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MEDIA & INVESTOR RELEASE

Novartis Kisqali® receives European Commission approval in a broad population of patients with HR+/HER2- early breast cancer at high risk of recurrence

- *Approval is based on Phase III NATALEE data showing Kisqali® (ribociclib) plus adjuvant endocrine therapy (ET) demonstrated clinically meaningful invasive disease-free survival (iDFS) benefit in patients with stage II or III HR+/HER2- early breast cancer (EBC), consistent across all subgroups*[1,2]

- *With this broad indication, nearly twice as many EBC patients in Europe, including those with node-negative disease, could now be eligible for treatment with Kisqali to help reduce their risk of recurrence*[3]

- *Despite ET, more than one-third of people diagnosed with stage II and III EBC will experience a return of their cancer in the long term, often as incurable advanced disease*[4,5]

- *Recently presented four-year analysis of the ongoing NATALEE trial showed a deepening iDFS benefit after completion of three-year treatment period*[6]

Basel, November 27, 2024 – Novartis announced today that the European Commission (EC) has approved Kisqali® (ribociclib) in combination with an aromatase inhibitor (AI) for the adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer (EBC) at high risk of recurrence[1,7].

The approval is based on results from the pivotal Phase III NATALEE trial, which included a broad patient population with HR+/HER2- stage II and III EBC, including those with node-negative disease[2]. The trial showed a significant and clinically meaningful 25.1% (HR=0.749; 95% CI: 0.628, 0.892; *P*=0.0006) reduction in risk of disease recurrence with adjuvant Kisqali plus endocrine therapy (ET) compared to ET alone[2]. The invasive disease-free survival (iDFS) benefit was consistently observed across all patient subgroups[2].

“For many patients diagnosed with stage II or III HR+/HER2- early breast cancer, the risk of their cancer coming back despite treatment with endocrine therapy remains high, even after decades,” said Michael Gnant, M.D., FACS, FEBS, Professor of Surgery at the Medical University of Vienna, Austria, and President of the Austrian Breast and Colorectal Study Group. “This approval represents a positive milestone for the early breast cancer community in Europe, including physicians who now have a new option to help reduce the risk of recurrence in a broader population of patients.”

In addition, Michael Untch, M.D., Professor and Head of the Clinic for Gynecology and Obstetrics, and Director of the Interdisciplinary Breast Cancer Center at Helios Klinikum Berlin-Buch, noted: “Adding a new treatment option to the HR+/HER2- early breast cancer

armamentarium is encouraging news for both physicians and their patients – including patients with node-negative disease and additional risk factors. Ribociclib may now help many patients who are at risk of their cancer returning."

Breast cancer is the most commonly diagnosed cancer in Europe[8], with approximately 70% of cases diagnosed in the early stages of the disease[9]. Despite current treatment options, people with stage II and III HR+/HER2- EBC remain at risk of experiencing a return of their cancer in the long term, often as incurable advanced disease[4,5].

"Breast cancer recurrence can be a lifelong concern for those living with the disease. Patients deserve access to treatment options that help minimize the risk of their cancer coming back and put their mind at ease," said Iris Zemzoum, M.D., President, Europe, Novartis. "We are proud of this approval, which will help to address a key unmet need and improve health outcomes for a broader population of patients in Europe."

This news follows the recent U.S. Food and Drug Administration (FDA) approval of Kisqali for EBC patients and recommendation as a Category 1 preferred breast cancer adjuvant treatment by the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®*)[10,11]. Kisqali has also achieved the highest score (A) on the European Society for Medical Oncology-Magnitude of Clinical Benefit Scale (ESMO-MCBS) for EBC[12].

Regulatory review of Kisqali in EBC is ongoing worldwide. Following recent data announcements at ESMO 2024[6], Novartis will continue to evaluate NATALEE patients for longer-term outcomes, including overall survival.

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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 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[8,14]. In the U.S., Kisqali is indicated in combination with an AI as an adjuvant treatment of adults with HR+/HER2- stage II and III early breast cancer (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 indication in combination with fulvestrant as initial ET or following disease progression on ET in post-menopausal women or in men[14]. 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. In pre- or perimenopausal women, or in men, the AI should be combined with a luteinising hormone-releasing hormone (LHRH) agonist; 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. In pre- or peri-menopausal women, the ET should be combined with a LHRH[8].

In EBC, it is the only CDK4/6 inhibitor recommended 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[8,14]. Kisqali, in combination with an AI, has the highest score (A) on the ESMO-Magnitude of Clinical Benefit Scale for the adjuvant treatment of adults with stage II and III HR+/HER2- EBC, at high risk of recurrence[12].

In MBC, Kisqali has consistently demonstrated statistically significant overall survival benefit across three Phase III trials[15-25]. 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 U.S. prescribers in HR+/HER2- MBC[26]. In addition, 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[27]. 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[28].

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 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 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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