New Novartis data presented at ASCO find nearly half of CML patients treated with Tasigna® remain in remission almost three years after stopping therapy

- *ENESTop and ENESTfreedom data evaluate Treatment-free Remission (TFR) rates at 144 weeks among eligible Ph+ CML-CP patients who stopped Tasigna®*

- *Findings further support durability and safety of TFR with Tasigna; nearly all patients who lost TFR regained major molecular response after restarting therapy*

- *Novartis commitment to seek new solutions in CML continues with update of Phase III trial evaluating asciminib, an investigational BCR-ABL1 inhibitor*

**Basel, June 2, 2018** – New Novartis data from two long-term Treatment-free Remission (TFR) studies in patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in the chronic phase (CP) will be presented during the 54th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago. Results from the open-label Phase II trials, ENESTop and ENESTfreedom, show sustained TFR in patients treated with both front-line and second-line Tasigna® (nilotinib) therapy. The 144-week trials evaluate the potential to maintain molecular response (MR) after stopping therapy in eligible adult patients with Ph+ CML-CP.

“Treatment-free Remission is a new treatment goal in CML,” said François-Xavier Mahon, Cancer Center of Bordeaux, Institut Bergonié and lead investigator of ENESTop. “Clinical studies like ENESTop and ENESTfreedom offer evidence that when a Ph+ CML-CP patient achieves a deep molecular response with Tasigna, along with other eligibility criteria, s/he can attempt TFR and have a nearly 50% chance of remaining treatment-free long-term. These results confirm an exciting opportunity for eligible patients – the opportunity to reduce time on drug for a chronic leukemia.”

Data from ENESTop, presented today in an oral session (Abstract #7003) show that approximately half (48.4%; CI 95%, 39.4%-57.5%) of patients with Ph+ CML-CP who are eligible to stop second-line Tasigna therapy maintained disease remission over a prolonged period of time in the absence of treatment at 144 weeks of follow up, almost 3 years1. Patients in this trial took Tasigna following a switch from Glivec® (imatinib)*. ENESTop data also show that of the patients who restarted Tasigna due to loss of major molecular response (MMR=BCR-ABL/ABL <=0.1% IS), during the study period, nearly all (97.1%) regained MMR1 and 95.8% regained MR4.5 (BCR-ABL1 IS ≤ 0.0032%)1. Study authors stress that frequent scheduled and compliant monitoring is necessary to assess for loss of response. Results of ENESTop at 144-weeks are consistent with previously reported data at both 96- and 48-weeks.

A second long-term clinical trial, ENESTfreedom, is also part of the ASCO Scientific Program this week. The authors will report on TFR results at 144 weeks in patients who started front-line CML therapy with Tasigna. Results from ENESTfreedom will be shared with ASCO attendees on Monday, June 4 (Abstract #7063). In this trial, researchers found that almost half
(46.8%; CI 95%: 39.6%-54.2%) of Ph+ CML-CP patients eligible to stop Tasigna treatment remained in MMR following treatment discontinuation2.

“Novartis continues to redefine treatment options for Ph+ CML patients,” said Samit Hirawat, MD, Head of Novartis Oncology Global Drug Development. “The importance of achieving deep and sustained responses with Tasigna has been demonstrated in our TFR clinical program, which is the largest among all oncology companies. These long-term trials deliver on our commitment to the patient community to continue to look for more and better solutions for CML.”

An update on the Phase III clinical trial design for Novartis’ investigational BCR-ABL1 inhibitor, asciminib, will also be presented as part of the ASCO Scientific Program (Abstract #TPS7081).

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 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-CP receiving Tasigna for at least three years, after patients had achieved and sustained deep molecular response (DMR) 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 upon discontinuation of Tasigna.

Findings from ENESTop at 144-weeks found that 48.4% (CI 95%, 39.4%-57.5%) of 126 patients were able to remain in TFR at 144 weeks1. In the study, 58 patients with confirmed loss of MR4 (n=24; BCR-ABL1 IS ≤ 0.01%) or loss of MMR (n=34) restarted Tasigna by the cut-off date1. Of the 34 patients who restarted treatment with Tasigna due to loss of MMR, 91.2% regained MR4.5 (n=31; BCR-ABL1 IS ≤ 0.0032%)1. Of the 24 patients with loss of MR4 who restarted Tasigna, 95.8% (n=23) regained MR4.51. No new major safety findings were observed in ENESTop in patients treated with Tasigna beyond those in the known safety profile of Tasigna1. Among patients who remained in the TFR phase of the trial for more than 96 weeks (n=68), 10.3%, 51.5%, 19.1%, and 11.8% experienced any-grade musculoskeletal pain–related adverse events in the consolidation phase and first, second, and third 48-week phases of TFR, respectively1.

