

**MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG****FDA approves Novartis drug Glivec® label recommending extending treatment to three years for certain GIST patients after surgery**

- *Phase III results showed 54% reduction in risk of recurrence and 55% reduction in risk of death after three years' adjuvant Glivec in adults with KIT+ GIST<sup>1</sup>*
- *Approval builds on vast experience with Glivec, first approved 10 years ago for treatment of adults with metastatic and/or unresectable KIT+ GIST<sup>2</sup>*
- *NCCN guidelines updated to include new adjuvant treatment duration in patients with KIT+ GIST<sup>2</sup>*

**Basel, February 1, 2012** – Novartis announced today that following a priority review, the US Food and Drug Administration (FDA) has approved an update to the Glivec® (imatinib)\* label to recommend 36 months of treatment after surgery for adult patients with KIT (CD117)-positive gastrointestinal stromal tumors (GIST) who met the risk of recurrence inclusion criteria of the pivotal trial. This treatment regimen has been shown to improve recurrence-free survival (RFS) and overall survival (OS) for KIT+ GIST patients compared to 12 months of treatment<sup>3</sup>.

The US approval was based on data from an international, multicenter, open-label, Phase III clinical trial. Results of the study showed that 36 months of Glivec treatment significantly prolonged RFS compared to 12 months of Glivec treatment, which was a 54% reduction in the risk of recurrence ( $p < 0.0001$ ). In addition, 36 months of Glivec treatment resulted in a 55% reduction in the risk of death compared to one year of treatment ( $p = 0.0187$ ). The median time of follow-up was 42 months for RFS and 48 months for OS<sup>3</sup>.

“This approval represents another important step in the progress of KIT+ GIST treatment that began a decade ago when Glivec was first approved to treat metastatic KIT+ GIST,” said Hervé Hoppenot, President, Novartis Oncology. “With the significant survival benefit resulting from three years of adjuvant treatment, GIST patients now have a more effective regimen to help manage their disease.”

Gastrointestinal stromal tumors are a rare, life-threatening cancer of the gastrointestinal tract. The major cause of GIST is an abnormal form of the protein KIT which causes cells to grow uncontrollably and become cancerous<sup>4</sup>. Patients with GIST are at risk of recurrence following complete resection of primary GIST<sup>5</sup>.

In August 2011, the US National Comprehensive Cancer Network (NCCN) updated its clinical practice guidelines to recommend consideration of at least three years of adjuvant therapy with Glivec for patients with high-risk GIST<sup>2</sup>.

In addition to extending the Glivec label to three-year treatment duration in patients with KIT+ GIST after surgery, the FDA has agreed that all accelerated post-approval

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

commitments for this indication have been met, confirming the clinical benefit of adjuvant treatment with Glivec.

### **Study details**

The SSG XVIII clinical trial was conducted by the Scandinavian Sarcoma Group (SSG) and the Sarcoma Group of the Arbeitsgemeinschaft Internistische Onkologie (AIO). This trial was a multicenter, prospective, randomized study for the evaluation of adjuvant treatment with Glivec of histologically confirmed KIT+ GIST<sup>6</sup>.

The primary endpoint of the study was to compare, within the first five years, recurrence-free survival in patients with a greater than 50% estimated risk of GIST disease recurrence, following diagnosis and treatment with adjuvant Glivec for either 12 or 36 months. The secondary endpoints included overall survival and treatment safety<sup>1</sup>.

Three hundred ninety-seven patients entered the study. Inclusion criteria for risk of recurrence was defined as tumor diameter >5.0 cm and mitotic count >5/50 high power fields (HPFs); or tumor diameter >10.0 cm, any mitotic count; or tumor of any size with a mitotic count >10/50 HPFs; or tumors ruptured into the peritoneal cavity.

Recurrence-free survival was longer in the 36-month group compared to the 12-month group (HR 0.46, 95% CI 0.32-0.65;  $p < 0.0001$ ). Patients assigned to 36 months of Glivec after surgery had longer overall survival (HR 0.45, 95% CI 0.22-0.89;  $p = 0.0187$ ). Almost all patients experienced side effects while taking Glivec. Glivec was generally well tolerated. The proportion of patients who discontinued Glivec during the assigned treatment period for reasons other than GIST recurrence was 26% over the full three-year treatment period in the 36-month group and 13% in the 12-month group<sup>1</sup>.

Novartis provided the study drug and supported the study financially. Additional funding was received from the Academy of Finland, Cancer Society of Finland, Sigrid Juselius Foundation and Helsinki University Research Funds.

### **About Glivec (imatinib)**

Glivec<sup>®</sup> (imatinib) is approved in more than 110 countries for the treatment of all phases of Ph+ CML, for the treatment of adult patients with KIT (CD117)-positive gastrointestinal stromal tumors (GIST), which cannot be surgically removed and/or have metastasized and for the treatment of adult patients following complete surgical removal of KIT+ GIST.

### **Glivec Important Safety Information**

Glivec can cause fetal harm in pregnant woman. Glivec has been associated with severe edema (swelling) and serious fluid retention. Cytopenias (anemia, neutropenia, thrombocytopenia) are common, generally reversible and usually managed by withholding Glivec or dose reduction. Monitor blood counts regularly. Severe congestive heart failure and left ventricle dysfunction, severe liver problems including cases of fatal liver failure and severe liver injury requiring liver transplants have been reported. Use caution in patients with cardiac dysfunction and hepatic dysfunction. Monitor carefully.

Bleeding may occur. Severe gastrointestinal (GI) bleeding has been reported in patients with KIT+ GIST. Skin reactions, hypothyroidism in patients taking levothyroxine replacement, GI perforation, in some cases fatal and tumor lysis syndrome, which can be life threatening, have also been reported with Glivec. Correct dehydration and high uric acid levels prior to treatment. Long-term use may result in potential liver, kidney, and/or heart toxicities; immune system suppression may also result from long-term use. In patients with hypereosinophilic syndrome and heart involvement, cases of heart disease have been associated with the initiation of Glivec therapy. Growth retardation has been reported in children taking Glivec. The long-term effects of extended treatment with Glivec on growth in children are unknown.

The most common side effects include fluid retention, muscle cramps or pain and bone pain, abdominal pain, loss of appetite, vomiting, diarrhea, decreased hemoglobin, abnormal bleeding, nausea, fatigue and rash. Glivec should be taken with food and a large glass of water.

Please see full Prescribing Information.

### **Disclaimer**

The foregoing release contains forward-looking statements that can be identified by terminology such as “recommending,” “to recommend,” or similar expressions, or by express or implied discussions 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 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; 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; unexpected manufacturing issues; 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 innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care, cost-saving generic pharmaceuticals, preventive vaccines and diagnostic tools, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2011, the Group’s continuing operations achieved net sales of USD 58.6 billion, while approximately USD 9.6 billion (USD 9.2 billion excluding impairment and amortization charges) was invested in R&D throughout the Group. Novartis Group companies employ approximately 124,000 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>.

### **References**

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