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PRESS RELEASE

Novartis Kisqali® 5-year NATALEE data demonstrate 28% reduction in risk of recurrence in the broadest early breast cancer patient population

- *After 5 years, Kisqali® plus endocrine therapy consistently shows significant and clinically meaningful benefit in invasive disease-free survival*[1]
- *Kisqali remains the only CDK4/6 inhibitor demonstrating consistent and clinically meaningful benefit across the broadest population of HR+/HER2- early breast cancer (EBC) patients, including those with node-negative disease*[1]
- *Data also show a 29.1% risk reduction in distant disease-free survival, and a positive trend in overall survival**[1]
- *With a median of around two years post-completion of treatment with Kisqali, no new safety signals were observed*[1]

Basel, October 17, 2025 – Novartis today announced results from the five-year analysis of the pivotal Phase III NATALEE trial of Kisqali® (ribociclib) that demonstrated a sustained benefit at a median of two years after a three-year treatment with Kisqali (median follow-up: 58.4 months). Results showed a 28.4% reduction in risk of recurrence (HR=0.716; 95% CI 0.618-0.829; nominal p-value <0.0001) in the broadest population of patients with high-risk stage II and III hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) early breast cancer (EBC) treated with Kisqali plus endocrine therapy (ET) compared to ET alone[1].

The five-year invasive disease-free survival (iDFS) rates were 85.5% in the Kisqali plus ET arm versus 81.0% in the ET alone arm, representing a clinically meaningful 4.5% improvement[1]. These late-breaking results will be presented at the European Society for Medical Oncology (ESMO) Congress 2025.

"For the thousands of people diagnosed with early breast cancer each year, the fear of recurrence, often as incurable advanced disease, weighs heavily on patients and their families," said Dr. John Crown, Consultant Medical Oncologist at St. Vincent's University Hospital, Dublin, and NATALEE investigator. "These five-year results show that the benefit of ribociclib persists well beyond the completion of treatment, offering these at-risk patients a greater chance of living breast cancer-free."

As follow-up continued, the confidence intervals (CIs) became narrower[1]. This pattern held across clinically relevant subgroups, reinforcing the robustness of the observed iDFS benefit[1].

"These data reinforce the potential of Kisqali to significantly reduce the long-term risk of breast cancer recurrence, extending well beyond the three-year treatment period. This provides physicians and patients with greater confidence in long-term disease management. Kisqali is redefining the standard of care in adjuvant therapy, including in patients with node-negative disease," said Dushen Chetty, Global Head of Oncology and Hematology Development at Novartis, Ad Interim. "The consistency of the benefit observed across both advanced and early breast cancer settings, together with Kisqali's established safety profile, underscores its position as the CDK4/6 inhibitor with the most comprehensive Phase III evidence base for improving patient outcomes."

Overall survival (OS) continues to show an encouraging trend, with further improvement in the hazard ratio (HR) to 0.800 and narrowing CI (95% CI: 0.637-1.003; one-sided nominal p-value 0.026) compared to the final iDFS analysis (OS HR = 0.892 (0.661-1.203)), demonstrating a 20% reduction in the risk of death compared to ET alone[1]. The NATALEE trial will continue follow-up to ensure sufficient data is collected for OS and other long-term endpoints.

iDFS results across pre-specified subgroups[1]:

Subgroups	Hazard ratio	95% CI	Absolute risk reduction at 5 years
Overall population	0.716	0.618-0.829	4.5%
Stage II	0.660	0.493-0.884	3.7%
Stage III	0.730	0.615-0.865	5.6%
Node-negative (N0)	0.606	0.372-0.986	5.7%
Node-positive (N1-3)	0.737	0.631-0.860	4.4%

With a median of around two years after all patients completed Kisqali treatment, long-term safety shows no new safety signals[1]. Overall, rates of secondary primary malignancies (SPMs) were 2.7% (Kisqali plus ET) and 3.0% (ET alone), while SPMs leading to deaths were reported in one patient in each group[1].

Kisqali remains the only CDK4/6 inhibitor to demonstrate statistically significant OS benefits across three randomized controlled trials in advanced breast cancer (MONALEESA-2, MONALEESA-3, and MONALEESA-7)[2-12].

