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MEDIA & INVESTOR RELEASE

Longer-term Novartis Kisqali® NATALEE data show durable reduction in distant recurrence in broad population of patients with early breast cancer

- *Reduction in distant recurrence consistently deepened beyond 3-year Kisqali treatment duration in patients with node-positive (N+) and high-risk node-negative (N0) disease, as well as between anatomical stages*[1]

- *Real-world 5-year distant recurrence data in high-risk patients with HR+/HER2- early breast cancer (EBC), regardless of nodal status, highlights importance of adding a CDK4/6 inhibitor to endocrine therapy for all eligible patients*[2]

- *Late-breaking Kisqali data presentations at SABCS follow recent FDA and EMA approvals and recognition by NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®*) as only Category 1 preferred adjuvant treatment for both N+ and high-risk N0 disease in combination with AI*[3]

Basel, December 10, 2024 – Novartis today announced results from an updated analysis of the pivotal Phase III NATALEE trial of Kisqali® (ribociclib) that underscore the extended efficacy beyond the duration of treatment in combination with endocrine therapy (ET). Results showed a sustained reduction in distant recurrence of 28.5% (HR=0.715; 95% CI 0.604-0.847; nominal P<0.0001), compared to ET alone, in patients with stage II and III hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) early breast cancer (EBC)[1].

Reduction in distant recurrence, known as distant disease-free survival (DDFS), is a decrease in the rate of cancer returning and spreading to other organs. The DDFS with Kisqali was consistent across all pre-specified patient subgroups, including those with node-negative (N0) disease[1]. These late-breaking data are being presented at the 2024 San Antonio Breast Cancer Symposium (SABCS).

"In day-to-day practice, we see a real and persistent risk of breast cancer coming back after early diagnosis, often as metastatic disease," said Paolo Tarantino, M.D., Advanced Fellow at Dana-Farber Cancer Institute and Harvard Medical School. "The latest NATALEE and real-world data presented at SABCS reaffirm we can better address risk of recurrence for all patients at high-risk, including selected patients with node-negative disease, by offering them adjuvant CDK4/6 inhibitor treatment in addition to endocrine therapy."

DDFS results across pre-specified subgroups[1,4**]**:**

Subgroup	Hazard Ratio	95% CI
Intention-To-Treat Population	0.715	0.604-0.847

AJCC Tumor Stage IIA	0.396	0.218-0.720
AJCC Tumor Stage IIB	0.806	0.524-1.238
AJCC Tumor Stage IIIA	0.697	0.524-0.926
AJCC Tumor Stage IIIB	0.569	0.326-0.994
AJCC Tumor Stage IIIC	0.878	0.649-1.188
Node-negative disease	0.696	0.403-1.204
Node-positive disease	0.726	0.608-0.867

Safety remains consistent with previous reports, and no new safety signals were identified[5]. Adverse events (AEs) of special interest (grade 3 or higher) were neutropenia (44.4%), liver-related AEs (e.g., elevated transaminases) (8.6%), and QT interval prolongation (1.0%)[5].

Real-World Risk of Distant Recurrence
Further, real-world evidence presented at the meeting highlights the relatively high incidence of distant recurrences within 5 years despite ET monotherapy for patients at high-risk, regardless of nodal involvement[2].

"On the heels of its U.S. FDA and EMA approvals in early breast cancer, it is encouraging to see the continued benefit of adding Kisqali to standard endocrine therapy to help reduce the risk of recurrence," said Jeff Legos, Executive Vice President, Global Head of Oncology Development, Novartis. "These data, together with the recent NCCN Guidelines® Category 1 preferred treatment recommendation for all eligible patients with early breast cancer, reinforce the opportunity to evolve adjuvant treatment to help a broader group of people."

Additional research presented at the meeting further demonstrates the ongoing focus of Novartis to advance the care of people with breast cancer, including studies investigating the potential of radioligand therapies in the treatment of metastatic breast cancer (MBC)[6].

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***The 4-year DDFS analysis was not prespecified and the trial was not powered to demonstrate statistical significance of these results.*

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[7,8]. The adjuvant ET in both treatment arms was a non-steroidal aromatase inhibitor (NSAI; anastrozole or letrozole) and goserelin if applicable[7,8]. The primary endpoint of NATALEE is invasive disease-free survival (iDFS) as defined by the Standardized Definitions for Efficacy End Points (STEEP) criteria[7,8]. A total of 5,101 adult patients with HR+/HER2- EBC across 20 countries were randomized in the trial[7,8].

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[9,10]. 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 in post-menopausal women or in men[9]. 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[10]. In pre- or peri-menopausal women, the ET should be combined with a luteinizing hormone-releasing hormone agonist[9,10].

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[3]. 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- when combined with an AI[3], 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 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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