Longer-term Phase III data show Novartis drug Tasigna® continues to surpass Gleevec® in slowing disease progression in patients with newly diagnosed CML

Dec 06, 2010

EAST HANOVER, N.J., Dec. 6, 2010 /PRNewswire/ --

- Fewer patients taking Tasigna for Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase progressed to advanced stages of the disease

- 24-month analysis confirms Tasigna induces deeper and more durable cytogenetic and molecular responses

- Tasigna now approved in the US and Switzerland for this indication; regulatory submissions under review in EU, Japan and other countries worldwide

Novartis announced today 24-month data showing that Tasigna® (nilotinib) 150 mg capsules continues to surpass Gleevec® (imatinib mesylate) tablets* in the treatment of adult patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (1). These new data, from the first Phase III comparison of the two oral therapies as initial treatment for this blood cancer, were presented at the 52nd Annual Meeting and Exposition of the American Society of Hematology (ASH) in Orlando, Florida.

With this longer-term follow-up at 24 months, first-line treatment with Tasigna at 300 mg twice daily was found to result in a lower incidence of progression to accelerated phase and blast crisis, compared to the standard approved dose of Gleevec 400 mg once daily. Patients receiving Tasigna also had a lower incidence of suboptimal response and treatment failure as defined by study criteria (1).

These data also showed that Tasigna induced deeper and more durable complete cytogenetic response (CCyR) and major molecular response (MMR) compared to Gleevec, as well as a significantly higher rate of an even deeper response – a trace amount of 0.0032% or less of the Bcr-Abl protein that causes Ph+ CML, which is considered a complete molecular response (CMR) (1). Fewer patients taking Tasigna in the study discontinued treatment due to adverse events compared to Gleevec (1). Tasigna and Gleevec were generally well tolerated.

"These 24-month Phase III data extend the evidence of clinical benefit for newly diagnosed patients with chronic phase Ph+ CML treated with Tasigna, compared to Gleevec," said Timothy P. Hughes, MD, ENESTnd study investigator and Clinical Professor at the University of Adelaide, Australia. "Now we can begin to evaluate the long-term treatment outcomes of patients who achieve and maintain deep reductions in Bcr-Abl on Tasigna."

Rates of MMR and CCyR remain statistically higher for Tasigna versus Gleevec at the 24-month minimum follow-up. MMR was achieved by 71% of patients taking Tasigna 300 mg twice daily and 67% of patients taking Tasigna 400 mg twice daily, compared to 44% of patients taking Gleevec by 24 months. Durable MMR rates were statistically significantly higher in the Tasigna 300 mg twice daily and Tasigna 400 mg twice daily arms compared to Gleevec 400 mg once daily (42%, 39% and 21% respectively). Significantly more patients achieved CCyR in the Tasigna 300 mg and 400 mg arms compared to the Gleevec arm at 87% and 85% vs. 77% respectively by 24 months.

The US Food and Drug Administration (FDA) and Swissmedic have approved Tasigna in this first-line indication. In September, Novartis received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) recommending European Commission approval for Tasigna for this indication. Regulatory submissions are under review in the European Union, Japan and other countries worldwide.

This year, Novartis also began a collaboration with molecular diagnostics company Cepheid to develop a new FDA cleared/approved Bcr-Abl test, which adheres to the International Scale. The goal of the collaboration is to help doctors more reliably monitor Ph+ CML patients. Cepheid and Novartis also will develop a next generation test, which is expected to enable even more sensitive testing, indicating the depth of a patient's response to tyrosine kinase inhibitors, including Tasigna and Gleevec. Currently there are no FDA cleared/approved tests to monitor for Bcr-Abl.

"The creation and introduction of Gleevec revolutionized the treatment of Ph+ CML by substantially improving overall survival rates for patients," said Herve Hoppenot, President, Novartis Oncology. "We are encouraged by the ongoing clinical development of Tasigna as a new treatment showing that at 24 months it continues to surpass Gleevec in slowing disease progression in patients with newly diagnosed chronic phase Ph+ CML."

