Novartis investigational STAMP inhibitor asciminib (ABL001) shows superior MMR rate to Bosulif®* in chronic myeloid leukemia trial

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- At 24 weeks, asciminib nearly doubled the major molecular response (MMR) rate compared to Bosulif® (bosutinib)*, in patients resistant to, or intolerant of, at least two prior tyrosine kinase inhibitor (TKI) therapies[1]
- Despite advances in chronic myeloid leukemia (CML) care, many patients are at risk of disease progression, and sequential TKI therapy may be associated with increased resistance and intolerance[2-7]
- Data further reinforce the potential of asciminib to help patients with CML who suffer from intolerable side effects in later lines of therapy1
- Data presented at ASH; submission to health authorities planned for first half of 2021

EAST HANOVER, N.J., Dec. 8, 2020 /PRNewswire/ -- Detailed results from the Phase III ASCEMBL study demonstrate that, at 24 weeks, asciminib (ABL001) – a novel investigational treatment specifically targeting the ABL myristoyl pocket (STAMP) – nearly doubled the major molecular response (MMR) rate compared to Bosulif® (bosutinib)* (25.5% vs. 13.2%, respectively ([95% CI, 2.19-22.3]; 2-sided P=0.029) in patients with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine-kinase inhibitors (TKIs)[1]. These data were presented today at a late-breaking abstracts session during the 62nd American Society of Hematology Annual Meeting & Exposition (ASH).

"These important comparative data are impressive, and they reinforce the critical role asciminib may play, if approved, in overcoming the treatment challenges we face in later treatment lines of chronic-phase CML," said Dr. Michael J. Mauro**, Member and Myeloproliferative Neoplasms Program Leader at Memorial Sloan Kettering Cancer Center and Professor at Weill Cornell Medicine. "While the advent and expansion of TKI therapies has resulted in tremendous progress for patients living with CML over the last decades, many of our patients in later treatment lines still face inadequate response, disease progression and intolerable side effects."

Despite the significant advances in the CML treatment landscape, many patients treated with two or more TKIs experience intolerance; for example, in an analysis of studies in patients who had previously failed two TKIs, up to 55% reported intolerance to treatment[8-13]. In addition, resistance rates for patients in later treatment lines remain high; and in the second-line setting, at least three out of five patients are unable to achieve MMR and up to 56% of patients do not achieve complete cytogenetic response (CCyR) within two years of follow-up[5,13-18]. With few remaining treatment options, and no currently established standard-of-care in the third-line setting per treatment guidelines, patients who are resistant or intolerant to two or more TKIs are at a high risk of progression[2-5,19-21].

In the ASCEMBL trial, 233 patients were randomized to receive asciminib 40 mg twice daily (n=157) or Bosulif 500 mg once a day (n=76)[1]. Data showed that, at 24 weeks, more patients achieved a CCyR in the asciminib arm (40.8%) than in the Bosulif arm (24.2%); and deep molecular response (DMR) rates were higher for

patients in the asciminib arm than in the Bosulif arm – with 10.8% and 8.9% patients achieving MR^4 and $MR^{4.5}$ on asciminib, respectively, vs. 5.3% and 1.3% on Bosulif[1].

Grade ≥3 adverse events (AEs) occurred in 50.6% and 60.5% of patients treated with asciminib and Bosulif, respectively[1]. Treatment discontinuation due to AEs in the asciminib arm was 5.8% compared to 21.1% for patients taking Bosulif [1]. Similarly, AEs requiring dose interruption and/or dose adjustments were reported less frequently with asciminib than with Bosulif (37.8% vs. 60.5%, respectively)[1]. At data cutoff, more patients were still on treatment in the asciminib arm vs. the Bosulif arm (61.8% vs. 30.3%, respectively)[1].

