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Novartis presents new data from large European study reinforcing the benefit of first-line Tasigna® in newly-diagnosed patients with CML

- *Patients on Tasigna achieved rapid and high rates of molecular response with a very low rate of progression to advanced disease*
- *ENEST1st data confirm the favorable benefit/risk profile of Tasigna in newly-diagnosed CML patients seen in the pivotal ENESTnd study*
- *Safety results in this Phase 3b study of more than 1,000 European patients were consistent with the known safety profile of Tasigna*

Basel, June 13, 2015 – Novartis today announced results from the Phase 3b ENEST1st study in over 1,000 patients with newly-diagnosed, BCR-ABL positive chronic myeloid leukemia (CML), confirming the benefits of first-line Tasigna treatment seen in earlier trials. The final results of this large study, conducted in 26 European countries, were presented at the 20th Congress of the European Hematology Association (EHA) in Vienna.

"These results show patients with BCR-ABL positive CML in chronic phase receiving first-line treatment with Tasigna achieved rapid and high rates of molecular response and had a very low rate of progression to advanced disease," said Dr. Andreas Hochhaus, Head of the Department of Hematology and Medical Oncology, Jena University Hospital, Germany. "These findings from 26 countries, which are a collaboration of 307 trial sites and 14 standardized laboratories monitoring the incidence of MR4.0 as primary endpoint, confirm and complement data from the pivotal ENESTnd trial."

The primary endpoint in ENEST1st was the rate of Molecular Response 4 (MR4.0) at 18 months. MR4.0, which is a 4 log reduction in BCR-ABL, represents a very low level of detectable BCR-ABL, the cause of Ph+ CML (measured as BCR-ABL ≤0.01% on the International Scale [BCR-ABL^{IS}] or undetectable BCR-ABL in cDNA with ≥10,000 ABL transcripts).

At 18 months, 38.4% of Tasigna-treated patients (n=1,052) reached MR4.0. These data demonstrate high rates of early and deep molecular response with Tasigna. The rate of disease progression in the study was low, with six patients, or 0.6%, advancing to the accelerated phase/blast crisis stage of the disease. Despite the higher median age of patients in ENEST1st than in previous Tasigna studies, the safety results were consistent with the known safety profile of Tasigna. The most common adverse events (AE) were rash, itch and headache. Grade 3/4 AEs related to hepatotoxicity and pancreatitis occurred in 0.4% and 0.6% of patients, respectively. Grade 3/4 thrombocytopenia (low blood platelet count) and neutropenia (low white blood cell count) occurred in 6.0% and 4.8% of patients, respectively.

"Our commitment to CML remains strong and is exemplified by this trial, as well as further study of deep molecular response with Tasigna and the possibility for some patients with Ph+ CML to stop their treatment and achieve sustained treatment-free

remission," said Bruno Strigini, President, Novartis Oncology. "In addition, we are developing new compounds with different mechanisms of action, which could help address the resistance to existing medications that some patients experience."

ENEST1st Study Details[1]
ENEST1st (Evaluating Nilotinib Efficacy and Safety Trial as First-Line Treatment) is a Phase 3b, open-label study that evaluated the efficacy and safety of Tasigna 300 mg twice daily (BID) in a large population of adult patients with newly diagnosed CML-chronic phase (CP) using a network of 14 European Treatment and Outcome Study (EUTOS) standardized laboratories to monitor MR.

The study was conducted in 26 European countries with 1,089 patients treated. Specifically, 90.3% of patients were Philadelphia chromosome positive (Ph+) and 97.0% had typical BCR-ABL transcripts. Sokal risk scores were low, intermediate and high in 34.6%, 37.5% and 18.1% of patients, respectively (9.8% missing). EUTOS scores were low in 82.6% and high in 8.6% of patients (8.7% missing). A total of 80.9% of patients completed 24 months of treatment; 19.1% discontinued early, most frequently due to AEs (10.7%). The AEs seen in this study were consistent with the known safety profile of Tasigna. Thirteen patients (1.2%) died by 24 months; of those 13 deaths, one was attributed to CML progression (16 months after study drug discontinuation).