Another study will be presented at this year's annual ASH meeting which provides further support for the use of Tasigna in patients with newly diagnosed Ph+ CML. The Gruppo Italiano Malattie Ematologiche dell'Adulto (GIMEMA) study, an ongoing, open-label, single-stage, multicenter Phase II clinical trial, will be presented on Monday, December 6, 2010 (2).

ENESTnd Study Details

The clinical trial, ENESTnd (Evaluating Nilotinib Efficacy and Safety in Clinical Trials of Newly Diagnosed Ph+ CML Patients), is a Phase III randomized, open-label, multicenter trial comparing the efficacy and safety of Tasigna versus Gleevec 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 Gleevec 400 mg once daily (n = 283). The primary endpoint was MMR at 12 months; the key secondary endpoint was durable MMR at 24 months (patients having MMR when evaluated at both 12 and 24 months) (1). 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 (1). Planned follow-up is for five years. Patients on the Gleevec treatment arm who had suboptimal response or treatment failure were allowed to escalate dose and/or switch to Tasigna via a protocol extension. These data, presented at ASH, were the 24-month minimum

follow-up.

Results showed that fewer patients progressed to accelerated phase or blast crisis while on treatment with Tasigna at 300 mg twice daily (n = 2) and 400 mg twice daily (n = 3) versus Gleevec at 400 mg once daily (n = 12) (1) with 24 months of minimum follow-up demonstrating a significant improvement in disease control.

These data also showed that nearly three times more patients taking Tasigna 300 mg twice daily achieved CMR – defined as a trace amount of 0.0032% or less of the Bcr-Abl protein that causes Ph+ CML – with Tasigna 300 mg twice daily (n = 70) than with Gleevec (n = 25) by 24-months (1).

All patients had a minimum of 24 months of treatment or discontinued early; the median follow-up was 25 months. Overall, 75%, 78% and 68% of patients remained in the study on Tasigna 300 mg twice daily, Tasigna 400 mg twice daily and Gleevec 400 mg once daily, respectively (1).

Both Tasigna and Gleevec were generally well tolerated overall. Rates of discontinuation due to adverse events or laboratory abnormalities were 9% for Tasigna 300 mg twice daily, 13% for Tasigna 400 mg twice daily and 11% for Gleevec 400 mg once daily (1). No patients treated with Tasigna in the study had prolongation of QT interval >500 milliseconds (1). No sudden deaths occurred in any of the treatment arms (1).

About Philadelphia Chromosome-Positive Chronic Myeloid Leukemia (Ph+ CML)

Chronic myeloid leukemia 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® (nilotinib) is indicated for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase. The effectiveness of Tasigna is based on major molecular response and cytogenetic response rates. The study is ongoing and further data will be required to determine long-term outcome.

Tasigna is indicated for the treatment of chronic phase and accelerated phase Philadelphia chromosome positive chronic myelogenous leukemia (Ph+ CML) in adult patients resistant or intolerant to prior therapy that included imatinib. The effectiveness of Tasigna is based on hematologic and cytogenetic response rates. There are no controlled trials demonstrating a clinical benefit, such as improvement in disease-related symptoms or increased survival.

Tasigna has been approved in more than 85 countries for the treatment of chronic phase and accelerated phase Ph+ CML in adult patients resistant or intolerant to at least one prior therapy, including Gleevec. The effectiveness of Tasigna for this indication is based on hematologic and cytogenetic response rates. There are no controlled trials demonstrating a clinical benefit, such as improvement in disease-related symptoms or increased survival.

