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MEDIA UPDATE

Novartis Scemblix® granted FDA Priority Review for the treatment of adults with newly diagnosed CML

- *Priority Review based on ASC4FIRST Phase III study with Scemblix® data first to show significantly improved molecular response and a favorable safety and tolerability profile compared to standard of care therapies (imatinib and 2G TKIs)*[1]
- *Treatment options combining high efficacy with safety and tolerability represent a critical gap in care for long-term CML management*[1]
- *Scemblix was previously granted FDA Breakthrough Therapy designation and is in review under the agency's Real-Time Oncology Review program*[2-4]

East Hanover, July 29, 2024 – Novartis announced today that Scemblix® (asciminib) has been granted Priority Review status by the US Food and Drug Administration (FDA) for treatment of newly diagnosed adult patients with Philadelphia chromosome-positive CML in chronic phase (Ph+ CML-CP).

The FDA grants Priority Review to medicines that address serious or life-threatening diseases or conditions and, if approved, would provide significant improvements in treatment safety or efficacy[5]. Scemblix previously received Breakthrough Therapy designation for the treatment of newly diagnosed adult patients and is currently being reviewed under the FDA's Real-Time Oncology Review (RTOR) program. Scemblix received Priority Review and Breakthrough Therapy designations at the time of the original new drug application for the treatment of adult patients with Ph+ CML-CP who have previously been treated with two or more TKIs[2-4,6,7].

"We welcome the FDA's decision to grant Priority Review and Breakthrough Therapy designations to Scemblix for newly diagnosed CML patients, which underscores the substantial need for additional effective, safe and tolerable treatment options," said Rodney Gillespie, Senior Vice President, Therapeutic Area Head, US Oncology, Novartis. "The ASC4FIRST data indicate that Scemblix, if approved, has the potential to address a critical gap in CML by offering a highly effective treatment along with a favorable safety and tolerability profile."

Priority Review designation is based on results from ASC4FIRST, a Phase III study that evaluated the efficacy, tolerability and safety of once daily Scemblix against investigator-selected (IS) tyrosine kinase inhibitors (TKIs) (imatinib, nilotinib, dasatinib, and bosutinib) representing the current standard of care (SoC) in newly diagnosed adult patients with Ph+ CML-CP[1]. Scemblix demonstrated superior major molecular response (MMR) rates in both primary endpoints at week 48 vs. IS SoC TKIs (68% vs. 49.0%) and imatinib alone (69% vs. 40%)[1]. Additionally, Scemblix is the first CML treatment to show superior efficacy along with a favorable safety and tolerability profile vs. imatinib and 2G TKIs, with fewer grade ≥3 AEs

(38% vs. 44% and 55%), dose adjustments (30% vs. 39% and 53%) and half the rate of AEs leading to treatment discontinuation (5% vs. 11% and 10%)[1]. In newly diagnosed patients, the safety profile was consistent with previous registration studies, with no new safety concerns observed[1].

Earlier this year, ASC4FIRST data were presented as a late-breaking abstract at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting, as a plenary at the European Hematology Association (EHA) 2024 Congress and published in The New England Journal of Medicine[1].

Scemblix is currently approved by the FDA, European Medicines Agency and other regulatory authorities for adult patients with Ph+ CML-CP who have been treated previously with two or more TKIs[2,4,6].

About ASC4FIRST Phase III Clinical Trial
ASC4FIRST (NCT04971226) is a Phase III, head-to-head, multi-center, open-label, randomized study of oral Scemblix® 80 mg QD vs. investigator-selected first- or second-generation TKIs (imatinib, nilotinib, dasatinib or bosutinib) in 405 adult patients with newly diagnosed Ph+ CML-CP[6]. The two primary endpoints of the study are to compare efficacy of asciminib vs. investigator-selected SoC TKIs and to compare efficacy vs. that of TKI within the stratum of participants with imatinib as pre-randomization selected TKI, based on proportion of patients that achieve MMR at week 48[6].

