Novartis drug Tasigna® approved by FDA to treat children with rare form of leukemia

- Tasigna® (nilotinib) approved for pediatric patients with newly diagnosed Ph+ CML-CP and children with Ph+ CML-CP resistant or intolerant to prior TKI therapy
- New indication approved under FDA Priority Review designation; provides clinicians with pediatric-specific safety and clinical data
- Novartis continues commitment to people living with CML, including pediatric patients with this cancer

Basel, March 22, 2018 – Novartis announced today that the US Food and Drug Administration (FDA) expanded the indication for Tasigna® (nilotinib) to include treatment of first- and second-line pediatric patients one year of age or older with Philadelphia chromosome-positive chronic myeloid leukemia in the chronic phase (Ph+ CML-CP).

In the United States, Tasigna is now indicated for the treatment of adult and pediatric patients one year of age or older with newly diagnosed Ph+ CML-CP. Tasigna is also indicated for the treatment of pediatric patients one year of age or older with Ph+ CML-CP resistant or intolerant to prior tyrosine kinase inhibitor (TKI) therapy, as well as adult patients with Ph+ CML in chronic phase and accelerated phase, resistant or intolerant to prior therapy that included imatinib.

This approval is the latest in a series of regulatory milestones that broadens the understanding and clinical use of Tasigna.

CML is a type of blood cancer where the body produces malignant white blood cells. Almost all patients with CML have an abnormality known as the "Philadelphia chromosome," which produces a protein called BCR-ABL. This protein aids the proliferation of malignant white blood cells in affected patients. Worldwide, CML accounts for approximately 3% of newly diagnosed childhood leukemia.⁴

“Novartis’ commitment to people living with CML is reinforced by today’s FDA approval of Tasigna in children,” said Liz Barrett, CEO, Novartis Oncology. "This expanded use, along with the other recent global regulatory Tasigna milestones, underscores our dedication to reimagining medicine and addressing the needs for people with CML, including children with this cancer.”

The new indications, granted under the FDA’s Priority Review designation, are based on two studies evaluating the efficacy and safety of nilotinib in pediatric patients (two years to less than 18 years of age) with Ph+ CML-CP. A total of 69 Ph+ CML-CP pediatric patients, either newly diagnosed (first-line) or who were resistant or intolerant to prior TKI therapy (second-line), received nilotinib. In newly diagnosed pediatric patients, the major molecular response (MMR; BCR ABL/ABL <=0.1% International Scale [IS]) rate was 60.0% (95% confidence interval [CI]: 38.7, 78.9) at 12 cycles, with 15 patients achieving MMR. The cumulative MMR rate among newly diagnosed pediatric patients was 64.0% by cycle 12, and the median time...
to first MMR was 5.6 months (range: 2.7 to 16.6). In pediatric patients with resistance or intolerance to prior TKI therapy, the MMR rate was 40.9% (95% CI: 26.3, 56.8) at 12 cycles, with 18 patients being in MMR². The cumulative MMR rate among pediatric patients with resistance or intolerance was 47.7% by cycle 12, and the median time to first MMR was 2.8 months (range: 0.0 to 11.3)².

Adverse reactions observed in these pediatric studies were generally consistent with those observed in adults, except for laboratory abnormalities of hyperbilirubinemia (Grade 3/4: 13%)—a condition where there is too much bilirubin in the blood—and transaminase elevation (AST Grade 3/4: 1%, ALT Grade 3/4: 9%), which were reported at a higher frequency than in adult patients. One resistant or intolerant pediatric CML patient progressed to advance phase/blast crisis (AP/BC) after about 10 months on treatment.

Novartis Commitment to CML
Novartis’ ongoing research in Ph+ CML has helped transform the disease from a fatal leukemia to a chronic condition in most patients. The company maintains an unwavering commitment to scientific innovation and access to care for patients worldwide. As an organization committed to patients, Novartis continues to reimagine CML by pursuing ambitious goals with courage, passion and commitment for the global CML community.

About Tasigna
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 Gilvec (imatinib)*, and in more than 110 countries for the treatment of adult patients with newly diagnosed Ph+ CML in chronic phase. Tasigna is approved in the United States (US) for the treatment of Ph+ CML in the chronic phase in pediatric patients one year of age or older with resistance or intolerance to prior therapy including imatinib and for the treatment of pediatric patients one year of age or older with newly diagnosed Ph+ CML in the chronic phase. Tasigna is also approved in the European Union (EU) for the treatment of Ph+ CML in the chronic phase in pediatric patients with resistance or intolerance to prior therapy including imatinib and for the treatment of pediatric patients with newly diagnosed Ph+ CML in the 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. If pregnancy is planned during the treatment-free remission phase, the patient must be informed of a potential need to re-initiate treatment with Tasigna during pregnancy. 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.
In pediatric patients the long-term effects of prolonged treatment with Tasigna is unknown.

Eligible patients who are confirmed to express the typical BCR-ABL transcripts, e13a2/b2a2 or e14a2/b3a2, can be considered for treatment discontinuation. Frequent monitoring of BCR-ABL transcript levels in patients eligible for treatment discontinuation must be performed with a quantitative diagnostic test validated to measure molecular response levels with a sensitivity of at least MR4.5 (BCR-ABL/ABL <=0.0032% IS). BCR-ABL transcript levels must be assessed prior to and during treatment discontinuation. Loss of major molecular response (MMR=BCR-ABL/ABL <=0.1% IS) or confirmed loss of MR4 (two consecutive measures separated by at least 4 weeks showing loss of MR4 (MR4=BCR-ABL/ABL <=0.01% IS) will trigger treatment re-initiation within 4 weeks of when loss of remission is known to have occurred. It is crucial to perform frequent monitoring of BCR-ABL transcript levels and complete blood count with differential in order to detect possible loss of remission. For patients who fail to achieve MMR after three months of treatment re-initiation, BCR-ABL kinase domain mutation testing should be performed.

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.

Musculoskeletal pain, myalgia, pain in extremity, arthralgia, bone pain and spinal pain may occur upon discontinuing treatment with Tasigna within the framework of attempting treatment-free remission.

Please see full Prescribing Information including Boxed WARNING at https://www.us.tasigna.com/.

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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, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2017, the Group achieved net sales of USD 49.1 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 122,000 full-time-equivalent associates. Novartis products are sold in approximately 155 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 and Canada.

References
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