Tasigna Important Safety Information

WARNING: QT PROLONGATION AND SUDDEN DEATHS

Tasigna prolongs the QT interval. Sudden deaths have been reported in patients receiving nilotinib. Tasigna should not be used in patients with hypokalemia, hypomagnesemia, or long QT syndrome. Hypokalemia or

hypomagnesemia must be corrected prior to Tasigna administration and should be periodically monitored. Drugs known to prolong the QT interval and strong CYP3A4 inhibitors should be avoided. Patients should avoid food 2 hours before and 1 hour after taking dose. A dose reduction is recommended in patients with hepatic impairment. ECGs should be obtained to monitor the QTc at baseline, seven days after initiation, and periodically thereafter, as well as following any dose adjustments.

Contraindications

Do not use in patients with hypokalemia, hypomagnesemia, or long QT syndrome.

Warnings and Precautions

Myelosuppression

Treatment with Tasigna (nilotinib) can cause Grade 3/4 thrombocytopenia, neutropenia and anemia. Perform complete blood counts every two weeks for the first 2 months and then monthly thereafter, or as clinically indicated. Myelosuppression was generally reversible and usually managed by withholding Tasigna temporarily or dose reduction.

QT Prolongation

Tasigna prolongs the QT interval. ECGs should be performed at baseline, seven days after initiation, periodically as clinically indicated, and following dose adjustments. Correct hypokalemia or hypomagnesemia prior to administration and monitor periodically.

Significant prolongation of the QT interval may occur when Tasigna is inappropriately taken with food, and/or strong CYP3A4 inhibitors and/or medicinal products with a known potential to prolong QT. Therefore, co-administration with food must be avoided and concomitant use with strong CYP3A4 inhibitors and/or medicinal products with a known potential to prolong QT should be avoided. The presence of hypokalemia and hypomagnesemia may further enhance this effect.

Sudden Deaths

Sudden deaths have been reported in patients with resistant or intolerant Ph+ CML receiving nilotinib (n = 867; 0.6%). A similar incidence was also reported in the expanded access program for patients with resistance or intolerant Ph+CML. The relative early occurrence of some of these deaths relative to the initiation of nilotinib suggests the possibility that ventricular repolarization abnormalities may have contributed to their occurrence.

Elevated Serum Lipase

Caution is recommended in patients with a history of pancreatitis. In case lipase elevations are accompanied by abdominal symptoms, doses should be interrupted and appropriate diagnostics should be considered to exclude pancreatitis. Check serum lipase levels monthly or as clinically indicated.

Hepatotoxicity

Serum bilirubin and hepatic transaminases

The use of Tasigna may result in elevations in bilirubin, AST/ALT, and alkaline phosphatase. Hepatic function tests should be checked monthly or as clinically indicated.

Electrolyte Abnormalities

Tasigna can cause hypophosphatemia, hypokalemia, hyperkalemia, hypocalcemia, and hyponatremia. Correct

electrolyte abnormalities prior to initiating Tasigna and monitor periodically during therapy.

Hepatic Impairment

Nilotinib exposure is increased in patients with impaired hepatic function. A lower starting dose is recommended for patients with mild to severe hepatic impairment and QT interval should be monitored closely.

Drug Interactions

The concomitant use of QT prolonging drugs and strong inhibitors or inducers of CYP3A4 should be avoided as they may affect serum concentration of Tasigna.

Concomitant strong CYP3A4 inhibitors

The concomitant use of strong CYP3A4 inhibitors or anti-arrhythmic drugs (including, but not limited to amiodarone, disopyramide, procainamide, quinidine and sotalol) and other drugs that may prolong QT interval (including, but not limited to chloroquine, clarithromycin, haloperidol, methadone, moxifloxacin, and pimozide) should be avoided. Should treatment with any of these agents be required, it is recommended that therapy with Tasigna be interrupted. If interruption of treatment with Tasigna is not possible, patients who require treatment with a drug that prolongs QT or strongly inhibits CYP3A4 should be closely monitored for prolongation of the QT interval. If patients must be co-administered a strong CYP3A4 inhibitor, based on pharmacokinetic studies, consider a dose reduction to 300 mg once daily in patients with resistant or intolerant Ph+ CML or to 200 mg once daily in patients with newly diagnosed Ph+ CML-CP. If the strong inhibitor is discontinued, a washout period should be allowed before Tasigna is adjusted upward to the indicated dose. Close monitoring for prolongation of the QT interval is indicated for patients who cannot avoid strong CYP3A4 inhibitors. Grapefruit products and other foods that are known to inhibit CYP3A4 should also be avoided.