The study remains ongoing with key secondary endpoints of proportion of patients that achieve MMR at week 96 and a safety endpoint of discontinuation of study treatment due to an AE (TTDAE) by week 96[6]. The study also assesses additional secondary safety and efficacy endpoints, including MMR, MR4, MR4.5, complete hematological response (CHR) and BCR::ABL1 ≤1% at and by all scheduled data collection time points; duration of and time to first MMR, MR4 and MR4.5; time to treatment failure; event-free survival, failure-free survival, progression-free survival and overall survival[6].

About Scemblix® (asciminib)
Scemblix® is the first CML treatment that works by Specifically Targeting the ABL Myristoyl Pocket (referred to as a STAMP inhibitor in scientific literature)[8-10]. The current approved CML treatments are TKIs that target the ATP-binding site (ATP-competitive)[10].

Scemblix is approved in more than 70 countries, including the US, the EU and JP, to treat adults with Ph+ CML-CP who have previously been treated with two or more TKIs[2,3,7]. In some countries, including the US, Scemblix is also approved in patients with Ph+ CML-CP with the T315I mutation[2-4].

Scemblix is an important treatment option for patients who experience resistance and/or intolerance after two prior TKI therapies[11-26], and it is being studied across multiple treatment lines for Ph+ CML-CP, both as a monotherapy and in combination[6,8,9,19,27-39].

About Novartis Commitment to CML
Novartis has a long-standing scientific commitment to patients living with CML. For more than two decades, our bold science has helped transform CML from a life-limiting to a chronic condition for many patients. Despite these advancements, there’s still work to be done. We continue to research ways to target the disease more selectively and to address the challenges of not reaching treatment efficacy goals, experiencing treatment resistance and/or intolerance that many patients face. Our legacy inspires our future innovation – we continue to lead the way in developing novel medicines to address serious unmet needs in CML. Our commitment also goes beyond science. Our 20+ year collaboration with the Max Foundation has provided access to Gleevec (imatinib), Tasigna (nilotinib) and now Scemblix and is delivering tremendous patient impact in low- and middle-income countries, with over 100,000 patients supported to date.

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. 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.

Disclaimer

This media update 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,” “seek,” “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; 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.

About Novartis

Novartis is an innovative medicines company. Every day, we work to reimagine medicine to improve and extend people’s lives so that patients, healthcare professionals and societies are empowered in the face of serious disease. Our medicines reach more than 250 million people worldwide.

Reimagine medicine with us: Visit us at **https://www.novartis.com** and **https://www.novartis.us** and connect with us on **LinkedIn**, **LinkedIn US**, **Facebook**, **X/Twitter**, **X/Twitter US** and **Instagram**.

References

1. Hughes TP, Hochhaus A, Takahashi N, et al. ASC4FIRST, a pivotal ph 3 study of asciminib (ASC) vs investigator-selected tyrosine kinase inhibitors (IS TKIs) in newly diagnosed patients (pts) with chronic myeloid leukemia (CML): primary results [abstract]. Presented at: American Society for Clinical Oncology (ASCO) 2024 Annual Meeting; May 31 – June 4, 2024; Chicago, IL.
2. Scemblix. US FDA Prescribing Information. Novartis Pharmaceuticals; 2021.
3. Novartis data on file.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Chronic Myeloid Leukemia Version 2.2024. December 5, 2023. Accessed April 3, 2024. https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf
5. U.S. Food and Drug Administration. Delivering Promising New Medicines Without Sacrificing Safety and Efficacy. August 27, 2019. Accessed July 17, 2024. https://www.fda.gov/news-events/fda-voices/delivering-promising-new-medicines-without-sacrificing-safety-and-efficacy.
6. A Study of Oral Asciminib Versus Other TKIs in Adult Patients With Newly Diagnosed Ph+ CML-CP (ASC4FIRST). ClinicalTrials.gov identifier: NCT04971226. Updated March 25, 2024. Accessed March 26, 2024. https://clinicaltrials.gov/study/NCT04971226
7. Scemblix. EMA Summary of Product Characteristics. Novartis Europharm Limited; 2022.
8. Rea D, Mauro MJ, Boquimpani C, et al. A Phase 3, Open-Label, Randomized Study of Asciminib, a STAMP Inhibitor, vs Bosutinib in CML After 2 or more prior TKIs. *Blood*. 2021;138(21):2031-2041. doi:10.1182/blood.2020009984

