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MEDIA & INVESTOR RELEASE

Novartis Kisqali® significantly reduced the risk of recurrence by 25% across a broad population of patients with early breast cancer; clinically meaningful benefit was consistent across subgroups

- *Kisqali is the first and only CDK4/6 inhibitor to demonstrate a consistent, clinically meaningful benefit across a broad population of patients with HR+/HER2- early breast cancer, regardless of disease stage, menopausal or nodal status*[1]
- *Results were also consistent across all secondary endpoints, including distant disease-free survival and recurrence-free survival, with a trend for improved overall survival*[*1]
- *The safety profile of Kisqali was favorable at 400 mg with low rates of symptomatic adverse events and limited treatment modifications when administered up to three years*[1]
- *Collectively, NATALEE results have the potential to more-than-double the number of patients who could benefit from treatment with a CDK4/6 inhibitor in the adjuvant setting*[2]

Basel, June 2, 2023 — Novartis today presents positive primary endpoint data from the pivotal Phase III NATALEE trial at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting. Data showed that Kisqali® (ribociclib) plus endocrine therapy (ET), compared to ET alone, lowered the risk of cancer recurrence by 25.2% in patients with stage II and III hormone receptor-positive/human epidermal growth factor receptor 2-negative (HR+/HER2-) early breast cancer (HR=0.748; 95% CI: 0.618, 0.906; p=0.0014) along with a consistent, clinically meaningful invasive disease-free survival (iDFS) benefit across key pre-specified subgroups (see table below)[1].

Kisqali iDFS benefit across key pre-specified subgroups[1]:

	Hazard Ratio	95% CI
Intention-To-Treat Population	**0.748**	**0.618, 0.906 (p=0.0014)**
AJCC Tumor Stage II	0.761	0.525, 1.103
AJCC Tumor Stage III	0.740	0.592, 0.925
Node-positive disease	0.771	0.630, 0.944
Node-negative disease	0.630	0.341, 1.165
Pre-menopausal women and men	0.722	0.530, 0.983
Post-menopausal women	0.781	0.613, 0.997

Kisqali data across all secondary efficacy endpoints was also consistent, including distant disease-free survival (DDFS) (26% risk reduction) and recurrence-free survival (RFS) (28%

risk reduction), with a trend for improvement in overall survival (OS) (HR=0.759; 95% CI: 0.539, 1.068)[*1].

The safety profile of Kisqali at 400 mg was favorable with low rates of symptomatic adverse events (AEs) and limited need for dose modifications when administered up to three years[1]. The most frequently reported AEs of special interest (grade 3 or higher) were neutropenia (43.8%) and liver-related AEs (e.g. elevated transaminases) (8.3%)[1]. Grade 3 or higher QT interval prolongation and diarrhea were low for Kisqali at 1.0% and 0.6%, respectively[1].

“These landmark results will fundamentally change how we treat patients with stage II and III HR+/HER2- early breast cancer who are in need of new, well-tolerated options that prevent their cancer from coming back,” said Dennis J. Slamon, M.D., Director of Clinical/Translational Research, UCLA Jonsson Comprehensive Cancer Center and Chairman and Executive Director of Translational Research In Oncology (TRIO) and NATALEE trial lead investigator. “Addressing this unmet need across such a broad patient population could help streamline treatment decisions for healthcare providers and keep many more at-risk patients cancer-free without disrupting their daily lives.”

“Patients diagnosed with HR+/HER2- early breast cancer remain at risk of cancer recurrence, given that one-third of patients diagnosed with stage II and more than half of those diagnosed with stage III will unfortunately experience a return of their cancer,” said Shreeram Aradhye, M.D., President, Global Drug Development and Chief Medical Officer, Novartis. “The compelling data from NATALEE highlight the potential of Kisqali to reduce the risk of cancer recurrence in this at-risk population, including node-negative patients, while maintaining a favorable safety profile. These potentially practice-changing results reinforce the unique and well-established profile of Kisqali as a proven treatment in HR+/HER2- metastatic breast cancer.”

"After an early breast cancer diagnosis, patients live with a persistent and lifelong worry that their cancer will return,” said Fran Visco, President, National Breast Cancer Coalition, and member of the NATALEE Steering Committee. “The National Breast Cancer Coalition partners with industry and scientists to help find treatments that will make certain that does not happen. Educated patient advocate participation in all phases of research, especially in designing and implementing clinical trials, is critical to making certain patients have meaningful options, and we are grateful that Novartis welcomed our collaboration and participation in all aspects of the NATALEE trial."

Novartis plans to submit these Phase III data to regulatory authorities in the US and Europe before end of year.