The primary endpoint was the rate of MR4.0 (BCR-ABL ≤0.01% on the International Scale [BCR-ABL^{IS}] or undetectable BCR-ABL in cDNA with ≥10,000 ABL transcripts) at 18 months. The MR4.0 rate in all treated patients with ≤3 months of prior Glivec treatment (n=1,052) was 38.4% at 18 months and 40.4% at 24 months. As assessed with multicenter molecular monitoring, MR rates in this study provided prospective confirmation of the centrally reviewed MR rates in the pivotal ENESTnd study. In ENESTnd, Tasigna demonstrated higher rates of early and deeper sustained molecular response, including MR4.5, and a reduced risk of progression compared to Glivec.

Consistent with prior studies, ENEST1st demonstrated the importance of early molecular response to frontline treatment. Molecular testing can vary in countries around the world, thus reinforcing the importance of these consistent findings. Patients with BCR-ABL1^{IS} ≤ 1% at 3 months achieved the highest rates of MMR, MR4.0, and MR4.5 at later time points, while no patient with BCR-ABL1^{IS} > 10% at 3 months achieved MR4.0 by 24 months.

Within the study duration of two years, the most common AEs of any cause were rash (21.4%), itch (16.5%), and headache (15.2%). Study investigators conclude relatively low rates of these AEs may reflect improvements in the management of Tasigna-treated patients. Peripheral artery disease (PAD) occurred in 1.9% of patients, ischemic heart disease (IHD) in 3.4%, and ischemic cerebrovascular conditions (ICVE) in 0.8%; 0.6% of patients had excess fluid around the lung. These findings are consistent with what was seen in ENESTnd at the same duration of therapy. The most frequently observed grade 3/4 biochemical abnormalities were decreased phosphate (14.3%) and increased lipase (7.2%); glucose and lipid monitoring was not mandated in the study protocol.

Novartis Commitment to CML
Over the past several decades, Novartis research in Ph+ CML has helped transform this fatal disease to a chronic condition and today, the company continues its long-standing commitment to the global CML community.

About Tasigna (nilotinib)
Tasigna® (nilotinib) is approved in more than 110 countries for the treatment of chronic phase and accelerated phase Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML) in adult patients resistant or intolerant to at least one prior therapy,

including Glivec® (imatinib), and in more than 85 countries for the treatment of adult patients with newly diagnosed Ph+ CML in chronic phase.

Tasigna Important Safety Information
Use with caution in patients with uncontrolled or significant cardiac disease and in patients who have or may develop prolongation of QTc. Low levels of potassium or magnesium must be corrected prior to Tasigna administration. Monitor closely for an effect on the QTc interval. Baseline ECG is recommended prior to initiating therapy and as clinically indicated. Uncommon cases (0.1 to 1%) of sudden death have been reported in clinical studies in patients with significant risk factors.

Use with caution in patients with liver impairment, with a history of pancreatitis and with total gastrectomy. Patients with rare hereditary problems of galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption should not use Tasigna. Tasigna may cause fetal harm in pregnant women. Women taking Tasigna should not breastfeed.

The most frequent Grade 3 or 4 adverse events are hematological (neutropenia and thrombocytopenia) which are generally reversible and usually managed by withholding Tasigna temporarily or dose reduction. Monitor blood counts regularly. Pancreatitis has been reported. The most frequent non-hematologic adverse events were rash, pruritus, nausea, fatigue, headache, alopecia, myalgia, constipation and diarrhea. Most of these adverse events were mild to moderate in severity.

Please see full Prescribing Information available at www.tasigna.com.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as “commitment,” “remains,” “further study,” “possibility,” “developing,” “could,” “continues,” “long-standing,” or similar terms, or by express or implied discussions regarding potential new indications or labeling for Tasigna, or regarding potential future revenues from Tasigna. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that Tasigna will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that Tasigna will be commercially successful in the future. In particular, management’s expectations regarding Tasigna could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company’s ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected manufacturing issues, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. 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 and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2014, the Group achieved net sales of USD 58.0 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 120,000 full-time-equivalent associates. Novartis products are available in more than 180 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

1. Tsai, J, et al. Efficacy and safety of frontline nilotinib in 1089 European patients with CML in chronic phase: ENEST1st Final Analysis. Oral Presentation. Abstract #S486. 20th Congress of the European Hematology Association. 2015. Vienna, Austria.

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