9. Cortes JE, Hughes TP, Mauro MJ, 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.
10. Schoepfer J, Jahnke W, Berellini G, 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. doi:10.1021/acs.jmedchem.8b01040
11. Hochhaus A, Saglio G, Hughes TP, et al. Long-term benefits and risks of frontline nilotinib vs imatinib for chronic myeloid leukemia in chronic phase: 5-year update of the randomized ENESTnd trial. *Leukemia*. 2016;30(5):1044-1054. doi:10.1038/leu.2016.5
12. Brümmendorf TH, Cortes JE, de Souza CA, et al. Bosutinib versus imatinib in newly diagnosed chronic-phase chronic myeloid leukaemia: results from the 24-month follow-up of the BELA trial. *Br J Haematol*. 2015;168(1):69-81. doi:10.1111/bjh.13108
13. Cortes JE, Gambacorti-Passerini C, Deininger MW, et al. Bosutinib Versus Imatinib for Newly Diagnosed Chronic Myeloid Leukemia: Results From the Randomized BFORE Trial. *J Clin Oncol*. 2018;36(3):231-237. doi:10.1200/JCO.2017.74.7162
14. Kota VK, Wei D, Yang D, et al. Treatment Patterns and Modifications of Tyrosine Kinase Inhibitors (TKI) Therapy in Early Lines in Patients with Chronic Myeloid Leukemia in Chronic Phase (CML-CP): Real-World Analysis from a Large Commercial Claims Database in the United States (US). *Blood.* 2023;142:5190.
15. Hehlmann R, Cortes JE, Zyczynski T, et al. Tyrosine kinase inhibitor interruptions, discontinuations and switching in patients with chronic-phase chronic myeloid leukemia in routine clinical practice: SIMPLICITY. *Am J Hematol*. 2019;94(1):46-54. doi:10.1002/ajh.25306
16. Claudiani S, Chughtai F, Khan A. et al. Long-term outcomes after upfront second-generation tyrosine kinase inhibitors for chronic myeloid leukemia: managing intolerance and resistance. *Leukemia.* 2024;38:796–802. doi:10.1038/s41375-024-02187-w
17. Kohlbrenner K, Galuschek N, Fabarius A, et al. Therapy in Patients with Chronic Myeloid Leukemia Outside of Clinical Trials: Results of the German CML-Registry (CML-VI). *Blood.* 2022;140(Supplement 1):947–949. doi:10.1182/blood-2022-15941
18. Cortes JE, Khoury HJ, Kantarjian HM, 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. doi:10.1002/ajh.24536
19. Garg RJ, Kantarjian H, O'Brien S, 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. doi:10.1182/blood-2009-05-221531
20. Steegmann JL., Baccarani M, Breccia M, et al. European LeukemiaNet recommendations for the management and avoidance of adverse events of treatment in chronic myeloid leukaemia. *Leuk.* 2016;30:1648-1671. doi:10.1038/leu.2016.104
21. Hochhaus A, Larson RA, Guilhot F, et al. Long-Term Outcomes of Imatinib Treatment for Chronic Myeloid Leukemia. *N Engl J Med.* 2017;376: 917–927. doi:10.1056/NEJMoa1609324
22. Cortes JE, Saglio G, Kantarjian HM, 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. doi:10.1200/JCO.2015.64.8899
23. Akard LP, Albitar M, Hill CE, Pinilla-Ibarz, J. 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 Routine Practice. *Clin Adv Hematol Oncol.* 2013;11(7):421-432.
24. Cortes JE, Kim DW, Pinilla-Ibarz J, et al. Ponatinib efficacy and safety in Philadelphia chromosome–positive leukemia: final 5-year results of the phase 2 PACE trial. *Blood.* 2018;132(4):393-404. doi:10.1182/blood-2016-09-739086
25. Hochhaus A, Baccarani M, Silver RT, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. *Leuk.* 2020;34:966-984. doi:10.1038/s41375-020-0776-2
26. Flis S, Chojnacki T. Chronic myelogenous leukemia, a still unsolved problem: pitfalls and new therapeutic possibilities. *Drug Des Devel Ther.* 2019;13:825-843. doi:10.2147/DDDT.S191303
27. Wylie AA, Schoepfer J, Jahnke W, et al. The allosteric inhibitor ABL001 enables dual targeting of BCR–ABL1. *Nature.* 2017;543(7647):733-737. doi:10.1038/nature21702
28. Hughes TP, Mauro MJ, Cortes JE, et al. Asciminib in Chronic Myeloid Leukemia after ABL Kinase Inhibitor Failure. *N Engl J Med.* 2019; 381(24):2315-2326. doi:10.1056/NEJMoa1902328
29. 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. Presented at: ASH Annual Meeting & Exposition; Dec. 5, 2016.
30. Ottmann OG, Alimena G, DeAngelo DJ, 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. doi:10.1182/blood.V126.23.138.138
31. Mauro MJ, Kim DW, Cortes J, 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. Presented at: EHA Annual Meeting; June 15, 2019.
32. Cortes JE, Lang F, Kim DW, et al. Combination Therapy Using Asciminib Plus Imatinib (IMA) in Patients (PTS) with Chronic Myeloid Leukemia (CML): Results from a Phase 1 Study. Presented at: EHA Annual Meeting; June 15, 2019.
33. Manley PW, Barys L, Cowan-Jacob SW. 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. *Leuk Res.* 2020;98:106458. doi:10.1016/j.leukres.2020.106458

