NOVARTIS

FDA approves Novartis Scemblix® (asciminib), with novel mechanism of action for the treatment of chronic myeloid leukemia

Nov 01, 2021

- Scemblix provides much-needed and long-awaited new option for patients with chronic myeloid leukemia (CML) who suffer with intolerance or inadequate response after at least two previous tyrosine kinase inhibitor (TKI) treatments1
- In the pivotal Phase III ASCEMBL trial, Scemblix demonstrated significant and clinically meaningful superiority in major molecular response (MMR) rate vs. Bosulif®* (bosutinib) (25% vs. 13%) at 24 weeks, and more than three times lower discontinuation rates due to side effects (7% vs. 25%)2,3
- Additional Phase I data in patients with CML with the T315I mutation supported the FDA approval for a second indication in this patient population4
- With a new mechanism of action known in scientific literature as a STAMP inhibitor and clinical trials across treatment lines - including in the first-line setting -, Scemblix reinforces Novartis' two-decade commitment to bring transformative therapies to people living with CML2-18

EAST HANOVER, N.J., Nov. 1, 2021 - Novartis announced today that the US Food and Drug Administration (FDA) approved Scemblix® (asciminib) for the treatment of chronic myeloid leukemia (CML) in two distinct indications. The FDA granted Scemblix accelerated approval for adult patients with Philadelphia chromosome-positive CML in chronic phase (Ph+ CML-CP), previously treated with two or more tyrosine kinase inhibitors (TKIs), based on major molecular response (MMR) rate at 24 weeks; and full approval for adult patients with Ph+ CML-CP with the T315I mutation[1]. In accordance with the Accelerated Approval Program, continued approval for the first indication may be contingent upon verification and description of clinical benefit from confirmatory evidence[1]. Scemblix is the first FDA-approved CML treatment that works by binding to the ABL myristoyl pocket, and represents an important development for patients who experience resistance and/or intolerance to currently available TKI therapies[1-3]. Also known as a STAMP inhibitor in scientific literature, Scemblix is being studied across multiple treatment lines for CML-CP, including the ASC4FIRST Phase III study evaluating Scemblix as a first-line treatment[2-18].

Experience the interactive Multichannel News Release here:
https://www.multivu.com/players/English/8950851-fda-approves-novartis-scemblix-asciminib-first-stamp-inhibitor-treatment-chronic-myeloid-leukemia/

"The introduction of TKIs twenty years ago revolutionized treatment for CML; however, there remain many patients who do not respond adequately to at least two available treatments and often experience challenging side effects that add a burden to their daily lives," said Lee Greenberger, Chief Scientific Officer at The Leukemia & Lymphoma Society. "The approval of Scemblix may offer hope to patients by addressing gaps in CML care."

For many patients, current treatment for CML may be limited by intolerance or resistance, and sequential use of available TKIs is associated with increased failure rates[19-26]. In an analysis of patients with CML treated

with two prior TKIs, approximately 55% reported intolerance to previous treatment[27]. Additionally, a pooled analysis in the second-line setting showed that up to 70% of patients are unable to achieve major molecular response (MMR) within two years of follow-up[28-30]. Moreover, patients who develop the T315I mutation are resistant to most available TKIs, leaving them at an increased risk of disease progression[4].

"CML can be difficult to treat when currently available treatments fail patients, when treatment side effects cannot be tolerated, or sometimes both," expressed Dr. Michael J. Mauro**, Hematologist and Myeloproliferative Neoplasms Program Leader at Memorial Sloan Kettering Cancer Center (MSK). "The addition of Scemblix into the CML treatment landscape gives us a novel approach to combat this blood cancer, helping address clinical challenges in patients struggling after switching to a second treatment, as well as in patients who develop the T315I mutation and face significantly worse outcomes."

The FDA approval of Scemblix is based on results from the Phase III ASCEMBL trial and a Phase I (NCT02081378) study that included patients with Ph+ CML-CP with the T315I mutation.