Concomitant strong CYP3A4 inducers

The concomitant use of strong CYP3A4 inducers should be avoided (including, but not limited to, dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifapentin, phenobarbital). Patients should also refrain from taking St John's Wort. Based on the nonlinear pharmacokinetic profile of nilotinib, increasing the dose of Tasigna when co-administered with such agents is unlikely to compensate for the loss of exposure. Tasigna is a competitive inhibitor of CYP3A4, CYP2C8, CYP2C9, CYP2D6, and UGT1A1. In vitro studies also suggest that nilotinib may induce CYP2B6, CYP2C8 and CYP2C9, and decrease the concentrations of drugs which are eliminated by these enzymes. Single-dose administration of Tasigna to healthy subjects did not change the pharmacokinetics and pharmacodynamics of warfarin (a CYP2C9 substrate). The ability of Tasigna to induce metabolism has not been determined in vivo. Caution should be exercised when co-administering Tasigna with substrates for these enzymes that have a narrow therapeutic index. Tasigna inhibits human P-glycoprotein. If Tasigna is administered with drugs that are substrates of Pgp, increased concentrations of the substrate are likely and caution should be exercised.

Proton pump inhibitors

Since proton pump inhibitors affect pH of the upper GI tract for an extended period, separation of doses may not eliminate the interaction, The concomitant use of proton pump inhibitors with Tasigna should be used with caution.

Food Effects

Food increases blood levels of Tasigna. Patients should avoid food 2 hours before and at least one hour after

the dose is taken.

Total Gastrectomy

The exposure of nilotinib is reduced in patients with total gastrectomy. More frequent follow-up of these patients should be considered. Dose increase or alternative therapy may be considered in patients with total gastrectomy.

Lactose

Since the capsules contain lactose, Tasigna is not recommended for patients with rare hereditary problems of galactose intolerance, severe lactose deficiency with a severe degree of intolerance to lactose-containing products, or of glucose-galactose malabsorption.

Use in Pregnancy

There are no adequate and well-controlled studies of Tasigna in pregnant women. However, Tasigna may cause fetal harm when administered to a pregnant woman. Women of child-bearing potential should avoid becoming pregnant while taking Tasigna and should be advised of the potential hazard to the fetus if they do.

Adverse Reactions

Newly Diagnosed Ph+ CML-CP:

The most common (>10%) non-hematologic Adverse Drug Reactions (ADRs) were rash , pruritus , headache, nausea, fatigue, and myalgia . Upper abdominal pain, alopecia, constipation, diarrhea, dry skin, muscle spasms, arthralgia, abdominal pain, peripheral edema, and asthenia were observed less commonly (≤10% and >5%) and have been mild to moderate severity, manageable, and generally did not require dose reduction. Pleural and pericardial effusions occurred in 1% of patients. Gastrointestinal hemorrhage was reported in 0.4% of patients.

The most common hematologic ADRs (all grades) were myelosuppression including: thrombocytopenia (17%), neutropenia (15%), and anemia (7%).

Resistant or Intolerant Ph+ CML-CP and CML-AP:

In chronic phase patients, the most commonly reported adverse drug reactions (>10%) were rash, pruritus, nausea, fatigue, headache, constipation, diarrhea, and vomiting. The common serious drug-related adverse reactions were thrombocytopenia and neutropenia.

In accelerated phase patients, the most commonly reported adverse drug reactions (>10%) were rash, pruritus, and constipation. The common serious adverse drug reactions were thrombocytopenia, neutropenia, pneumonia, febrile neutropenia, leukopenia, intracranial hemorrhage, elevated lipase and pyrexia.

