Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

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

Longer-term data for Novartis Scemblix® reinforce superior efficacy with favorable safety and tolerability profile in adults with newly diagnosed CML

- *Scemblix demonstrated sustained superior major molecular response (MMR) vs. all investigator-selected TKIs (74.1% vs. 52%) and vs. imatinib alone (76.2% vs. 47.1%), meeting both ASC4FIRST 96-week key secondary endpoints*[1]
- *Scemblix showed a clinically relevant 15.1% higher MMR rate vs. second generation (2G) TKIs (72.0% vs. 56.9%)*[1]
- *96-week data extend favorable safety and tolerability profile for Scemblix vs. imatinib and 2G TKIs, with fewer grade ≥3 AEs and less than half the discontinuation rate due to AEs*[1]
- *Latest results strengthen Scemblix as a standard of care following expanded indication in newly diagnosed and previously treated adult patents with Ph+ CML-CP and NCCN category 1 recommendation*[1-3]

Basel, December 8, 2024 – Novartis today announced positive, longer-term results from the pivotal Phase III ASC4FIRST trial with Scemblix® (asciminib) showing superior major molecular response (MMR) rates at week 96[1]. The study compared the MMR rate of Scemblix to investigator-selected standard-of-care (SoC) tyrosine kinase inhibitors (TKIs) (imatinib, nilotinib, dasatinib and bosutinib) and to imatinib alone in adult patients with newly diagnosed Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP) at the week 96 evaluation, the study's key secondary endpoints[1]. The longer-term results showed an increasing difference in Scemblix MMR rate vs. SoC, vs. imatinib and vs. 2G TKIs (nilotinib, dasatinib and bosutinib)[1]. Results were presented at the 66th American Society of Hematology Annual Meeting & Exposition (ASH)[1].

"These 96-week results are very encouraging for clinicians who aspire to obtain a balance of efficacy and tolerability profiles to help newly diagnosed adult CML patients achieve and maintain treatment goals," said Jorge Cortes, M.D., Director, Georgia Cancer Center. "The sustained superior efficacy, deeper and more durable responses, and favorable safety and tolerability profile compared to standard of care TKIs continue to support the promise of Scemblix as a potentially practice-changing treatment option."

The median follow-up was 2.2 years for Scemblix and investigator-selected SoC TKIs[1]. Over 22% more patients treated with once-daily Scemblix achieved MMR at week 96 vs. all

investigator-selected SoC TKIs, and nearly 30% more patients achieved MMR at week 96 vs. imatinib alone[1]. The Scemblix MMR rate was 15.1% (95% CI: 2.3, 28.0; not crossing zero) higher vs. 2G TKIs (72% vs. 56.9%)[1]. Patients treated with Scemblix also achieved deeper rates of molecular responses (MR4 and MR4.5) compared with investigator-selected SoC TKIs[1].

		Overall [a] Scemblix (n=201) vs. IS 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)
Key secondary endpoints	MMR rates at week 96	74.1% vs. 52%	76.2% vs. 47.1%	
Secondary endpoints[d]	MMR rates at week 96			72% vs. 56.9%
	MR4 at week 96	48.8% vs. 27.5%	52.5% vs. 23.5%	45% vs. 31.4%
	MR4.5 at week 96	30.9% vs. 17.7%	35.6% vs. 11.8%	26% vs. 23.5%

[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.

The safety profile of Scemblix at 96-weeks was consistent with the 4-year follow-up of the Phase III ASCEMBL trial, with no new safety concerns observed to date[1,2,4]. Fewer grade ≥3 AEs and dose adjustments to manage AEs were reported for Scemblix, and discontinuation due to AEs was more than 50% lower for Scemblix vs. both imatinib and 2G TKIs[1]. The most frequent AEs (≥15%) were diarrhea, headache, fatigue, musculoskeletal pain, and rash[1].

Week 96	Scemblix n=200	Imatinib n=99	2G TKIs n=102
Grade ≥ AEs[a]	44.5%	49.5%	59.8%
Discontinuation due to AEs[a]	5.5%	13.1%	12.7%
AEs leading to dose adjustments/interruptions[a]	33%	41.4%	57.8%

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

Novartis also presented today at ASH interim data from the Phase II ASC2ESCALATE dose-escalation study in both the second line (2L) and newly diagnosed Ph+ CML-CP settings[5]. In the analysis of 2L patients at week 24 (n=28) Scemblix demonstrated MMR rates of 42.9% and deep molecular responses (MR4 25% and MR4.5 10.7%), with a consistent safety and tolerability profile[5]. The most common AEs (>15%) were nausea, hypertension, and vomiting[5].