**OS data remain immature at the five-year NATALEE analysis*

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 adjuvant treatment versus ET alone in the broadest range of patients with stage II and III HR+/HER2- EBC, being conducted in collaboration with TRIO[13,14]. The adjuvant ET in both treatment arms was a non-steroidal aromatase inhibitor (NSAI; anastrozole or letrozole) and goserelin if applicable[13,14]. The primary endpoint of NATALEE is invasive disease-free survival (iDFS) as defined by the Standardized Definitions for Efficacy End Points (STEEP) criteria[13,14]. A total of 5,101 adult patients with HR+/HER2- EBC across 20 countries were randomized in the trial[13,14].

About Kisqali® (ribociclib)
Kisqali® (ribociclib) is a selective cyclin-dependent kinase inhibitor, helping slow the progression of cancer by inhibiting two proteins called cyclin-dependent kinase 4 and 6 (CDK4/6). These proteins, when over-activated, enable cancer cells to grow and divide quickly. Targeting CDK4/6 with enhanced precision plays a role in tumor control.

Kisqali has been approved as a treatment for breast cancer by regulatory authorities in more than 100 countries worldwide, including the U.S. FDA and the European Commission[15,16]. 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[15]. 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[16]. In pre- or peri-menopausal women, the ET should be combined with a luteinizing hormone-releasing hormone agonist[15,16].

In EBC, Kisqali is the only CDK4/6 inhibitor recommended by the NCCN Guidelines® for breast cancer as Category 1 preferred 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[17]. Kisqali approvals in EBC from regulatory authorities worldwide are ongoing, including recent approval from China's National Medical Products Administration[18]. In MBC, Kisqali has consistently demonstrated statistically significant overall survival benefit across three Phase III trials[2-12]. The NCCN Guidelines® also recommend 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, making Kisqali the preferred first-line treatment of choice for US prescribers in HR+/HER2- MBC[17].

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[19]; and has the highest rating of any CDK4/6 inhibitor on the ESMO Magnitude of Clinical Benefit Scale, achieving a score of four out of five for first-line pre-menopausal patients with HR+/HER2- advanced breast cancer[20]. 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[21].

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 discovery of new therapies and combinations in HR+/HER2- breast cancer, the most common form of the disease.

Disclaimer
This is a legal statement identifying forward-looking statements involving known and unknown risks and uncertainties. You should include the standard disclaimer in your release as outlined in the Global Press Release Approval Guidelines.

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.

References

1. Crown J, Stroyakovskii D, Yardley DA, et al. Adjuvant Ribociclib Plus Nonsteroidal Aromatase Inhibitor Therapy in Patients With HR+/HER2− Early Breast Cancer: NATALEE 5-Year Outcomes. Presented at the European Society for Medical Oncology (ESMO) Congress; October 17-21, 2025; Berlin, Germany.
2. Yardley DA et al. Pooled exploratory analysis of survival in patients (pts) with HR+/HER2- advanced breast cancer (ABC) and visceral metastases (mets) treated with ribociclib (RIB) + endocrine therapy (ET) in the MONALEESA (ML) trials. Poster presented at the European Society of Medical Oncology Congress. September 9-13, 2022. Paris, France.
3. Neven P et al. Updated overall survival (OS) results from the first-line (1L) population in the Phase III MONALEESA-3 trial of postmenopausal patients with HR+/HER2- advanced breast cancer (ABC) treated with ribociclib (RIB) + fulvestrant (FUL). Mini oral presented at the European Society for Medical Oncology Breast Cancer Congress. May 4, 2022. Paris, France.
4. Hortobagyi GN, Stemmer SM, Burris HA, et al. Overall Survival with Ribociclib plus Letrozole in Advanced Breast Cancer. *N Engl J Med*. 2022;386(10):942-950. doi:10.1056/NEJMoa2114663.
5. Hortobagyi GN et al. Overall survival (OS) results from the phase III MONALEESA (ML)-2 trial of postmenopausal patients with hormone receptor positive/human epidermal growth factor receptor 2 negative (HR+/HER2−) advanced breast cancer (ABC) treated with endocrine therapy (ET) ± ribociclib. LBA 17. Proffered paper presented at the European Society of Medical Oncology Congress, September 16-21, 2021. Lugano, Switzerland.
6. Im SA, Lu YS, Bardia A, et al. Overall survival with ribociclib plus endocrine therapy in breast cancer. *N Engl J Med*. 2019;381(4):307-316. doi:10.1056/NEJMoa1903765.
7. Slamon DJ, Neven P, Chia S, et al. Overall Survival with Ribociclib plus Fulvestrant in Advanced Breast Cancer. *N Engl J Med*. 2020;382(6):514-524. doi:10.1056/NEJMoa1911149.

