENESTnd study achieved undetectable disease at the molecular level (BCR-ABL levels at 4.5-log reduction) with Tasigna than with Glivec at the 18-month median follow-up(1). CCyR indicates that no CML cells containing the diagnostic Philadelphia chromosome can be seen in a sample of bone marrow taken from the patient.

All patients had a minimum of 16 months of treatment or discontinued early; the median follow-up was 18 months. Overall, 80%, 81% and 75% 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 well tolerated overall. Rates of discontinuation due to adverse events or laboratory abnormalities were 7% for Tasigna 300 mg twice daily, 11% for Tasigna 400 mg twice daily, and 9% for Glivec 400 mg once daily(1). Fewer patients taking Tasigna discontinued due to adverse events compared to Glivec. No patients in the study had prolongation of QT interval >500 milliseconds(1). No sudden deaths occurred in any of the treatment arms(1).

## About Ph+ CML

CML 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 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 for the treatment of newly diagnosed Ph+ CML-CP.

### **Tasigna important 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.

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, 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. Close monitoring for an effect on the QTc interval is advisable and a baseline echocardiogram is recommended prior to initiating therapy with Tasigna and as clinically indicated.

### **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 (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 "priority review," "will," "can," "to be," 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 clinical trial results, unexpected regulatory actions or delays or government regulation generally; 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>.

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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: June 4, 2010

By: /s/ MALCOLM B. CHEETHAM

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