

PRESS RELEASE

Kisqali® shows clinically meaningful overall survival in broadest HR+/HER2- early breast cancer population at high risk of recurrence

- *Six-year NATALEE analysis showed ~20% reduction in risk of death compared to ET alone¹*
- *Benefit increased over time in invasive disease-free survival and across key secondary endpoints¹⁻³*
- *Patients off Kisqali for a median of three years, with clinical benefit continuing to deepen after treatment completion¹⁻³*

Basel, October 23, 2026 – Novartis today announced results from the six-year follow-up analysis of the Phase III NATALEE trial, reporting positive, clinically meaningful overall survival (OS) data with Kisqali® (ribociclib) plus endocrine therapy (ET) compared to ET alone¹. The study was in the broadest early breast cancer (eBC) population of patients with stage II and III HR+/HER2- early breast cancer at high risk of recurrence, including those with high-risk node-negative (N0) disease and all node-positive patients^{1,2}. Kisqali plus ET reduced the risk of death by nearly 20% (19.1%) compared to ET alone (HR=0.809; 95% CI: 0.661-0.989), with consistent overall survival benefit observed across all key subgroups¹. These late-breaking results will be presented at the European Society for Medical Oncology (ESMO) Annual Meeting 2026.

Patients have been off Kisqali for a median of three years (38 months) and have passed the five-year protocol-specified ET duration^{1,2}. The invasive disease-free survival (iDFS) benefit increased from 4.1% at five years to 5.3% at six years, underscoring the long-term value of dual inhibition, with benefit observed years after treatment completion^{1,3}.

Fewer patients treated with Kisqali plus ET experienced metastatic recurrence compared to ET alone, and OS continued to increase over time, with the absolute difference increasing from 1.2% at five years to 2.1% at six years^{1,3}. Breast-cancer specific survival (BCSS) was supportive of OS benefit, showing a ~30% reduction in risk of breast cancer-specific deaths (HR=0.709; 95% CI: 0.559-0.890) compared to ET alone¹.

Six-year NATALEE results reinforce long-term clinical benefit

"The NATALEE six-year data clearly demonstrate a clinically meaningful improvement in overall survival with ribociclib plus endocrine therapy," said Dennis J. Slamon, MD, Chief of the Division of Hematology/Oncology, UCLA Department of Medicine. "These findings have very important implications for patients as well as health care providers worldwide and further strengthen the role of ribociclib in treating patients with HR+/HER2- early breast cancer at high risk of recurrence."

Benefits observed across major efficacy endpoints, with sustained or increasing improvements over six years^{1,3}.

Endpoint	Hazard Ratio	95% CI	Absolute Benefit at 5Y	Absolute Benefit at 6Y
Overall Survival (OS)	0.809	0.661-0.989	1.2%	2.1%

Breast-Cancer Specific Survival (BCSS)	0.709	0.559-0.890	1.5%	2.6%
Invasive Disease-Free Survival (iDFS)	0.741	0.646-0.849	4.1%	5.3%
Distant Disease-Free Survival (DDFS)	0.744	0.646-0.858	3.7%	4.9%
Distant Recurrence-Free Survival (DRFS)	0.738	0.631-0.846	3.5%	4.4%

“The clinically meaningful overall survival benefit observed in NATALEE underscores Kisqali as a standard of care for eligible patients and its foundational role in early breast cancer treatment,” said Andrea Myers, Global Head, Oncology Development, Novartis, Ad Interim. “These findings demonstrate the value of combining CDK4/6i with endocrine therapy in the broadest population of patients at high risk of recurrence, including those with high-risk node-negative disease and all node-positive patients.”

With longer follow-up, the safety profile remained consistent with previous analyses, and no new safety signals were observed¹⁻³. Overall, rates of secondary primary malignancies (SPMs) were 3.0% with Kisqali plus ET and 3.3% with ET alone¹. SPMs leading to death were 0.2% in both the Kisqali plus ET and ET alone arms¹.

Building on established Kisqali overall survival evidence

Kisqali is the only CDK4/6 inhibitor to demonstrate statistically significant OS benefit across three randomized controlled trials (MONALEESA-2, MONALEESA-3, and MONALEESA-7) in metastatic breast cancer and clinically meaningful OS in the broadest early breast cancer population at high risk of recurrence, including node-negative and node-positive disease^{1,4-14}.

"For those diagnosed with early breast cancer who face a higher risk of recurrence, having meaningful long-term overall survival data is invaluable," said Jean A. Sachs, Chief Executive Officer, Living Beyond Breast Cancer. "These new insights help with important, shared decision-making conversations with their medical team, and make clear the importance of continued research to support those navigating complex decisions."

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^{15,16}. The adjuvant ET in both treatment arms was a non-steroidal aromatase inhibitor (NSAI; anastrozole or letrozole) and goserelin, if applicable^{15,16}. The primary endpoint of NATALEE is invasive disease-free survival (iDFS) as defined by the Standardized Definitions for Efficacy End Points (STEEP) criteria^{15,16}. A total of 5,101 adult patients with HR+/HER2- eBC across 20 countries were randomized in the trial^{15,16}.

