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MEDIA RELEASE

Novartis Kisqali® reduces risk of recurrence in younger patients with early breast cancer in NATALEE subgroup analysis

- *33% reduction in relative risk of invasive disease observed in pre-menopausal early breast cancer (EBC) patients receiving Kisqali in 1-year post-treatment analysis*[1]
- *Tolerability remained consistent, with fewer treatment discontinuations due to adverse events among pre-menopausal patients*[1]
- *Rising breast cancer diagnosis rates and more aggressive disease in younger women underscore importance of early detection and care with effective and tolerable treatments that help prevent cancer recurrence*[2]
- *Separate real-world analysis presented at ASCO demonstrates differences in treatment outcomes that underscore critical need to improve care for Black patients with EBC*[3]

Basel, June 1, 2025 – Novartis is announcing data from a new subgroup analysis of the Phase III NATALEE trial evaluating the efficacy and safety of Kisqali® (ribociclib) plus endocrine therapy (ET, a non-steroidal aromatase inhibitor) in patients with stage II and III hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) early breast cancer (EBC) at high risk of recurrence across age and menopausal status[1]. The data will be presented today at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting.

Results at median follow-up of 44.2 months show that patients receiving Kisqali continued to see consistent reductions in risk of recurrence across all efficacy measures, regardless of age and menopausal status[1]. In this one-year post-treatment analysis, pre-menopausal and younger patients, who often present with more aggressive disease characteristics, experienced greater reductions in risk of recurrence and fewer treatment discontinuations due to adverse events (AEs) than post-menopausal patients[1].

“As the incidence of early onset breast cancer increases, it is encouraging to see that ribociclib continues to deliver durable risk reduction for a broad population of patients with EBC, including younger patients,” said Dr. Kevin Kalinsky, Division Director of Medical Oncology and Director of the Glenn Family Breast Center at Winship Cancer Institute of Emory University. “Coupled with the lower rates of discontinuation due to AEs seen in this subgroup, these data reinforce the benefit of three-year adjuvant treatment with ribociclib as a well-tolerated intervention for patients seeking to reduce the likelihood of their cancer coming back.”

	Pre-menopausal patients	Post-menopausal patients

	(n = 2238)	(n = 2844)
Hazard ratio[a] (95% CI)	**All Kisqali = 1115 ET = 1123**	**All Kisqali = 1424 ET = 1420**
Invasive disease-free survival (iDFS)	0.671 (0.518-0.870)	0.746 (0.607-0.917)
Distant disease-free survival (DDFS)	0.655 (0.498-0.861)	0.759 (0.612-0.941)
Recurrence-free survival (RFS)	0.641 (0.486-0.845)	0.735 (0.588-0.919)
Disposition in Kisqali arm, n (%)		
Discontinuation due to AE	179 (16.1)	326 (22.9)
Dose reduction due to AE	248 (22.4)	332 (23.6)

[a] Hazard ratios between treatment arms (RIB + NSAI; NSAI alone), stratified by stage, prior chemotherapy, and geographic region.

Addressing Recurrence in Other At-Risk Groups

A separate real-world analysis of EBC patients who met the NATALEE trial eligibility criteria and received ET monotherapy found that Black patients were more likely to be younger, pre-menopausal, have stage III tumors, and have more extensive nodal involvement than white patients. After adjusting for these factors, Black patients also had worse RFS, DDFS, and overall survival than their white counterparts. These findings reinforce the critical need to improve care for Black patients with the addition of a CDK4/6 inhibitor to their adjuvant treatment[3].

Novartis is continuing to add to the body of evidence on the efficacy and safety of Kisqali in different patient populations. Trial design details will be presented at ASCO for the Adjuvant WIDER study, which is enrolling patients that closely reflect the population seen in clinical practice, including more patients from racial and ethnic minority groups[4].

“There is an undeniable and urgent need to improve outcomes for vulnerable patient populations, including younger and Black patients, who often face more aggressive forms of breast cancer and remain at high risk of recurrence," said Reshema Kemps-Polanco, Executive Vice President and Chief Commercial Officer, Novartis US. "With Kisqali, we have the opportunity to reduce the risk of recurrence for these patients with early breast cancer, while we continue to offer significant survival benefit to patients living with metastatic disease.”