In patients with Ph+ CML-CP who had experienced resistance or intolerance to at least two TKIs, the ASCEMBL trial showed that[1-3]:

- Scemblix nearly doubled the MMR rate vs. Bosulif® (bosutinib)* at 24 weeks (25% vs. 13% [P=0.029])
- The proportion of patients who discontinued treatment due to adverse reactions was more than three times lower in the Scemblix arm (n = 156) vs. patients in the Bosulif arm (n = 76) (7% vs. 25%)
- The most common (incidence ≥ 20%) adverse reactions and laboratory abnormalities in the Scemblix arm were, respectively: upper respiratory tract infections and musculoskeletal pain; decrease in platelet and neutrophil counts, decrease in hemoglobin; increase in triglycerides, creatine kinase and alanine aminotransferase (ALT)

"After more than two decades of reimagining CML care, we continue to boldly push the boundaries of innovation to transform the standard-of-care and help even more patients living with this disease," said Susanne Schaffert, PhD, President, Novartis Oncology. "We would like to thank all those who have been involved in helping to advance this new and important breakthrough."

Scemblix is currently available for physicians to prescribe to appropriate patients in the US.

Additional efficacy and safety details for Scemblix, including data on patients with the T315I mutation, and full Prescribing Information can be found at

https://www.novartis.us/sites/www.novartis.us/files/scemblix.pdf.

About Scemblix® (asciminib)

Scemblix (asciminib) is indicated for the treatment of adult patients with Ph+ CML-CP pre-treated with two or more TKIs, as well as adult patients with Ph+ CML-CP with the T315I mutation[1]. The first indication is approved under the US FDA Accelerated Approval Program based on MMR rate at 24 weeks; continued approval for the first indication may be contingent upon verification and description of clinical benefit from confirmatory evidence.

Scemblix is the first FDA-approved CML treatment that binds to the ABL myristoyl pocket[1]. This novel mechanism of action, also known in scientific literature as a STAMP inhibitor, may help address resistance in patients with CML previously treated with two or more TKIs and overcome mutations at the defective BCR-ABL1 gene, which is associated with the over-production of leukemic cells[2-11]. Scemblix has also been shown

to limit off-target activity in pre-clinical studies[31].

Novartis has initiated regulatory filings for Scemblix in multiple countries and regions across the globe.

Scemblix represents an important development for patients who experience resistance and/or intolerance to currently available TKI therapies, and it is being studied across multiple treatment lines for CML-CP [2-18]. Specifically, the ASC4FIRST Phase III study (NCT04971226) evaluates Scemblix as a first-line treatment and is in the recruitment phase[13].

About Novartis Commitment to CML

Novartis has a long-standing scientific commitment to patients living with CML. For more than 20 years, our bold science has helped transform CML into a chronic disease for many patients. Despite these advancements, we're not standing still. We continue to research ways to target the disease, seeking to address the challenges with treatment resistance and/or intolerance that many patients face. Novartis also continues to reimagine CML care through its commitment to sustainable access for patients and collaboration with the global CML community.

Indication

SCEMBLIX® (asciminib) tablets is a prescription medicine used to treat adults with Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with 2 or more tyrosine kinase inhibitor (TKI) medicines. The effectiveness of SCEMBLIX in these patients is based on a study that measured major molecular response (MMR) rates. No clinical information is available to show if these patients treated with SCEMBLIX live longer or if their symptoms improve. Ongoing studies exist to find out how SCEMBLIX works over a longer period of time.

SCEMBLIX is also approved for use in adults with Ph+ CML in CP with the T315I mutation.

It is not known if SCEMBLIX is safe and effective in children.

Important Safety Information

SCEMBLIX® (asciminib) tablets may cause low platelet counts (thrombocytopenia), low white blood cell counts (neutropenia), and low red blood cell counts (anemia). Patients should tell their doctor right away if they have unexpected bleeding or easy bruising; blood in their urine or stools; fever; or any signs of an infection. SCEMBLIX may increase enzymes in the patient's blood called amylase and lipase, which may be a sign of inflammation of the pancreas (pancreatitis). Patients should tell their doctor right away if they have sudden stomach-area pain or discomfort, nausea, or vomiting. During treatment with SCEMBLIX, doctors may check their patients' blood pressure and treat any high blood pressure as needed. Patients should tell their doctor if they develop elevated blood pressure or symptoms of high blood pressure including confusion, headaches, dizziness, chest pain, or shortness of breath.

