Novartis data shows Treatment-free Remission rates are consistently above 50% regardless of reason for switch to Tasigna® from Glivec®

- **ENESTop post-hoc analysis provides further insights into Treatment-free Remission (TFR) among Ph+ CML switch patients**

- **The Tasigna TFR trials, including ENESTop, demonstrate our continued commitment to the CML community**

**Basel, December 5, 2016** - Novartis today announced at the 58th American Society of Hematology (ASH) Annual Meeting & Exposition new data from the Tasigna® (nilotinib) ENESTop Treatment-free Remission (TFR) study, which demonstrate that TFR rates are consistent among Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) patients who switched from Glivec® (imatinib)* due to intolerance, resistance or physician preference. ENESTop evaluated stopping Tasigna treatment in eligible Ph+ CML adults with chronic phase disease after they achieved and sustained deep molecular response (MR) for at least one year with Tasigna but had not achieved and sustained this response previously1,2. Results of this post-hoc analysis were presented today in an oral session (ASH Abstract #792).

“Findings from this post-hoc analysis of ENESTop suggest that the reason for switching from Glivec to Tasigna did not impact a patient's chance of maintaining TFR,” said Timothy P. Hughes, MD, ENESTop study investigator, Cancer Theme Leader at the South Australian Health and Medical Research Institute and Clinical Professor at the University of Adelaide, Australia. “CML is considered a chronic disease due to the success of tyrosine kinase inhibitors (TKIs), but there remains a need for continued advancements and these findings are an exciting and important contribution to clinical research in CML treatment.”

This new post-hoc analysis of ENESTop evaluated rates of TFR at 48 weeks after stopping treatment with Tasigna among subgroups of patients who switched from Glivec due to intolerance, resistance or physician preference. The analysis, which included 125 patients, found that more than 50% of patients in each of the subgroups maintained TFR at 48 weeks and that the proportion of patients who maintained TFR at 48 weeks was similar across the three subgroups: 30 of 51 (58.8%; 95% confidence interval [CI], 44.2%-72.4%) in the intolerance subgroup, 16 of 30 (53.3%; 95% CI, 34.3%-71.7%) in the resistance subgroup, and 27 of 44 (61.4%; 95% CI, 45.5%-75.6%) in the physician preference subgroup1. One patient who stopped treatment in the ENESTop trial was found to have had atypical transcripts and was excluded from this analysis3.

ENESTop is part of a larger Tasigna TFR clinical trial program to evaluate the potential to maintain molecular response after stopping therapy in adult patients with Ph+ CML in the chronic phase who achieved a sustained deep level of molecular response with Tasigna. In the primary analysis of ENESTop, nearly 6 out of 10 (57.9%) patients (95% CI, 48.8%-66.7%) who achieved a sustained deep molecular response following at least three years of Tasigna therapy maintained a molecular response 48 weeks after stopping treatment4. No new major safety findings were observed in ENESTop in patients treated with Tasigna beyond those in...
the known safety profile of Tasigna. The rates of all grade musculoskeletal pain were 42.1% in
the first year of the TFR phase versus 14.3% while still taking Tasigna in the consolidation
phase. No patients progressed to advanced phase/blast crisis. These results were previously
presented at the American Society of Clinical Oncology (ASCO) Annual Meeting and the
Annual Congress of European Hematology Association (EHA) in June 2016. Results from
additional studies in the Tasigna TFR clinical trial program were also presented at ASH in
poster sessions, including ENESTpath (Abstract #3094) and ENESTfreedom (Abstract
#3066).

“Our mission at Novartis is to help transform cancer therapy through bold science and
innovation, and there is no better example of this than our support of eight TFR studies in
patients with CML,” said Bruno Strigini, CEO of Novartis Oncology. “Our further exploration of
results from the ENESTop trial, beyond the primary analysis, reinforces our ongoing
commitment to CML patients and contributes to the growing body of science that goes into
treating this cancer.”

Regular and frequent molecular monitoring with a well-validated assay able to measure BCR-
ABL transcript levels down to MR4.5 is an important part of Tasigna TFR studies. Frequent
patient monitoring during TFR allows timely determination of loss of MR4.0 or major molecular
response (MMR) and the need for treatment initiation.

