Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

https://www.novartis.com
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MEDIA & INVESTOR RELEASE

Novartis Scemblix® demonstrates sustained response rate in 48-week follow-up in patients with chronic myeloid leukemia

- *Updated 48-week data from Phase III ASCEMBL trial consistent with improved major molecular response (MMR) rate of Scemblix® (asciminib) vs. Bosulif®* (bosutinib) and lower discontinuation rate due to adverse reactions demonstrated in 24-week primary analysis*[1]

- *Data support longer-term use of Scemblix in patients with chronic myeloid leukemia (CML) who have previously struggled with intolerance and resistance to at least two prior tyrosine kinase inhibitor treatments*[2-4]

- *Differentiated by novel mechanism of action, Scemblix is the first FDA-approved CML treatment that works by binding to the ABL myristoyl pocket*[2-4]

- *Clinical development program continues, evaluating Scemblix across multiple treatment lines in CML*[2-19]

Basel, December 11, 2021 — Novartis today announced new 48-week data from the Phase III ASCEMBL trial of Scemblix® (asciminib) demonstrating that the results observed in the primary analysis (24 weeks) vs. Bosulif®* (bosutinib) were maintained in longer-term follow up for patients with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP) previously treated with two or more tyrosine kinase inhibitors (TKIs)[1-4].

In this analysis, presented at the 63rd American Society of Hematology Annual Meeting & Exposition (ASH), the major molecular response (MMR) rate at 48 weeks was 29.3% for patients treated with Scemblix vs. 13.2% for patients in the Bosulif arm, which is consistent with a doubling of the efficacy at 24 weeks (25% vs. 13% [*P*=0.029])[1-4]. The proportion of patients treated with Scemblix who experienced adverse reactions leading to discontinuation was more than three times lower than those in the Bosulif arm (7.1% vs. 25%)[1].

Scemblix is the first FDA-approved CML treatment that works by binding to the ABL myristoyl pocket[2]. This novel mechanism of action, also known in scientific literature as a STAMP inhibitor, can help address resistance to TKI therapy in patients with CML and overcome mutations at the defective *BCR-ABL1* gene, which is associated with the over-production of leukemic cells[2-4]. Scemblix continues to be studied across multiple lines of treatment for CML-CP[3-12].

“We often see that sequential use of TKI treatments can be associated with increased failure rates and greater concerns regarding potential treatment side effects as patients move to later lines. Scemblix offers an increasingly proven option for patients living with CML who have

previously tried two or more TKIs, and takes a different approach to targeted inhibition to better manage CML," said Dr. Michael J. Mauro**, Hematologist and Myeloproliferative Neoplasms Program Leader at Memorial Sloan Kettering Cancer Center (MSK).

In this updated analysis, responses were also durable, with 60 out of 62 patients on Scemblix maintaining MMR at time of their last assessment[1]. Scemblix continued to deliver more favorable deep molecular responses (MRs) with MR^4 and $MR^{4.5}$ rates at 48 weeks of 10.8% and 7.6%, compared to 3.9% and 1.3% in patients treated with Bosulif, respectively[1]. Additionally, the cumulative proportion of patients achieving a level of $BCR\text{-}ABL1^{IS} \leq 1\%$ at 48 weeks – a predictor of better long-term outcomes in this heavily pretreated patient population – was higher in the Scemblix arm than in the Bosulif arm (50.8% vs 33.7%)[1].

The most common reason for treatment discontinuation was lack of efficacy in 37 (23.6%) patients treated with Scemblix and 27 (35.5%) patients treated with Bosulif[1]. Median duration of exposure was 15.4 months (range, 0.0–37.3 months) for Scemblix and 6.8 months (range, 0.2–34.3 months) for Bosulif[1]. With a longer duration of exposure, the safety and tolerability profile remains consistent with the primary analysis of the ASCEMBL trial[1-4]. The most common (incidence ≥ 20%) adverse reactions reported in this analysis were thrombocytopenia (29.5%) and neutropenia (23.1%) in the Scemblix arm; and diarrhea (71.1%), nausea (46.1%), increased ALT (28.9%), vomiting (26.3%), rash (23.7%), increased AST (21.1%) and neutropenia (21.1%) in the Bosulif arm[1].

"We are excited to see the continued benefit with Scemblix for this long-underserved patient population," said Jeff Legos, Executive Vice President, Global Head of Oncology & Hematology Development at Novartis. "These data are encouraging as we continue to challenge the current standard of care in CML by exploring if and how Scemblix can help more patients living with this disease."

Scemblix received FDA approval in October 2021 and is currently available for physicians to prescribe to appropriate patients in the US[2]. Scemblix is also being evaluated in studies across multiple treatment lines and indications for CML-CP, including the ASC4FIRST Phase III study for newly diagnosed adult patients, as well as in a Phase Ib/II dose assessment study in pediatric patients with Ph+ CML-CP. Trial-in-progress posters for both are being presented at ASH[13-22].

To learn more about our long-standing commitment to transforming the lives of patients with CML with bold science, the latest information from Novartis and access to our ASH 2021 scientific presentations, visit the Novartis Oncology Congress Hub at https://www.hcp.novartis.com/virtual-congress/ash-2021/.

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. 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[2].

Scemblix is the first FDA-approved CML treatment that binds to the ABL myristoyl pocket[2]. This novel mechanism of action, also known in scientific literature as a STAMP inhibitor, can 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[3-12].

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[3-20]. Specifically, the ASC4FIRST Phase III study (NCT04971226) evaluates Scemblix as a first-line treatment and is in the recruitment phase[14,21].

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.

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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,” “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 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.

About Novartis

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 products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at

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

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

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

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

Julie Masow
Novartis US External Communications
+1 862 579 8456
julie.masow@novartis.com

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

Central		North America	
Samir Shah	+41 61 324 7944	Sloan Simpson	+1 862 345 4440
Thomas Hungerbuehler	+41 61 324 8425	Alina Levchuk	+1 862 778 3372
Isabella Zinck	+41 61 324 7188	Parag Mahanti	+1 973-876-4912