“Novartis’ decades-long work in CML and deep relationships within the community have informed our Scemblix clinical trial program of over 10 years, the centerpiece of our continuing drive to address ongoing unmet medical needs for people with CML,” said Jeff Legos, Executive Vice President, Global Head of Oncology Development, Novartis. “These latest

findings reinforce the differentiated efficacy, safety and tolerability profile of Scemblix in newly diagnosed and previously treated adult CML patients."

Scemblix was recently granted accelerated approval in the US to treat newly diagnosed adults with Ph+ CML-CP, which together with its approval in previously treated adult patients with Ph+ CML-CP expands the population of Scemblix-eligible patients by four-fold [2]. In addition, the National Comprehensive Cancer Network (NCCN) updated its Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for the treatment of CML, recommending asciminib as a *category 1 – preferred* treatment for newly diagnosed Ph+ CML-CP and across all risk categories[3].

About the 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. IS first- or second-generation TKIs (imatinib, nilotinib, dasatinib or bosutinib) in 405 adult patients with newly diagnosed Ph+ CML-CP[2,6]. The trial met both primary endpoints with Scemblix demonstrating 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%) as well as the secondary, non-powered endpoint for the 2G TKI stratum of (66% vs 57.8%)[1,6]. The study remains ongoing with further efficacy and safety readouts planned.

About the ASC2ESCALATE Phase II Study
ASC2ESCALATE (NCT05384587) is a Phase II, multicenter, single-arm, dose-escalation study of oral Scemblix® 80 mg QD in both the second line (2L) and newly diagnosed (1L) Ph+ CML-CP settings in the US [5,7]. While Scemblix is already approved across lines of therapy, this is the first prospective trial to assess asciminib in the 2L setting and a dose-escalation strategy of asciminib as 2L and 1L treatment for patients with CML-CP not meeting molecular milestones [5]. The proportion of patients achieving MMR at 12 months in the 2L setting will be measured as the primary endpoint [5]. The study remains ongoing and has completed enrollment with 196 patients (100 patients in 2L, 96 patients in 1L)[5].

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)[4,8,9]. Other currently approved CML treatments are TKIs that target the ATP-binding site (ATP-competitive)[9].

In the US, Scemblix was granted accelerated approval to treat newly diagnosed adults with Ph+ CML-CP and is also approved for previously treated adult patients with Ph+ CML-CP. Outside the US, it is approved in more than 75 countries, including the EU, to treat those who have previously been treated with two or more TKIs with Ph+ CML-CP[2,10,11]. In some countries, including the US, Scemblix is also approved in patients with Ph+ CML-CP with the T315I mutation[2,3,10].

Scemblix is being studied across multiple treatment lines for Ph+ CML-CP, both as a monotherapy and in combination[2,4,6,8,10,12-24].

Patient Access and Support
Novartis, with its 20+ year history in CML, is committed to continuing to address areas of unmet patient need and reducing barriers to patient access and affordability that prevent patients from benefiting from innovation. Novartis Patient Support is available to help guide eligible patients through the various aspects of getting started on treatment including help understanding insurance coverage and identifying potential financial assistance options. Patients or providers can call 866-433-8000 or visit support.scemblix.com to learn more.

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 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.

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,” “may,” “committed,” “contingent,” “lead,” “continue,” “ongoing,” “to deliver,” “allowing,” “continuing,” “commitment,” 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.

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# # #

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

Central		North America	
Anja von Treskow	+41 79 392 9697	Michael Meo	+1 862 274 5414
Anna Schäfers	+41 79 801 7267		
Switzerland			
Satoshi Sugimoto	+41 79 619 2035		

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

Central		North America	
Isabella Zinck	+41 61 324 7188	Sloan Simpson	+1 862 345 4440
Nicole Zinsli-Somm	+41 61 324 3809	Jonathan Graham	+1 201 602 9921
Imke Kappes	+41 61 324 8269	Parag Mahanti	+1 973 876 4912