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MEDIA & INVESTOR RELEASE

Novartis Scemblix® shows superior major molecular response (MMR) rates vs. standard-of-care TKIs in Phase III trial for newly diagnosed patients with chronic myeloid leukemia

Ad hoc announcement pursuant to Art. 53

- *ASC4FIRST trial met both primary endpoints with clinically meaningful and statistically significant results; Scemblix® (asciminib) shows superior MMR rates at week 48 vs. standard-of-care TKIs (imatinib, nilotinib, dasatinib, and bosutinib) in newly diagnosed Ph+CML-CP patients*[1]

- *Scemblix demonstrated a favorable safety and tolerability profile with fewer adverse events (AEs) and treatment discontinuations vs. standard-of-care TKIs; no new safety signals were observed*[1]

- *With current standard-of-care TKIs, more than 60% of newly diagnosed patients with CML fail to meet molecular response goals at one year; intolerance and AEs remain a primary reason for discontinuing TKI therapy, with discontinuation rates due to AEs of up to 25% by five years*[2-13]

- *Data will be presented at an upcoming medical conference and submitted to regulatory authorities in 2024*

Basel, January 08, 2024 — Novartis today announced positive results from the primary analysis of ASC4FIRST, a pivotal Phase III trial comparing Scemblix® (asciminib) with investigators' choice of tyrosine kinase inhibitor (TKI) treatment in newly diagnosed patients with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP)[1]. ASC4FIRST is the first and only randomized head-to-head Phase III trial comparing a CML treatment vs. approved standard-of-care first- and second-generation TKIs[1].

The trial met both primary endpoints of major molecular response (MMR) rate for Scemblix compared to investigator-selected TKIs (imatinib, nilotinib, dasatinib, and bosutinib) and compared to imatinib, demonstrating clinically meaningful and statistically significant results for both endpoints[1]. Scemblix showed a favorable safety and tolerability profile with fewer adverse events (AEs) and treatment discontinuations vs. investigator selected standard-of-care TKIs[1]. The ASC4FIRST data showed no new safety signals compared to the established safety profile of Scemblix[1,14].

"We are very encouraged by these results given that a significant proportion of patients with newly diagnosed chronic myeloid leukemia, or CML, do not achieve their treatment goals," said Prof. Tim Hughes, MD, South Australian Health & Medical Research Institute (SAHMRI). "There remains a significant need in first-line therapy of CML for tolerable treatment options, allowing people with CML to balance their treatment alongside their quality of life."

Improvements in treatment have transformed CML into a chronic disease, with a life expectancy similar to that of the general population, making tolerability an important treatment goal[9]. While many patients with CML may benefit from available TKI therapy, intolerance and AEs remain a primary reason for TKI therapy discontinuation, with discontinuation rates due to AEs of up to 25% by five years[2-6]. Additionally, over 60% of newly diagnosed CML patients fail to meet 12-month molecular response goals [5-13].

“We are excited that Scemblix may help people newly diagnosed with CML achieve their treatment goals while continuing to live their lives,” said Shreeram Aradhye, M.D., President, Development and Chief Medical Officer, Novartis. “Given the chronic nature of their condition, patients often need to be on TKI therapy for many years, so treatment options that are well tolerated and highly efficacious are crucial to support adherence. This study outcome builds on our 20-year legacy in CML innovation as we strive to continue to address the remaining unmet needs for people living with this blood cancer.”

The trial remains ongoing, with the next scheduled data readout planned for week 96, which will evaluate the key secondary endpoint (MMR at week 96) as well as additional secondary endpoints.

Details will be presented at an upcoming medical conference and included as part of regulatory submissions in 2024.

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 versus investigator-selected first- or second-generation TKI (imatinib, nilotinib, dasatinib, or bosutinib) in 405 adult patients with newly diagnosed Ph+ CML-CP[1]. The two primary endpoints of the study are to compare efficacy of asciminib vs. investigator-selected TKI 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[1]. The study remains ongoing with a key secondary endpoint 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. 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[1].

About Scemblix® (asciminib)
Scemblix® is the first CML treatment that works by specifically targeting the ABL myristoyl pocket[15,16] and was intentionally designed to be highly specific and minimize off-target kinase mediated effects, which translates into an improved safety and tolerability profile compared to current standard of care.

Scemblix is approved in more than 60 countries, including the US and the EU, to treat adults with Ph+ CML-CP who have previously been treated with two or more TKIs[14,19]. In some countries including the US, Scemblix is also approved in patients with Ph+ CML-CP with the T315I mutation[2-14,18,19].

Scemblix represents an important potential treatment option for patients who experience resistance and/or intolerance to currently available TKI therapies, and it is being studied across multiple treatment lines for Ph+ CML-CP, both as monotherapy and in combination[15-18,20-33].

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, versus 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 90,000 patients supported to date.

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," "planned," "may," "commitment," "remain," "goals," "upcoming," "excited," "potentially," "continuing," "continue," "strive," "ongoing," "to address," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for Scemblix, or regarding potential future revenues from Scemblix. 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 Scemblix 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 Scemblix will be commercially successful in the future. In particular, our expectations regarding Scemblix 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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