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Tasigna® gains European approval for patients with a life-threatening form of leukemia who are resistant or intolerant to existing therapies

- *Tasigna produced response in 49% of patients with Philadelphia chromosome-positive chronic myeloid leukemia resistant or intolerant to existing therapies*
- *Phase III trials launched to explore potential of Tasigna in newly diagnosed CML patients and also those with sub-optimal response to prior treatment*

Basel, November 28, 2007 – Tasigna® (nilotinib) has received European Union approval as a new anti-cancer therapy for patients with a life-threatening form of leukemia who are resistant or intolerant to prior treatment including Glivec® (imatinib)*.

The EU approval was supported by data showing that Tasigna produced a positive response in 49% of patients in the chronic phase of Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML). Most patients achieved this response within three months of starting Tasigna treatment.

“The approval of Tasigna gives us the opportunity to help more CML patients and, with Glivec as our first line agent, provide comprehensive treatment options for prescribers,” said David Epstein, President and CEO of Novartis Oncology. “Tasigna drives home our commitment to develop compounds to fulfill unmet medical needs by pursuing indications for patients with limited treatment options.”

The European Commission decision applies in all 27 EU member states plus Norway and Iceland, and follows recent approvals in the US and Switzerland. Tasigna is now approved in a total of 37 countries, and was also submitted for approval in Japan in June.

CML is one of the four most common types of leukemia, responsible for about 15% of all leukemia cases worldwide¹. Without treatment, CML typically progresses over three to five years from the initial (chronic) phase through a transition (accelerated) phase to a rapidly fatal form called blast crisis¹. Tasigna is indicated in the EU for the treatment of adults who are in chronic or accelerated phase Ph+ CML and have resistance or intolerance to prior therapy including Glivec.

Taken twice daily, Tasigna works by inhibiting the proliferation of cells containing an abnormal chromosome in patients with CML. 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 driver of the overproduction of cancer-causing white blood cells in patients with Ph+ CML.

Tasigna was designed to target the Bcr-Abl protein more preferentially than Glivec without adding new mechanisms of action.

* Known as Gleevec® (imatinib mesylate) tablets in the US, Canada and Israel.

Earlier this year, a Phase III clinical trial program was launched to compare Tasigna with Glivec for the treatment of newly diagnosed patients with chronic phase Ph+ CML. A study is also underway comparing these two targeted therapies in chronic phase Ph+ CML patients who had sub-optimal responses to previous therapy. Separately, a Phase III program has been launched involving the use of Tasigna in patients with gastrointestinal stromal tumors (GIST) who are resistant or intolerant to prior treatment.

The EU approval of Tasigna was based on a pivotal clinical trial evaluating the rates of cytogenetic response (i.e. reduction or elimination of the Philadelphia chromosome) and confirmed hematologic response (i.e. normalization of white blood cell counts) in Glivec-resistant or -intolerant patients with Ph+ CML in chronic and accelerated phase.

The major cytogenetic response rate with Tasigna was 49% for chronic phase patients and 27% for accelerated phase patients. The complete hematologic response rate was 70% for chronic phase patients who were not already in complete hematologic response at the start of the trial, and the confirmed hematologic response rate was 42% for accelerated phase patients.

The US Food and Drug Administration (FDA) approved Tasigna in October 2007 based on the same pivotal clinical trial that supported the EU filing, but using a different analysis (including shorter duration of follow-up) that produced slightly different response rates.

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.

In countries where it is approved, Tasigna is indicated for the treatment of chronic phase and accelerated phase Philadelphia chromosome-positive chronic myeloid leukemia in adult patients resistant or intolerant to at least one prior therapy including Glivec. The effectiveness of Tasigna is based on confirmed 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. Close monitoring for an effect on the QTc interval is advisable and a baseline ECG is recommended prior to initiating therapy with Tasigna and as clinically indicated.

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 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, 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 “should”, “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 Tasigna. 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 Tasigna to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Glivec or Tasigna will be approved for any additional indications or labelling in any market or that Glivec or Tasigna will reach any particular level of sales. In particular, management’s expectations regarding Glivec or Tasigna 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>.

Reference

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Novartis Media Relations

John Gilardi

Novartis Global Media Relations
+41 61 324 3018 (direct)
+41 79 596 1408 (mobile)
john.gilardi@novartis.com

Kim Fox

Novartis Oncology
+1 862 778 7692 (direct)
kim.fox@novartis.com

e-mail: media.relations@novartis.com

Novartis Investor Relations

International

Ruth Metzler-Arnold
Katharina Ambuehl
Pierre-Michel Bringer
Jason Hannon
Thomas Hungerbuehler
Richard Jarvis
Isabella Zinck

North America

Ronen Tamir +1 212 830 2433
Jill Pozarek +1 212 830 2445
Edwin Valeriano +1 212 830 2456

Central phone no: +41 61 324 7944

e-mail: investor.relations@novartis.com

e-mail: investor.relations@novartis.com