About NATALEE

NATALEE is a global Phase III multi-center, randomized, open-label trial to evaluate the efficacy and safety of Kisqali with ET as an investigational adjuvant treatment versus ET alone in patients with stage II and III HR+/HER2- EBC, being conducted in collaboration with TRIO[5,6]. The adjuvant ET in both treatment arms was a non-steroidal aromatase inhibitor (NSAI; anastrozole or letrozole) and goserelin if applicable[5,6]. The primary endpoint of NATALEE is invasive disease-free survival (iDFS) as defined by the Standardized Definitions for Efficacy End Points (STEEP) criteria[5,6]. A total of 5,101 adult patients with HR+/HER2- EBC across 20 countries were randomized in the trial[5,6].

About Kisqali® (ribociclib)
Kisqali® (ribociclib) is a selective cyclin-dependent kinase inhibitor, a class of drugs that help slow the progression of cancer by inhibiting two proteins called cyclin-dependent kinase 4 and 6 (CDK4/6). These proteins, when over-activated, can enable cancer cells to grow and divide too quickly. Targeting CDK4/6 with enhanced precision may play a role in ensuring that cancer cells do not continue to replicate uncontrollably.

Kisqali has been approved as a treatment for breast cancer by regulatory authorities in 99 countries worldwide, including the U.S. FDA and the European Commission[7,8]. In the US, Kisqali is indicated in combination with an AI as an adjuvant treatment for adults with HR+/HER2- stage II and III early breast cancer at high risk of recurrence, as well as for the treatment of adults with HR+/HER2- advanced or MBC as initial ET; Kisqali is also approved in the metastatic indication in combination with fulvestrant as initial ET or following disease progression on ET[7]. In the EU, Kisqali is approved in combination with an AI for the adjuvant treatment of patients with HR+/HER2- early breast cancer at high risk of recurrence; and for the treatment of women with HR+/HER2- advanced or MBC in combination with either an AI or fulvestrant as initial ET or following disease progression[8]. In pre- or peri-menopausal women, the ET should be combined with a luteinizing hormone-releasing hormone agonist[7,8].

In EBC, ribociclib (Kisqali) is the only CDK4/6 inhibitor recommended by the NCCN Guidelines® for breast cancer for both all node-positive disease as well as for patients with no nodal involvement with high-risk disease characteristics, such as tumor size >5 cm, or for tumors sized 2-5 cm, either Grade 2 with high genomic risk/Ki-67 ≥20% or Grade 3[9]. Kisqali approvals in EBC from regulatory authorities worldwide are ongoing, including recent approval from China's National Medical Products Administration[10]. In MBC, Kisqali has consistently demonstrated statistically significant overall survival benefit across three Phase III trials[11-21]. The NCCN Guidelines® also recommend ribociclib (Kisqali) as the only Category 1 preferred CDK4/6 inhibitor for first-line treatment of people living with HR+/HER2- MBC when combined with an AI[9], making Kisqali the preferred first-line treatment of choice for US prescribers in HR+/HER2- MBC.

In addition, Kisqali has achieved the highest score (A) on the European Society for Medical Oncology-Magnitude of Clinical Benefit Scale (ESMO-MCBS) for EBC[22]; and has the highest rating of any CDK4/6 inhibitor on the ESMO Magnitude of Clinical Benefit Scale, achieving a score of five out of five for first-line pre-menopausal patients with HR+/HER2- advanced breast cancer[23]. Further, Kisqali in combination with either letrozole or fulvestrant has uniquely, among other CDK4/6 inhibitors, received a score of four out of five for post-menopausal patients with HR+/HER2- advanced breast cancer treated in the first line[24].

Kisqali was developed by Novartis under a research collaboration with Astex Pharmaceuticals.

Please see full Prescribing Information for Kisqali, available at www.Kisqali.com.

About Novartis in Breast Cancer
For more than 30 years, Novartis has been at the forefront of driving scientific advancements for people touched by breast cancer and improving clinical practice in collaboration with the global community. With one of the most comprehensive breast cancer portfolios and pipeline, Novartis leads the industry in the discovery of new therapies and combinations in HR+/HER2- breast cancer, the most common form of the disease. Beyond medicines, Novartis is leading efforts to encourage early detection and working to remove access barriers faced by patients along their care journey.

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,” “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 nearly 300 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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