If a patient has an allergic reaction while on SCEMBLIX, they should stop taking SCEMBLIX and get medical help right away. Signs or symptoms of an allergic reaction include trouble breathing or swallowing; feeling dizzy or faint; swelling of the face, lips, or tongue; fever; skin rash or flushing; or a fast heartbeat. SCEMBLIX may cause heart and blood vessel problems, including heart attack; stroke; blood clots or blockage of patient's arteries; heart failure; and abnormal heartbeat which can be serious and may sometimes lead to death. These heart and blood vessel problems can happen in people with risk factors or a history of these problems and/or previously treated with multiple TKI medicines. Patients should tell their doctor right away if they get shortness of breath; chest pain or pressure; a feeling like their heart is beating too fast or they feel abnormal heartbeats;

swelling in their ankles or feet; dizziness; weight gain; numbness or weakness on one side of their body; decreased vision or loss of vision; trouble talking; pain in their arms, legs, back, neck, or jaw; headache; or severe stomach-area pain.

Before taking SCEMBLIX, patients should tell their doctor about all of their medical conditions, including if they have a history of pancreatitis; a history of heart problems; or blood clots in their arteries and veins (types of blood vessels). SCEMBLIX can harm an unborn baby. Women should tell their doctor right away if they become pregnant or think they may be pregnant during treatment with SCEMBLIX. Women who are able to become pregnant should have a pregnancy test before they start SCEMBLIX and should use effective birth control during treatment and for 1 week after the last dose of SCEMBLIX. Women should not breastfeed during treatment and for 1 week after their last dose of SCEMBLIX.

Patients should tell their doctor about all the medicines they take, including prescription medicines, over-the-counter medicines, vitamins, and herbal supplements. SCEMBLIX and other medicines may affect each other, causing side effects. The most common side effects of SCEMBLIX include nose, throat, or sinus (upper respiratory tract) infections; muscle, bone, or joint pain; rash; tiredness; nausea; and diarrhea. The most common blood test abnormalities include decreased blood counts of platelets, white blood cells, and red blood cells; and increased blood levels of triglycerides, creatine kinase, liver enzymes, or pancreas enzymes (amylase and lipase).

Please see full Prescribing Information for SCEMBLIX, available at https://www.novartis.us/sites/www.novartis.us/files/scemblix.pdf.

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 nearly 15,000 people in the United States. For more information, please visit https://www.novartis.us.

Novartis and Novartis US is on Twitter. Sign up to follow @Novartis at https://twitter.com/novartisnews and @NovartisUS at https://twitter.com/NovartisUS.

For Novartis multimedia content, please visit https://www.novartis.com/news/media-library.

For questions about the site or required registration, please contact media.relations@novartis.com.

# # #

Novartis Media Relations

E-mail: media.relations@novartis.com

Julie Masow

Head, US External Engagement
+1 862 579 8456
julie.masow@novartis.com

Floriana Riccio Furnari

Novartis Oncology Communications
+1 862 778 1866 (direct)
+1 862 210 5317 (mobile)
floriana.riccio_furnari@novartis.com

Anja von Treskow
Novartis Strategy & Financial Communications
+41 79 392 8697 (mobile)
anja.von_treskow@novartis.com