8. Slamon DJ et al. Overall survival (OS) results of the Phase III MONALEESA-3 trial of postmenopausal patients (pts) with hormone receptor-positive (HR+), human epidermal growth factor 2-negative (HER2-) advanced breast cancer (ABC) treated with fulvestrant (FUL) ± ribociclib (RIB). LBA7_PR. Presented at the European Society of Medical Oncology Congress. September 29, 2019. Barcelona, Spain.
9. Slamon DJ et al. Updated overall survival (OS) results from the Phase III MONALEESA-3 trial of postmenopausal patients (pts) with HR+/HER2− advanced breast cancer (ABC) treated with fulvestrant (FUL) ± ribociclib (RIB). Presented at the American Society of Clinical Oncology Annual Meeting. June 5, 2021. Chicago, USA.
10. Tripathy D et al. Updated overall survival (OS) results from the phase III MONALEESA-7 trial of pre- or perimenopausal patients with HR+/HER2− advanced breast cancer (ABC) treated with endocrine therapy (ET) ± ribociclib. Presented at the San Antonio Breast Cancer Symposium. December 9, 2020. Texas, USA.
11. Yardley D et al. Overall survival (OS) in patients (pts) with advanced breast cancer (ABC) with visceral metastases (mets), including those with liver mets, treated with ribociclib (RIB) plus endocrine therapy (ET) in the MONALEESA (ML) -3 and -7 trials. Presented at the American Society of Clinical Oncology Annual Meeting. June 2020. Chicago, USA.
12. O'Shaughnessy J et al. Overall survival subgroup analysis by metastatic site from the Phase III MONALEESA-2 study of first-line ribociclib + letrozole in postmenopausal patients with HR+/HER2− advanced breast cancer. Presented at the San Antonio Breast Cancer Symposium. December 7-10, 2021. Texas, USA.
13. Slamon D, Lipatov O, Nowecki Z, et al. Ribociclib plus Endocrine Therapy in Early Breast Cancer. *N Engl J Med*. 2024;390(12):1080-1091. doi:10.1056/NEJMoa2305488
14. Clinicaltrials.gov. NCT03701334. A Trial to Evaluate Efficacy and Safety of Ribociclib With Endocrine Therapy as Adjuvant Treatment in Patients With HR+/ HER2- Early Breast Cancer (NATALEE). Accessed October 2025. https://clinicaltrials.gov/study/NCT03701334
15. Kisqali. Prescribing Information (US FDA). Novartis Pharmaceuticals Corporation; 2017. Accessed October 2025. https://www.novartis.com/us-en/sites/novartis_us/files/kisqali.pdf
16. Kisqali. Summary of product characteristics (SmPC). Novartis Europharm Limited; 2017. Accessed October 2025. https://www.ema.europa.eu/en/documents/product-information/kisqali-epar-product-information_en.pdf
17. NCCN Guidelines. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) - Breast Cancer. Accessed October 2025. https://www.nccn.org
18. National Medical Products Administration. Drug Evaluation Information Disclosure: Drug Evaluation Approval Results. National Medical Products Administration. Published May 21, 2025. Accessed October 2025. https://www.nmpa.gov.cn/zwfw/sdxx/sdxxyp/yppjfb/20250521151427103.html
19. European Society of Medical Oncology (ESMO). ESMO MCBS scorecards; NATALEE. Accessed October 2025. https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-for-solid-tumours/esmo-mcbs-scorecards/scorecard-468-1
20. European Society for Medical Oncology. Magnitude of Clinical Benefit Scale Scorecard. Accessed October 2025. https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-for-solid-tumours/esmo-mcbs-scorecards?scorecard=158-1
21. European Society for Medical Oncology. Magnitude of Clinical Benefit Scale Scorecard. Accessed October 2025. https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-for-solid-tumours/esmo-mcbs-scorecards?scorecard=9-1

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