Stopping CML treatment is currently not a clinical recommendation and should only be
attempted in the context of a clinical study. Discontinuation of treatment in ENESTop was
conducted under the conditions of the trial and in patients who met the rigorous predefined
criteria of the trial.

Novartis commitment to CML
Novartis is supporting eight studies as part of its TFR clinical trial program, which includes
ENESTop, as well as three other ongoing company-sponsored TFR studies and four
investigator-initiated studies that are now underway in more than 100 global sites across 40
countries. Over the past several decades, Novartis research in Ph+ CML has helped
transform the disease from a fatal leukemia to a chronic condition and, today, the company
continues its long-standing commitment to the global CML community. Novartis follows the
science and builds upon existing evidence to explore what could be the next major
contribution in the treatment of Ph+ CML through these TFR trials as well as investigational
compounds.

About ENESTop
ENESTop (Evaluating Nilotinib Efficacy and Safety Trial) is an open-label Phase II study
involving 163 Ph+ CML patients, conducted at 63 sites across 18 countries. The trial
evaluated stopping treatment in 126 adults with Ph+ CML in the chronic phase after patients
had achieved and sustained deep molecular response for one year with Tasigna following
Glivec. The study is ongoing with planned follow-up to evaluate the ability of patients to
sustain remission for longer durations following discontinuation of Tasigna.

About Tasigna (nilotinib)
Tasigna (nilotinib) is approved in more than 122 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 120 countries for the treatment of adult patients with newly
diagnosed Ph+ CML in chronic phase.

IMPORTANT SAFETY INFORMATION for TASIGNA (nilotinib) Capsules
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. Cases of sudden death have been reported in clinical studies in patients with significant risk factors. Avoid use of concomitant drugs known to prolong the QT interval and strong CYP3A4 inhibitors. Avoid food 2 hours before and 1 hour after taking dose. Reactivation of hepatitis B can occur in patients who are chronic carriers of this virus after receiving TKI treatment.

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.

Cases of cardiovascular events included ischemic heart disease-related events, peripheral arterial occlusive disease, and ischemic cerebrovascular events have been reported. Serious cases of hemorrhage from various sites including gastrointestinal were reported in patients receiving Tasigna. Grade 3 or 4 fluid retention including pleural effusion, pericardial effusion, ascites and pulmonary edema have been reported. Cases of tumor lysis syndrome have been reported in Tasigna-treated patients who were resistant or intolerant to prior CML therapy.

The most frequent Grade 3 or 4 adverse events are hematological (neutropenia, thrombocytopenia, anemia) which are generally reversible and usually managed by withholding Tasigna temporarily or dose reduction. Chemistry panels, including electrolytes, lipid profile, liver enzymes, and glucose should be checked prior to therapy and periodically. Tasigna can cause increases in serum lipase. The most frequent non-hematologic adverse events were rash, pruritus, nausea, fatigue, headache, alopecia, myalgia, constipation and diarrhea.

Please see full Prescribing Information including Boxed WARNING at www.tasigna.com.

About Glivec (imatinib)
Glivec (imatinib) is approved in more than 110 countries, for the treatment of adult patients in all phases of Ph+ CML, for the treatment of patients with KIT (CD117)-positive gastrointestinal 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.

Not all indications are available in every country.

Glivec Important Safety Information
Glivec is contraindicated in patients who are hypersensitive to imatinib or any of the excipients.

Glivec can cause fetal harm when administered to a pregnant woman. Women should not become pregnant, and should be advised of the potential risk to the unborn child.

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. Caution in patients with cardiac dysfunction and hepatic dysfunction. Monitor carefully. Reactivation of hepatitis B can occur in patients who are chronic carriers of this virus after receiving TKI treatment.

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, 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 available at www.glivec.com.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as "commitment," "exciting," "potential," "mission," "exploration," "growing," "currently," "continues," "could be," "investigational," "ongoing," "planned," or similar terms, or by express or implied discussions regarding potential new indications or labeling for Tasigna or Glivec, or regarding potential future revenues from Tasigna and Glivec. 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 either Tasigna or Glivec 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 either Tasigna or Glivec will be commercially successful in the future. In particular, management’s expectations regarding Tasigna and Glivec 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 safety, quality or 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 2015, the Group achieved net sales of USD 49.4 billion, while R&D throughout the Group amounted to approximately USD 8.9 billion (USD 8.7 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 118,000 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.

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