Dose Adjustments or Modifications

Tasigna may need to be temporarily withheld and/or dose reduced for QT prolongation, hematological toxicities that are not related to underlying leukemia, clinically significant moderate or severe nonhematologic toxicities, laboratory abnormalities, or concomitant use of strong CYP3A4 inhibitors.

For Grade 3 to 4 lipase elevations, dosing should be withheld, and may be resumed at 400 mg once daily. For Grade 3 to 4 bilirubin or hepatic transaminase elevations, dosing should be withheld, and may be resumed at 400 mg once daily.

Hepatic impairment

If possible, consider alternative therapies. If Tasigna must be administered to patients with hepatic impairment, a lower starting dose is recommended in patients with hepatic impairment and QT interval should be monitored. The following dose reduction should be considered:

Newly diagnosed Ph+ CML-CP

For patients with mild (Child-Pugh Class A), moderate (Child-Pugh Class B) and severe hepatic impairment (Child-Pugh Class C) , an initial dosing regimen of 200 mg twice daily followed by dose escalation to 300 mg twice daily based on tolerability.

Resistant or intolerant Ph+ CML-CP and CML-AP

For patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment, an initial dosing regimen of 300 mg twice daily followed by dose escalation to 400 mg twice daily based on tolerability should be considered. For patients with severe hepatic impairment (Child-Pugh Class C), a starting dose of 200 mg twice daily followed by a sequential dose escalation to 300 mg twice daily and then to 400 mg twice daily based on tolerability should be considered.

Other Patients in whom Tasigna Should be Used with Caution

Tasigna should not be used during pregnancy. Sexually active female patients should use effective contraception during treatment. Women should not breast feed while taking Tasigna. The safety and effectiveness of Tasigna in pediatric patients have not been established.

Please see accompanying full prescribing information.

About Gleevec (7)

Gleevec® (imatinib mesylate) tablets are indicated for newly diagnosed adult patients with Philadelphia chromosome–positive chronic myeloid leukemia (Ph+ CML) in the chronic phase (CP). Gleevec is also indicated for the treatment of patients with Ph+ CML in blast crisis (BC), accelerated phase (AP), or in CP after failure of interferon-alpha therapy.

Who Should Not Take Gleevec

Gleevec should not be taken by women who are or could be pregnant. Fetal harm can occur when administered to pregnant women; therefore, women should not become pregnant, as well as be advised of the potential risk to the unborn child if Gleevec is used during pregnancy. Gleevec should also not be taken by women who are breast-feeding because of the potential for serious adverse reactions in nursing infants. Sexually active females should use adequate birth control while taking Gleevec.

Be sure to talk to your doctor and/or healthcare professional about these issues before taking Gleevec.

Warnings and Precautions

Gleevec is often associated with edema (swelling) and serious fluid retention. It is important that patients be weighed and monitored regularly for signs and symptoms of serious fluid retention, or unexpected weight gain. Patients experiencing unexpected rapid weight gain should speak to their doctor about appropriate supportive care treatment. Studies have shown that edema (swelling) tended to occur more often among patients who are 65 and older or those taking higher doses of Gleevec. If you experience severe fluid retention, your doctor may stop your treatment with Gleevec until the fluid retention has been managed.

Cytopenias (reduction or lack of certain cell elements in blood circulation), such as anemia, have occurred. Your doctor will perform complete blood counts weekly for the first month, biweekly for the second month, and periodically thereafter. In most cases, your doctor will reduce or interrupt your Gleevec therapy; in rare cases, your doctor may discontinue treatment. If the cytopenia is severe, your doctor may reduce your dose or temporarily stop your treatment with Gleevec.

Severe congestive heart failure and left ventricle dysfunction have been reported, particularly in patients with other health issues and risk factors. Patients with heart disease or risk factors will be monitored and treated for the condition.

Severe liver problems (hepatotoxicity) may occur. Your doctor will check your liver function before beginning treatment and continue to monitor liver function as needed. If you experience severe liver problems, your doctor may stop your treatment with Gleevec until the liver problem has been managed.

