

**MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG**

## **Glivec® recommended for use in Europe as first post-surgery treatment for gastrointestinal stromal tumors (GIST)**

- *Use of Glivec after surgery (adjuvant setting) shows substantial benefit for GIST patients, reducing risk of recurrence by 89%<sup>1</sup>*
- *GIST, a life-threatening cancer, recurs in as many as one out of two patients<sup>2</sup>*
- *Positive opinion for Europe follows recent approvals of Glivec in the adjuvant setting in the US and Switzerland*

**Basel, March 19, 2009** – Novartis has received a positive opinion supporting European Union (EU) approval of Glivec® (imatinib)\* as a post-surgery treatment for patients at significant risk of relapse following removal of gastrointestinal stromal tumors (GIST).

The Committee for Medicinal Products for Human Use (CHMP) has recommended approval for Glivec based on positive findings from a pivotal Phase III study, which showed that use of Glivec after surgery reduces risk of recurrence by approximately 89%<sup>1</sup>. The European Commission generally follows the recommendations of the CHMP and delivers its final decision within two to three months. The decision will apply in all 27 EU member states plus Iceland and Norway.

“This positive opinion is an important step forward for GIST patients,” said David Epstein, President and CEO, Novartis Oncology, Novartis Molecular Diagnostics. “If approved in Europe, Glivec would provide an immediate option for post-surgical protection against the return of this highly aggressive disease.”

GIST is a life-threatening cancer of the gastrointestinal tract. After initial removal, it can return in as many as one out of two patients<sup>2</sup> within a median of two years<sup>3</sup>. If approved for this new use, Glivec would be the first and only treatment indicated for use after surgery to delay the return of this highly aggressive cancer. In the EU, Glivec is currently indicated for the first-line treatment of metastatic or unresectable (inoperable) Kit (CD117)-positive GIST, the treatment of all phases of Philadelphia chromosome-positive chronic myeloid leukemia (CML), and other rare cancers<sup>4</sup>. This would be the tenth indication approved for Glivec in the EU. Glivec is already approved for this new indication in the US, Switzerland and several other countries.

### **Filing data**

The CHMP reviewed data from a double-blind, randomized, multicenter study, which was just published in *The Lancet*. The study was conducted throughout the US and Canada by the American College of Surgeons Oncology Group (ACOSOG) and included 713 GIST patients whose tumors had been surgically removed. The study compared the recurrence-free survival (RFS) of patients taking Glivec 400 mg daily versus placebo for one year immediately following surgery. The results showed that after one year, 97.7% of those receiving Glivec remained recurrence-free, compared with 82.3% of those

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

receiving placebo ( $P < 0.0001$ ). Therefore, risk of recurrence was reduced by approximately 89% with Glivec as compared to placebo<sup>1</sup>.

The investigators reported that treatment with Glivec was well tolerated by most patients, with side effects similar to those observed in previous clinical trials with Glivec. These include nausea, diarrhea and swelling (edema)<sup>1</sup>.

### **About gastrointestinal stromal tumors**

GIST belong to a group of cancers known as soft tissue sarcomas<sup>3</sup>. The most common sarcomas, they can be found most often in the stomach and small bowel<sup>3</sup>. In the EU, the incidence of GIST is estimated to be more than 5,000 cases per year<sup>5,6</sup>, of which approximately 95% are Kit-positive<sup>3</sup>. Kit is the protein that, when mutated, has been identified as one of the major causes of GIST. Glivec inhibits the activity of several proteins, including Kit<sup>3</sup>.

### **About Glivec**

Glivec is approved in more than 90 countries including the US, EU and Japan for the treatment of all phases of Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML). Glivec is also approved in the US, EU and other countries for the treatment of patients with Kit (CD117)-positive GIST which cannot be surgically removed and/or have already spread to other parts of the body (metastasized). In the US, Glivec was recently approved for the post-surgery treatment of adult patients following complete surgical removal of 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 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.

### **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," "risk," "generally follows," "recommendations," "will," "if approved," "would," "estimated," or similar expressions, or by express or implied discussions regarding potential new indications or labeling for Glivec, regarding the long-term impact of a patient's use of Glivec, or regarding potential future revenues from 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 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 labeling in any market. Neither can there be any guarantee regarding the long-term impact of a patient's use of Glivec. Nor can there be any guarantee that Glivec will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Glivec could be affected by, among other things, unexpected regulatory actions or delays or government regulation generally, including actions or delays by the European Commission; 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 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, preventive vaccines, diagnostic tools, cost-saving generic pharmaceuticals and consumer health products. Novartis is the only company with leading positions in these areas. In 2008, the Group's continuing operations achieved net sales of USD 41.5 billion and net income of USD 8.2 billion. Approximately USD 7.2 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 96,700 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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