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 adjuvant treatment versus ET alone in patients with HR+/HER2- EBC, being conducted in collaboration with TRIO[1]. The adjuvant ET in both treatment arms was a non-steroidal aromatase inhibitor (NSAI; anastrozole or letrozole) and goserelin if applicable[1]. The primary endpoint of NATALEE is iDFS as defined by the Standardized Definitions for Efficacy End Points (STEEP) criteria[1]. A total of 5,101 adult patients with HR+/HER2- EBC across 20 countries were randomized in the trial[1].

Results showed Kisqali plus ET, compared to ET alone, lowered the risk of cancer recurrence by 25.2% (HR=0.748; 95% CI: 0.618, 0.906; p=0.0014), along with consistent clinically meaningful iDFS benefit across key pre-specified subgroups: AJCC Tumor Stage II (HR=0.761; 95% CI: 0.525, 1.103), AJCC Tumor Stage III (HR=0.740; 95% CI: 0.592, 0.925), node-negative disease (HR=0.630; 95% CI: 0.341, 1.165), node-positive disease (HR=0.771; 95% CI: 0.630, 0.944), pre-menopausal women and men (HR=0.722; 95% CI: 0.530, 0.983), post-menopausal women (HR=0.781; 95% CI: 0.613, 0.997)[1]. Kisqali data across all secondary efficacy endpoints was also consistent, including DDFS (26% risk reduction) and

RFS (28% risk reduction), with a trend for improvement in OS (HR=0.759; 95% CI: 0.539, 1.068)*[1].

Median study duration of follow up was 34 months (range 21-48 months) with clinical benefits observed after approximately two years[1]. NATALEE explored a lower starting dose (400 mg) of Kisqali than the dose approved for treatment in metastatic breast cancer (MBC) (600 mg) with the goal to minimize disruptions to patient quality of life without compromising efficacy. The safety profile of Kisqali at 400 mg was favorable with low rates of symptomatic AEs and limited need for dose modifications when administered up to three years[1]. The most frequently reported AEs of special interest (grade 3 or higher) were neutropenia (43.8%) and liver-related AEs (e.g. elevated transaminases) (8.3%)[1]. Grade 3 or higher QT interval prolongation and diarrhea were low for Kisqali at 1.0% and 0.6%, respectively[1].

**Results based on pre-specified interim analysis for OS at time of primary iDFS analysis; additional follow up is planned to obtain more mature OS data[1].*

About Early Breast Cancer
More than 90% of patients diagnosed with breast cancer have EBC[3]. Despite standard-of-care adjuvant therapy, approximately one-third of those diagnosed with stage II and more than half of those diagnosed with stage III HR+/HER2- EBC experience cancer recurrence[4,5]. The risk of recurrence continues over decades with more than half of breast cancer recurrences occurring five or more years after diagnosis[4,6]. For many of these patients, there are currently no targeted therapeutic options outside of the standard chemotherapy and ET[7].

About Kisqali® (ribociclib)
Kisqali has consistently demonstrated OS benefit while preserving or improving quality of life across three Phase III trials in MBC[8-19]. Updates to the NCCN Guidelines® for breast cancer, released in January 2023, recommend ribociclib (Kisqali) as the only Category 1 preferred CDK4/6 inhibitor for first-line treatment of patients with HR+/HER2- MBC when combined with an aromatase inhibitor (AI)[20]. 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[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 line[22].

Kisqali has been approved in 99 countries worldwide, including by the United States Food and Drug Administration (FDA) and the European Commission. In the U.S., Kisqali is approved for the treatment of adult patients 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. 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. In pre- or peri-menopausal women, the ET should be combined with a luteinizing hormone-releasing hormone agonist[19].

Novartis is committed to continuing to study Kisqali in breast cancer. Novartis is collaborating with SOLTI, which is leading the HARMONIA study to test whether Kisqali changes tumor biology to enable a better response to ET compared to Ibrance®** (palbociclib) for patients with HR+/HER2-, HER2-enriched subtype[23] MBC, and with the Akershus University Hospital in Norway on the NEOLETRIB trial, a neoadjuvant Phase II trial studying the effects of Kisqali in HR+/HER2- EBC to discover the potentially unique underlying mechanism of action[24].

Kisqali was developed by the Novartis Institutes for BioMedical Research (NIBR) under a research collaboration with Astex Pharmaceuticals.

Please see full Prescribing Information for Kisqali, available at www.Kisqali.com

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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,” “seek,” “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 such as COVID-19; 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 reimagining medicine to improve and extend people’s lives. We deliver high-value medicines that alleviate society’s greatest disease burdens through technology leadership in R&D and novel access approaches. In our quest to find new medicines, we consistently rank among the world’s top companies investing in research and development. About 103,000 people of more than 140 nationalities work together to bring Novartis products to nearly 800 million people around the world. Find out more at https://www.novartis.com

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