The most common grade ≥3 AEs (occurring in >10%) of patients treated with asciminib were thrombocytopenia (17.3%) and neutropenia (14.7%), while for Bosulif they were increased alanine aminotransferase (ALT) (14.5%), neutropenia (11.8%) and diarrhea (10.5%)[1]. On-treatment deaths on the asciminib arm occurred in two (1.3%) patients (ischemic stroke and arterial embolism); there was one (1.3%) death on Bosulif (septic shock)[1]. The most frequent AEs (all grades; ≥20%) were thrombocytopenia (28.8%) and neutropenia (21.8%) in the asciminib arm, compared to diarrhea (71.1%), nausea (46.1%), increased ALT (27.6%), vomiting (26.3%), rash (23.7%), increased aspartate aminotransferase (21.1%), neutropenia (21.1%) and thrombocytopenia (18.4%) in the Bosulif arm[1].

"Though some patients with CML may be told they have a 'good cancer' because of the wonderful advances in care that have been made over the years, this doesn't capture the full picture for everyone with the disease," said Greg Stephens, Executive Director and Founder of the US National CML Society. "The results of the ASCEMBL study are very encouraging to the CML community, and help underscore the crucial need for additional treatment options to address real challenges that patients face."

Pre-clinical data suggests that asciminib has specificity for BCR-ABL[22]. Additional data accepted for online publication highlight that, as an investigational STAMP inhibitor, asciminib is designed to help overcome mutations on the ATP-binding site of BCR-ABL1, which may help address resistance in later treatment lines of CML and may potentially address off-target activity[22].

"Novartis has been at the forefront of CML research for years – significantly changing the prognosis for patients. We are very proud to once again advance a potentially transformative medicine, a novel STAMP inhibitor, for those who do not adequately respond or are intolerant to currently available TKIs," said John Tsai, Head Global Drug Development and Chief Medical Officer, Novartis. "There is a clear need in later lines of therapy, and based on these results, we believe asciminib may become an important new development for patients. We look forward to sharing the data with regulatory authorities and moving forward with submissions worldwide."

The US Food and Drug Administration (FDA) has granted Fast Track designation for asciminib. Submission to the US and EU health authorities is planned for the first half of 2021.

Visit https://www.virtualcongress.novartis.com/ash20 for the latest information from Novartis including our bold approach to reimagining care in hematology, and access to our ASH Virtual Congress 2020 symposia and data presentations (for registered participants).

About asciminib (ABL001)

Asciminib (ABL001) is an investigational treatment specifically targeting the ABL myristoyl pocket (STAMP). As a STAMP inhibitor, asciminib may help address tyrosine-kinase inhibitor (TKI)-resistance and intolerance in later treatment lines of chronic myeloid leukemia (CML), and it is being studied in several clinical trials in

hopes of helping patients across multiple treatment lines of CML[23-30].

About ASCEMBL

ASCEMBL is a Phase III, multicenter, open-label, randomized study comparing the oral investigational treatment asciminib (ABL001) versus bosutinib in patients with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine-kinase inhibitors (TKIs)[1]. Patients with failure or intolerance to the most recently administered TKI therapy were included in the trial[1].

About Novartis Commitment to CML

Our ongoing research in Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) has helped transform the disease from a fatal leukemia to a chronic condition in most patients. Novartis 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 care by pursuing ambitious goals with courage, passion and commitment for the global CML community.

* Bosulif is a registered trademark of Pfizer.
** Disclosure: Dr. Mauro has provided consulting services to Novartis.

About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of Novartis – is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis employs more than 15,000 people in the United States. For more information, please visit https://www.novartis.us.

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Novartis Media Relations
E-mail: media.relations@novartis.com

Eric Althoff
Head, US Corp & Country External Comms,
Global Media & Corp Communications
+1 646 438 4335
eric.althoff@novartis.com

Jamie Bennett
Director, US Media Relations
+1 862 217 3976
jamie.bennett@novartis.com

Novartis Investor Relations
E-mail: investor.relations@novartis.com

Sloan Simpson +1 862 778 5052

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