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MEDIA & INVESTOR RELEASE

Novartis Scemblix® Phase III data first to show superior efficacy with a favorable safety and tolerability profile vs. standard-of-care TKIs in adults with newly diagnosed CML

- *Phase III ASC4FIRST trial met both primary endpoints with clinically meaningful and statistically significant results; Scemblix® (asciminib) demonstrated superior MMR rates at week 48 vs. investigator-selected SoC TKIs (imatinib, nilotinib, dasatinib and bosutinib) (67.7% vs. 49.0%) and imatinib alone (69.3% vs. 40.2%)[1]*

- *Scemblix also demonstrated a favorable safety and tolerability profile vs. imatinib and 2G TKIs, with fewer grade ≥3 AEs, dose adjustments, and half the rate of AEs leading to treatment discontinuation[1]*

- *TKIs have transformed CML treatment, but unmet need remains; many newly diagnosed patients do not meet molecular response goals, and many discontinue or change treatment due to intolerance[2-17]*

- *Scemblix was granted US FDA Breakthrough Therapy Designation, submission is now in review under the agency's Oncology Center of Excellence RTOR program; data will be presented as a plenary at EHA and today as a late-breaking abstract at ASCO*

Basel, May 31, 2024 – Novartis today presents positive results from the pivotal Phase III ASC4FIRST trial as a late-breaking abstract at the 2024 American Society of Clinical Oncology (ASCO) meeting. Scemblix® (asciminib) demonstrated superior major molecular response (MMR) rates at week 48 compared to investigator-selected standard-of-care (SoC) tyrosine kinase inhibitors (TKIs) imatinib, nilotinib, dasatinib and bosutinib, and compared to imatinib alone in patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP)[1]. Scemblix also showed a numerical improvement in MMR at week 48 vs. second generation (2G) TKIs (nilotinib, dasatinib and bosutinib)[1]. Additionally, Scemblix demonstrated a favorable safety and tolerability profile, with fewer adverse events (AEs) and treatment discontinuations vs. both imatinib and 2G TKIs[1].

"Scemblix is the first CML treatment to show significantly better efficacy compared to investigator-selected standard-of-care TKIs," said Prof. Tim Hughes, MD, South Australian Health & Medical Research Institute (SAHMRI). "When you combine superior response with the excellent safety and tolerability profile of Scemblix, we have a very promising potential frontline option for newly diagnosed patients to support them in achieving their treatment goals."

The median follow-up was 16.3 and 15.7 months for Scemblix and investigator-selected SoC TKIs, respectively[1]. Nearly 20% more patients treated with Scemblix achieved MMR at week 48 vs. investigator-selected SoC TKIs and nearly 30% more patients achieved MMR at week 48 vs. imatinib alone[1]. Patients treated with Scemblix also achieved deeper rates of molecular responses (MR4 and MR4.5) compared with investigator-selected SoC TKIs and imatinib alone[1].

		Overall[a] Scemblix (n=201) vs. investigator-selected SoC TKIs (n=204)	**Imatinib stratum[b]** Scemblix (n=101) vs. imatinib (n=102)	**2G TKI stratum[c]** Scemblix (n=100) vs. 2G TKIs (n=102)
Primary endpoints	Week 48 MMR rates	67.7% vs. 49.0%	69.3% vs. 40.2%	–
	Week 48 MMR Treatment difference (95% CI)	18.9% (9.6%–28.2%)	29.6% (16.9%–42.2%)	–
	Adjusted 1-sided *p*-value	<.001	<.001	–
Secondary endpoints[d]	Week 48 MMR rates	–	–	66.0% vs. 57.8%
	Week 48 MR4	39% vs. 21%	43% vs. 15%	35% vs. 26%
	Week 48 MR4.5	17% vs. 9%	18% vs. 5%	16% vs. 13%

[a] All patients receiving Scemblix (n=201) or investigator-selected SoC TKIs (n=204). Treatment difference after adjusting for pre-randomization selected TKI and EUTOS long-term survival (ELTS) risk groups at baseline.
[b] The 203 patients within the pre-randomization-selected imatinib stratum were randomized to receive either Scemblix (n=101) or imatinib (n=102). Treatment difference after adjusting for ELTS risk groups at baseline.
[c] The 202 patients within the pre-randomization selected 2G TKIs stratum were randomized to receive either Scemblix (n=100) or 2G TKIs (n=102: nilotinib, 48%; dasatinib, 41%; bosutinib, 11%).
[d] Secondary endpoints were not powered for statistical significance.

In newly diagnosed patients, the safety profile was consistent with previous registration studies with no new safety concerns observed[1]. Fewer grade ≥3 AEs, dose adjustments to manage AEs, and half the rate of AEs leading to treatment discontinuation were reported for Scemblix vs. both imatinib and 2G TKIs[1].

	Scemblix	**Imatinib**	**2G TKIs**
Grade ≥3 AEs[a]	38%	44%	55%
AEs leading to treatment discontinuation[a]	5%	11%	10%
AEs leading to dose adjustments/ interruptions[a]	30%	39%	53%

[a] In patients who experienced ≥1 adverse event.

“Patients living with CML need efficacious and well-tolerated treatment options that help them achieve meaningful outcomes as they manage their chronic condition,” said Shreeram Aradhye, M.D., President, Development and Chief Medical Officer, Novartis. “The compelling ASC4FIRST data highlight the potential of Scemblix to achieve better results than standard-of-care in newly diagnosed adults, while maintaining a favorable safety and tolerability profile. These results reinforce Scemblix as a proven treatment in Ph+CML-CP, as we continue to build on our 20-year legacy in CML innovation.”

“CML is a chronic condition and the side effects of standard-of-care can be challenging for patients. They often affect their daily life and can lead to high rates of treatment switching,” said Gerald Clements, CML caregiver, patient advocate and Steering Committee Treasurer at CML Advocates Network. “Effective care that can be tolerated long-term is a key unmet need. By potentially bringing Scemblix to patients when they are first diagnosed, they may have an

opportunity to be on a highly effective treatment while also maintaining their day-to-day from the start."

The trial remains ongoing, with the next scheduled analysis at week 96 to evaluate the key secondary endpoint (MMR at week 96) and additional secondary endpoints[18].

These results have been submitted to the US Food and Drug Administration (FDA) via the Oncology Center of Excellence Real-Time Oncology Review (RTOR) program and Scemblix has been granted Breakthrough Therapy Designation. They will also be presented as a plenary at the European Hematology Association (EHA) 2024 Congress in June.

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[18]. 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[18].

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[18]. 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[18].

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)[19-21]. The current approved CML treatments are TKIs that target the ATP-binding site (ATP-competitive) [21].

Scemblix is approved in more than 70 countries, including the US and the EU, to treat adults with Ph+ CML-CP who have previously been treated with two or more TKIs[22-24]. In some countries, including the US, Scemblix is also approved in patients with Ph+ CML-CP with the T315I mutation[23-25].

Scemblix is an important treatment option for patients who experience resistance and/or intolerance after two prior TKI therapies[2-17], and it is being studied across multiple treatment lines for Ph+ CML-CP, both as a monotherapy and in combination[18-20,24,26-38].

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 into a chronic, vs. a life-limiting, 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 collaboration with the Max Foundation has provided access to Glivec, Tasigna and now Scemblix, starting over 20 years ago, and delivering tremendous patient impact in low- and middle-income countries, with over 100,000 patients supported to date.

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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,” “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 connect with us on **LinkedIn**, **Facebook**, **X/Twitter** and **Instagram**.

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