Bleeding may occur. Severe gastrointestinal (GI) bleeding has been reported in patients with Ph+ CML.

In patients with hypereosinophilic syndrome (a condition with increased eosinophils, which are a type of white blood cell) and heart involvement, cases of heart disease (cardiogenic shock/left ventricular dysfunction) have been associated with the initiation of Gleevec therapy. Speak to your doctor regarding appropriate supportive care or discontinuing Gleevec.

Skin reactions, such as fluid-filled blisters, have been reported with the use of Gleevec.

Clinical cases of hypothyroidism (reduction in thyroid hormones) have been reported in patients taking levothyroxine replacement during treatment with Gleevec. Your doctor should closely monitor your thyroid hormone levels.

Long-term use may result in potential liver, kidney, and/or heart toxicities; immune system suppression may also result from long-term use.

Gleevec can cause fetal harm when administered to a pregnant woman. Women should be aware of the potential harm to the fetus. Be sure to inform your doctor if you are or think you may be pregnant. You should not breast-feed while taking Gleevec.

GI perforation (small holes or tears in the walls of the stomach or intestine), in some cases fatal, has been reported.

Gleevec Important Safety Information

The following serious side effects have been reported in patients taking Gleevec: severe fluid retention, (which can cause swelling around the eyes or swelling of the lower legs, lungs, and heart; fatal in rare cases), increased pressure in the heart or brain (fatal in rare cases), low levels of certain blood cells, heart failure/cardiogenic shock, liver problems, hemorrhage (abnormal bleeding), skin blistering and low levels of thyroid hormone.

Your doctor will check you closely for any side effects to stop more serious complications from occurring. Patients with heart disease or risk factors for heart failure should also be monitored carefully.

Gleevec is sometimes associated with stomach or intestinal irritation. Gleevec should be taken with food and a large glass of water to minimize this problem. There have been rare reports, including deaths, of stomach or intestinal perforation (a small hole or tear).

If you are experiencing any of the above-mentioned side effects, please be sure to speak with your doctor

immediately.

Common Side Effects of Gleevec

Almost all patients treated with Gleevec experience side effects at some time. Most side effects are mild to moderate in severity. Some common side effects you may experience include fluid retention, muscle cramps or pain and bone pain, vomiting, diarrhea, decreased hemoglobin, nausea, fatigue, rash and anorexia (loss of appetite).

If you are experiencing any of the above-mentioned side effects, please be sure to speak with your doctor immediately.

The severity of some side effects may be reduced with the help of other medicines and advice from your doctor, while others may require stopping Gleevec therapy for a while or changing the dose. However, in some cases, Gleevec therapy may need to be discontinued.

Tell your doctor if you experience side effects during therapy with Gleevec, including fever, shortness of breath, blood in your stools, jaundice (yellowing of the skin and/or eyes), sudden weight gain, symptoms of heart failure, or if you have a history of heart disease or risk factors for heart disease.

After the approval of Gleevec, the following adverse events have been reported in patients treated with Gleevec: compression of the heart due to increased fluid, swelling of the brain, GI perforation (holes in the stomach or intestine), and sudden lung failure. These events, including some fatalities, may or may not have been drug related.

Take Gleevec exactly as prescribed. Do not change your dose or stop taking Gleevec unless you are told to do so by your doctor. If you miss a dose, take your dose as soon as possible, unless it is almost time for your next dose. In this case, your missed dose should not be taken. A double dose should not be taken to make up for any missed dose. You should take Gleevec with a meal and a large glass of water.

Do not take any other medications without talking to your doctor or pharmacist first, including over-the-counter medications such as Tylenol® (acetaminophen); herbal products (St. John's wort, Hypericum perforatum); Coumadin® (warfarin sodium); rifampin; erythromycin; metoprolol; ketoconazole; and Dilantin® (phenytoin). Taking these with Gleevec may affect how they work, or affect how Gleevec works.