About ENESTfreedom
ENESTfreedom (Evaluating Nilotinib Efficacy and Safety in Clinical Trials – Following REsponse in De nOvo CML-CP Patients) is an open label Phase II study involving 215 Ph+ CML patients in the chronic phase, conducted at 132 sites across 19 countries. ENESTfreedom evaluated stopping treatment in 190 adults with Ph+ CML-CP receiving Tasigna for at least three years, after the patients had achieved a response of MR4.5 with Tasigna and a sustained DMR for one year as a first-line treatment. The study is ongoing with planned follow-up to evaluate the ability of patients to sustain remission for longer durations following discontinuation of Tasigna.

Findings from ENESTfreedom at 144-weeks found that 46.8% of 190 eligible CML patients (CI 95%; 39.6%-54.2%) remained in MMR following discontinuation of Tasigna2. Of the 91 patients who restarted treatment with Tasigna due to loss of MMR by the cut-off date, 98.9% (n=90) and 92.3% (n=84) were able to regain MMR and MR4.5, respectively2. No new major
safety findings were observed in ENESTfreedom in patients treated with Tasigna beyond those in the known safety profile of Tasigna\(^2\). Among patients who remained in TFR for more than 96 weeks (n=94), any-grade musculoskeletal pain-related AEs were 16.0%, 40.4%, 9.6% and 4.3% in the consolidation phase and first, second and third 48-week phases of TFR, respectively\(^2\).

**About Tasigna**

Tasigna (nilotinib) is approved in more than 130 countries for the treatment of adult patients with newly diagnosed Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML) in chronic phase and with chronic and accelerated phase Ph+ CML resistant or intolerant to at least one prior therapy, including Glivec (imatinib). Tasigna is also approved for the treatment of pediatric patients with newly diagnosed Ph+ CML in the chronic phase and with resistance or intolerance to prior TKI therapy.

**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 should not breastfeed while taking Tasigna and for 2 weeks after the last dose.

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 MR\(^4.5\) (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 MR\(^4\) (two consecutive measures separated by at least 4 weeks showing loss of MR\(^4\) (MR\(^4\)=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.
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.

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 at http://www.tasigna.com/.

https://www.us.tasigna.com/.

About asciminib
Asciminib (ABL001) is an investigational compound. Efficacy and safety have not been established. There is no guarantee this compound will become commercially available.

Disclaimer
This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as “potential,” “can,” “will,” “plan,” “expect,” “anticipate,” “look forward,” “believe,” “committed,” “investigational,” “pipeline,” “launch,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations 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 the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products could be affected by, among other things, the uncertainties inherent in research and development, including clinical trial results and additional analysis of existing clinical data; regulatory actions or delays or government regulation generally; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political and economic conditions; safety, quality or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, 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, 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 124,000 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
1. Mahon, F.X. et al. Long-term treatment-free remission (TFR) in patients (pts) with chronic myeloid leukemia in chronic phase (CML-CP) after stopping second-line (2L) nilotinib: ENESTop 144-wk results. Abstract #P601. 2 June 2018 American Society of Clinical Oncology Annual Meeting (ASCO) in Chicago, IL.
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Novartis Media Relations
Central media line: +41 61 324 2200
E-mail: media.relations@novartis.com

Eric Althoff
Novartis Global Media Relations
+41 61 324 7999 (direct)
+41 79 593 4202 (mobile)
eric.althoff@novartis.com

Mary Curtin Creaser
Novartis Oncology Communications
+ 1 862 778-2550 (direct)
+ 1 862 345-4102 (mobile)
mary.curtin_creaser@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central
Samir Shah +41 61 324 7944
Pierre-Michel Bringer +41 61 324 1065
Thomas Hungerbuehler +41 61 324 8425
Isabella Zinck +41 61 324 7188

North America
Richard Pulik +1 212 830 2448
Cory Twining +1 212 830 2417