Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

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

Novartis receives positive CHMP opinion for Kisqali® to help reduce risk of recurrence in people with HR+/HER2- early breast cancer

- *If approved, patients in Europe with stage II or III HR+/HER2- early breast cancer (EBC) at high risk of recurrence, including those with node-negative disease, will be eligible for adjuvant treatment with Kisqali® (ribociclib) in combination with an aromatase inhibitor*[1]
- *Recommendation is based on the Phase III NATALEE trial, where Kisqali added to endocrine therapy (ET) significantly reduced the risk of recurrence by 25% versus ET alone across a broad population of patients with HR+/HER2- early breast cancer* [2]
- *People with stage II or III HR+/HER2- EBC face significant risk of recurrence – often as incurable metastatic disease – despite adjuvant ET and regardless of nodal involvement*[3,4]
- *In September, Kisqali was approved by the FDA in this setting*[5]*; at ESMO 2024, an updated analysis from NATALEE was presented, showing a deepening invasive disease-free survival benefit*[6]

Basel, October 18, 2024 – Novartis announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion and recommended granting marketing authorization for Kisqali® (ribociclib) for the adjuvant treatment of adults with hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) early breast cancer (EBC), at high risk of disease recurrence, including those with node-negative disease[1].

“One-third of people diagnosed with stage II breast cancer and more than half of those diagnosed with stage III will unfortunately experience a return of their cancer in the long term, often as metastatic disease,” said Peter A. Fasching, M.D., Professor of Translational Medicine, University Hospital Erlangen and Comprehensive Cancer Center Erlangen-EMN and NATALEE trial investigator. “If approved, Kisqali could provide an effective and tolerable adjuvant treatment option to mitigate the risk of recurrence in a broader patient population, particularly for patients who currently have limited treatment options, including those with high-risk node-negative disease.”

Breast cancer is the most commonly diagnosed cancer in Europe[7]. HR+/HER2- is the most common subtype, accounting for approximately 70% of all breast cancers, and more than 40% of these are diagnosed in stage II or III[8-10].

The positive CHMP decision is based on robust data from the Phase III NATALEE trial[2,11,12].

In the trial, Kisqali plus endocrine therapy (ET), compared to ET alone, lowered the risk of cancer recurrence by 25.1% in patients with stage II and III HR+/HER2- EBC (HR=0.749; 95% CI: 0.628, 0.892; *P*=0.0006) and demonstrated a consistent, clinically meaningful invasive disease-free survival (iDFS) benefit across key pre-specified subgroups[2,11]. Data from the pivotal trial also showed the safety profile of Kisqali at the 400mg dose was well-tolerated with generally low-grade symptomatic adverse events[2,11].

An updated analysis from the NATALEE trial recently presented at the European Society for Medical Oncology (ESMO) Congress 2024 adds to the growing body of evidence supporting the potential of Kisqali to consistently reduce risk of recurrence across a broad population[6]. In the updated analysis, the iDFS benefit continued to deepen beyond the three-year Kisqali treatment period in all patient subgroups, including those with node-negative disease[2].

“Today, many people diagnosed with HR+/HER2- early breast cancer in Europe lack options beyond endocrine therapy to help reduce their risk of cancer coming back. If approved, Kisqali could nearly double the number of patients eligible for CDK4/6 inhibitor adjuvant therapy,” said Patrick Horber M.D., President, International, Novartis. “Together with the recent FDA approval and late-breaking NATALEE data presented at ESMO, today’s positive CHMP recommendation further reinforces the differentiated profile of Kisqali as a new treatment option for a broad population of patients, including those with node-negative disease.”

Following the CHMP’s recommendation to approve Kisqali in a broad population of patients diagnosed with HR+/HER2- EBC at high risk of recurrence, the European Commission (EC) will take a final decision within approximately two months.

About NATALEE
NATALEE is a global Phase III multi-center, randomized, open-label trial to evaluate the efficacy and safety of Kisqali® (ribociclib) 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[2,13]. The adjuvant ET in both treatment arms was a non-steroidal aromatase inhibitor (NSAI; anastrozole or letrozole) and goserelin if applicable[2,13]. The primary endpoint of NATALEE is invasive disease-free survival (iDFS) as defined by the Standardized Definitions for Efficacy End Points (STEEP) criteria[2,13]. A total of 5,101 adult patients with HR+/HER2- EBC across 20 countries were randomized in the trial[2,13].

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 was approved as a treatment for early breast cancer by the U.S. Food and Drug Administration (FDA) in September 2024[5]. Regulatory reviews for Kisqali as an EBC treatment are ongoing worldwide, including in the EU and China.

Kisqali has been approved as a treatment for metastatic breast cancer (MBC) patients in 99 countries worldwide, including by the U.S. FDA and the European Commission[14,15]. In the U.S., Kisqali is indicated for the treatment of adults with HR+/HER2- advanced or MBC in combination with an AI as initial ET or fulvestrant as initial ET or following disease progression on ET in post-menopausal women or in men[14]. In the EU, Kisqali is approved 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[15]. In pre- or peri-menopausal women, the ET should be combined with a luteinizing hormone-releasing hormone agonist[14,15].

In MBC, Kisqali has consistently demonstrated statistically significant overall survival benefit across three Phase III trials[16-26]. The NCCN Guidelines® for breast cancer recommend ribociclib (Kisqali) as the only Category 1 preferred CDK4/6 inhibitor for first-line treatment of people living with HR+/HER2- when combined with an AI, making Kisqali the preferred first-

line treatment of choice for US prescribers in HR+/HER2- MBC[27]. Additionally, Kisqali 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[28]. 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[29].

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.

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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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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 3247944
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