You should also tell your doctor if you are taking or plan to take iron supplements. Patients should also avoid grapefruit juice and other foods that may affect how Gleevec works.

Tylenol (acetaminophen) is a registered trademark of McNeil Consumer & Specialty Pharmaceuticals, a division of McNeil PPC, Inc. Coumadin (warfarin sodium) is a registered trademark of Bristol-Myers Squibb Company. Dilantin (phenytoin) is a registered trademark of Parke-Davis, a division of Pfizer Inc.

*For more detailed study information, please see full Prescribing Information.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as "under review," "expected," "goal," 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 Gleevec. 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 Gleevec 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 Gleevec will achieve any particular levels of revenue in the future. In particular, management's expectations regarding Tasigna and Gleevec 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; 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

Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which provides healthcare solutions that address the evolving needs of patients and societies. Focused solely on healthcare, the Novartis Group offers a diversified portfolio to best meet these needs: innovative medicines, preventive vaccines, diagnostic tools, cost-saving generic pharmaceuticals and consumer health products. The Novartis Group is the only company with leading positions in each of 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.us.novartis.com.

Novartis is on Twitter. Sign up to follow @Novartis at http://twitter.com/novartis.

* Known as Glivec® (imatinib) outside the US, Canada and Israel.

References

1. Hughes T, et al. ENESTnd Update: Continued Superiority of Nilotinib Versus Imatinib In Patients with Newly Diagnosed Chronic Myeloid Leukemia In Chronic Phase (CML-CP). 52nd Annual Meeting of the American Society of Hematology. Abstract No. 207. December 6, 2010.
2. Rosti G, et al. Excellent Outcomes at 3 Years with Nilotinib 800 Mg Daily In Early Chronic Phase, Ph+ Chronic Myeloid Leukemia (CML): Results of a Phase 2 GIMEMA CML WP Clinical Trial. 52nd Annual Meeting of the American Society of Hematology. Abstract No. 359. December 6, 2010.
3. National Cancer Institute. General Information About Chronic Myelogenous Leukemia (PDQ). http://www.cancer.gov/cancertopics/pdq/treatment/CML/patient/. Accessed March 2009.
4. American Cancer Society. Detailed Guide: CML. What are the key statistics about CML? (Sept 2008 revision) Available at: http://www.cancer.org/cancer/leukemia-chronicmyeloidcml/detailedguide/leukemia-chronic-myeloid-myelogenous-key-statistics. Accessed April 2009.
5. Central European Leukemia Study Group. About CML. [Cited 2009 Jan 13] Available from: http://www.cml-info.com/de/healthcare-professionals/about-cml.html.
6. Tasigna (nilotinib) Prescribing Information. East Hanover, New Jersey, USA: Novartis Pharmaceuticals Corporation; November 2010. http://www.pharma.us.novartis.com/product/pi/pdf/tasigna.pdf.
7. Gleevec® (imatinib mesylate) Tablets Prescribing Information. East Hanover, New Jersey, USA: Novartis

Pharmaceuticals Corporation; November 2010.
http://www.pharma.us.novartis.com/product/pi/pdf/gleevec_tabs.pdf.

Novartis Media Relations

Media only:	Investors only:
Amy Vinci	Richard Jarvis
Novartis Oncology	Novartis Corporation
P: +1 862 778 6309	P: +1 212 830 2433

Dana Kahn Cooper

P: +1 732 817 1800

e-mail: media.relations@novartis.com e-mail: investor.relations@novartis.com

SOURCE Novartis

---

myelogenous-key-statistics
6. http://www.cml-info.com/de/healthcare-professionals/about-cml.html
7. http://www.pharma.us.novartis.com/product/pi/pdf/tasigna.pdf
8. http://www.pharma.us.novartis.com/product/pi/pdf/gleevec_tabs.pdf
9. mailto:media.relations@novartis.com
10. mailto:investor.relations@novartis.com