34. Study of Efficacy of CML-CP Patients Treated with ABL001 Versus Bosutinib, Previously Treated With 2 or More TKIs. ClinicalTrials.gov identifier: NCT03106779. Updated February 7, 2024. Accessed April 3, 2024. https://clinicaltrials.gov/ct2/show/NCT03106779
35. Asciminib in Monotherapy for Chronic Myeloid Leukemia in Chronic Phase (CML-CP) With and WithoutT315I Mutation (AIM4CML). ClinicalTrials.gov identifier: NCT04666259. Updated September 7, 2023. Accessed April 3, 2024. https://clinicaltrials.gov/ct2/show/NCT04666259
36. Study of Efficacy And Safety Of Asciminib In Combination With Imatinib In Patients With Chronic Myeloid Leukemia In Chronic Phase (CML-CP). ClinicalTrials.gov identifier: NCT03578367. Updated March 22, 2024. Accessed April 3, 2024. https://clinicaltrials.gov/ct2/show/NCT03578367
37. 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. ClinicalTrials.gov identifier: NCT04795427. Updated October 19, 2023. Accessed April 3, 2024. https://clinicaltrials.gov/ct2/show/NCT04795427
38. A Phase I Study of Oral ABL001 in Patients With CML or Ph+ ALL. ClinicalTrials.gov identifier: NCT02081378. Updated March 18, 2024. Accessed April 3, 2024. https://clinicaltrials.gov/ct2/show/NCT02081378
39. Asciminib Treatment Optimization in ≥ 3rd Line CML-CP. ClinicalTrials.gov identifier: NCT04948333. Updated February 28, 2024. Accessed April 3, 2024. https://clinicaltrials.gov/ct2/show/NCT04948333

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