Novartis Investor Relations

E-mail: investor.relations@novartis.com

North America

Sloan Simpson
+1 862 778 5052

SOURCE Novartis

References

1. Scemblix [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2021.
2. Rea D, et al. A Phase 3, Open-Label, Randomized Study of Asciminib, a STAMP Inhibitor, vs Bosutinib in CML After≥ 2 Prior TKIs. Blood. 2021. DOI: 10.1182/blood.2020009984. PMID: 34407542.
3. Novartis Data on File, 2021.
4. Cortes JE, et al. Asciminib, a First-in-Class STAMP Inhibitor, Provides Durable Molecular Response in Patients (pts) with Chronic Myeloid Leukemia (CML) Harboring the T315I Mutation: Primary Efficacy and Safety Results from a Phase 1 Trial. Oral presentation at: ASH Annual Meeting; Dec. 7, 2020
5. Wylie AA, et al. The allosteric inhibitor ABL001 enables dual targeting of BCR–ABL1. Nature. 2017;543(7647):733-737.
6. Schoepfer J, et al. Discovery of Asciminib (ABL001), an Allosteric Inhibitor of the Tyrosine Kinase Activity of BCR-ABL1. J Med Chem. 2018;61(18):8120-8135.
7. Hughes TP, et al. Asciminib in Chronic Myeloid Leukemia after ABL Kinase Inhibitor Failure. N Engl J Med. 2019; 381(24):2315-2326.
8. Hughes TP, et al. Expanded Phase 1 Study of ABL001, a Potent, Allosteric Inhibitor of BCR-ABL, Reveals Significant and Durable Responses in Patients with CML-Chronic Phase with Failure of Prior TKI Therapy. Poster presented at: ASH Annual Meeting & Exposition; Dec. 5, 2016.
9. Ottmann OG, et al. ABL001, a Potent, Allosteric Inhibitor of BCR-ABL, Exhibits Safety and Promising Single- Agent Activity in a Phase I Study of Patients with CML with Failure of Prior TKI Therapy. Blood. 2015;126(23):138.
10. Mauro MJ, et al. Combination of Asciminib Plus Nilotinib (NIL) or Dasatinib (DAS) in Patients (PTS) with Chronic Myeloid Leukemia (CML): Results from a Phase 1 Study. Poster presented at: EHA Annual Meeting; June 15, 2019.
11. Cortes JE, et al. Combination Therapy Using Asciminib Plus Imatinib (IMA) in Patients (PTS) with Chronic Myeloid Leukemia (CML): Results from a Phase 1 Study. Poster presented at: EHA Annual Meeting; June 15, 2019.
12. ClinicalTrials.gov. 2017. Study of Efficacy of CML-CP Patients Treated with ABL001 Versus Bosutinib, Previously Treated With 2 or More TKIs. [online] Available at: https://clinicaltrials.gov/ct2/show/NCT03106779.
13. ClinicalTrials.gov. 2021. A Study of Oral Asciminib Versus Other TKIs in Adult Patients With Newly Diagnosed Ph+ CML-CP. [online] Available at: https://clinicaltrials.gov/ct2/show/NCT04971226.
14. ClinicalTrials.gov. 2020. Asciminib in Monotherapy for Chronic Myeloid Leukemia in Chronic Phase (CML-CP) With and WithoutT315I Mutation (AIM4CML). [online] Available at:

https://clinicaltrials.gov/ct2/show/NCT04666259.
15. ClinicalTrials.gov. 2018. Study of Efficacy And Safety Of Asciminib In Combination With Imatinib In Patients With Chronic Myeloid Leukemia In Chronic Phase (CML-CP). [online] Available at: https://clinicaltrials.gov/ct2/show/NCT03578367.
16. ClinicalTrials.gov. 2021. Study of Efficacy and Safety of CML-CP Patients Treated With Asciminib Versus Best Available Therapy, Previously Treated With 2 or More Tyrosine Kinase Inhibitors. [online] Available at: https://clinicaltrials.gov/ct2/show/NCT04795427.
17. ClinicalTrials.gov. 2014. A Phase I Study of Oral ABL001 in Patients With CML or Ph+ ALL. [online] Available at: https://clinicaltrials.gov/ct2/show/NCT02081378.
18. ClinicalTrials.gov. 2021 Asciminib Treatment Optimization in ≥ 3rd Line CML-CP. [online] Available at: https://clinicaltrials.gov/ct2/show/NCT04948333
19. Flis S, et al. Chronic myelogenous leukemia, a still unsolved problem: pitfalls and new therapeutic possibilities. Drug Des Devel Ther. 2019;13:825-843.
20. Akard LP, et al. The "Hit Hard and Hit Early" Approach to the Treatment of Chronic Myeloid Leukemia: Implications of the Updated National Comprehensive Cancer Network Clinical Practice Guidelines for RoutinePractice. Clin Adv Hematol Oncol. 2013;11(7):421-432.
21. Cortes JE, et al. Long-term bosutinib for chronic phase chronic myeloid leukemia after failure of imatinib plus dasatinib and/or nilotinib. Am J Hematol. 2016;91(12):1206-1214.
22. Cortes JE, et al. Ponatinib efficacy and safety in Philadelphia chromosome–positive leukemia: Final 5-yearresults of the phase 2 PACE trial. Blood. 2018;132(4):393-404.
23. Garg RJ, et al. The use of nilotinib or dasatinib after failure to 2 prior tyrosine kinase inhibitors: long-term follow-up. Blood. 2009;114(20):4361-4368
24. Hochhaus A, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. Leukemia. 2020;34:966-984
25. Cortes JE., et al. Final 5-Year Study Results of DASISION: The Dasatinib Versus Imatinib Study in Treatment-Naïve Chronic Myeloid Leukemia Patients Trial. J Clin Oncol. 2016;34:2333-2340.
26. Steegmann JL., et al. European LeukemiaNet recommendations for the management and avoidance of adverse events of treatment in chronic myeloid leukaemia. Leukemia. 2016;30:1648-1671.
27. Giles FJ, et al. Nilotinib is active in chronic and accelerated phase chronic myeloid leukemia following failure of imatinib and dasatinib therapy. Leukemia. 2010; 24(7):1299–1301.
28. Kantarjian HM, et al. Nilotinib is effective in patients with chronic myeloid leukemia in chronic phase after imatinib resistance or intolerance: 24-month follow-up results. Blood. 2011;117(4):1141-1145.
29. Shah NP, et al. Potent, transient inhibition of BCR-ABL with dasatinib 100 mg daily achieves rapid and durable cytogenetic responses and high transformation-free survival rates in chronic phase chronic myeloid leukemia patients with resistance, suboptimal response or intolerance to imatinib. Haematologica. 2010;95:232-240
30. Gambacorti-Passerini C., et al. Bosutinib efficacy and safety in chronic phase chronic myeloid leukemia after imatinib resistance or intolerance: Minimum 24-month follow-up. Am J Hematol. 2014;89:732-742.
31. Manley P., et al. The specificity of asciminib, a potential treatment for chronic myeloid leukemia, as a myristate-pocket binding ABL inhibitor and analysis of its interactions with mutant forms of BCR-ABL1 kinase. Leukemia Research. 2020;98

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," "may," "could," "would," "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 and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity 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.

Source URL: *https://www.novartis.com/us-en/news/media-releases/fda-approves-novartis-scemblix-asciminib-novel-mechanism-action-treatment-chronic-myeloid-leukemia*

List of links present in page

- https://www.novartis.com/us-en/us-en/news/media-releases/fda-approves-novartis-scemblix-asciminib-novel-mechanism-action-treatment-chronic-myeloid-leukemia
- https://www.multivu.com/players/English/8950851-fda-approves-novartis-scemblix-asciminib-first-stamp-inhibitor-treatment-chronic-myeloid-leukemia/
- https://www.novartis.com/us-en/us-en/sites/novartis_us/files/2022-03/scemblix_0.pdf
- https://www.novartis.com/us-en/us-en/home
- https://twitter.com/novartisnews
- https://twitter.com/NovartisUS
- https://www.novartis.com/news/media-library
- mailto:media.relations@novartis.com
- mailto:julie.masow@novartis.com
- mailto:floriana.riccio_furnari@novartis.com
- mailto:anja.von_treskow@novartis.com
- mailto:investor.relations@novartis.com
- https://clinicaltrials.gov/ct2/show/NCT03106779
- https://clinicaltrials.gov/ct2/show/NCT04971226
- https://clinicaltrials.gov/ct2/show/NCT04666259
- https://clinicaltrials.gov/ct2/show/NCT03578367
- https://clinicaltrials.gov/ct2/show/NCT04795427
- https://clinicaltrials.gov/ct2/show/NCT02081378
- https://clinicaltrials.gov/ct2/show/NCT04948333