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 US FDA and the European Commission^{16,17}. In the US, Kisqali is indicated in combination with an AI as an adjuvant treatment for adults with HR+/HER2- stage II and III eBC at high risk of recurrence, as well as for the treatment of adults with HR+/HER2- advanced or metastatic breast cancer (mBC) as initial ET; Kisqali is also approved in the metastatic setting in combination with fulvestrant as initial ET or following disease progression on ET¹⁶. In the EU, Kisqali is approved in combination with an AI for the adjuvant treatment of patients

with HR+/HER2- eBC at high risk of recurrence; and for the treatment of women with HR+/HER2- locally advanced or mBC in combination with either an AI or fulvestrant as initial ET or following disease progression who have prior endocrine therapy¹⁷. In pre- or peri-menopausal women, the ET should be combined with a luteinizing hormone-releasing hormone agonist^{16,17}.

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 3¹⁸. Kisqali approvals in eBC from regulatory authorities worldwide are ongoing, including recent approval from China's National Medical Products Administration¹⁹. In mBC, Kisqali has consistently demonstrated statistically significant overall survival benefit across three Phase III trials⁴⁻¹⁴. 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- mBC¹⁸.

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; 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^{20,21}. 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 line²².

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

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

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," or similar expressions, or by express or implied discussions regarding: potential new products; potential new indications for existing products; potential product launches or potential future revenues from any such products; results of ongoing clinical trials; or potential future, pending or announced transactions; potential future sales or earnings; strategy, plans, expectations or intentions, including discussions regarding our continued investment into new R&D capabilities and manufacturing; or our capital structure. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management 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 could be affected by, among other things, uncertainties concerning: global healthcare cost containment, including ongoing government, payer and general public pricing and reimbursement pressures and requirements for increased pricing transparency; the success of our key products, commercial priorities and strategy; research and development of new products, including clinical trial results and additional analysis of existing clinical data; our ability to obtain or maintain proprietary intellectual property protection, including the ultimate extent of the impact on Novartis of the loss of patent protection and exclusivity on key products; our ability to realize the strategic benefits, operational efficiencies or opportunities expected from our external business opportunities; the development or adoption of new technologies, including artificial intelligence, and new business models; potential significant breaches of information security or disruptions of our information technology systems; actual or potential legal proceedings, including regulatory actions or delays or government regulation related to the products and pipeline products

described in this press release; safety, quality, data integrity, or manufacturing issues; major macroeconomic and geo- and socio-political developments, including the impact of any potential tariffs on our products or the impact of war in certain parts of the world; future global exchange rates; future demand for our products; and other risks and factors referred to in Novartis AG's most recently filed Form 20-F and in subsequent reports filed with, or furnished to, 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 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 300 million people worldwide.

Reimagine medicine with us: Visit us at www.novartis.com and connect with us on **LinkedIn**, **Facebook**, **X/Twitter** and **Instagram**.

References

1. Slamon D et al. Adjuvant ribociclib + nonsteroidal aromatase inhibitor in patients with HR+/HER2- early breast cancer: NATALEE 6-year overall survival and efficacy outcomes. Presented at the European Society of Medical Oncology (ESMO) Congress. October 23-27, 2026. Madrid, Spain.
2. 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
3. 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.
4. 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.
5. 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.
6. 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.
7. 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.
8. 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.
9. 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.
10. 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.
11. 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.
12. 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.
13. 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.
14. 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.
15. 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 September 2026. <https://clinicaltrials.gov/study/NCT03701334>
16. Kisqali. Prescribing Information (US FDA). Novartis Pharmaceuticals Corporation; 2017. Accessed November 2025. https://www.novartis.com/us-en/sites/novartis_us/files/kisqali.pdf
17. Kisqali. Summary of product characteristics (SmPC). Novartis Europharm Limited; 2017. Accessed November 2025. https://www.ema.europa.eu/en/documents/product-information/kisqali-epar-product-information_en.pdf

18. NCCN Guidelines. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]/AE) - Breast Cancer. Accessed November 2025.
<https://www.nccn.org>
19. National Medical Products Administration. Drug Evaluation Information Disclosure: Drug Evaluation Approval Results. National Medical Products Administration. Published May 21, 2025. Accessed November 2025.
<https://www.nmpa.gov.cn/zwfw/sdxx/sdxxyp/yppjfb/20250521151427103.html>
20. European Society of Medical Oncology (ESMO). ESMO MCBS scorecards; NATALEE. Available from:
<https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-for-solid-tumours/esmo-mcbs-scorecards/scorecard-468-1> Accessed November 2025.
21. European Society for Medical Oncology. Magnitude of Clinical Benefit Scale Scorecard. Updated February 7, 2025. Available from:
<https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-scorecards/scorecard-158-1>. Accessed November 2025.
22. European Society for Medical Oncology. Magnitude of Clinical Benefit Scale Scorecard. Updated February 7, 2025. Available from:
<https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-scorecards/scorecard-9-1>. Accessed November 2025.

Novartis Media Relations

E-mail: media.relations@novartis.com

Novartis Investor Relations

Central investor relations line: [+41 61 324 7944](tel:+41613247944)

E-mail: investor.relations@novartis.com