Novartis presents updated data that reinforce the efficacy and safety of Kisqali® (ribociclib) plus letrozole as a first-line option for HR+/HER2- advanced or metastatic breast cancer

- At a subsequent analysis of the MONALEESA-2 trial, after nearly one year of additional follow-up, Kisqali plus letrozole demonstrated median progression-free survival (PFS) of 25.3 months compared to 16.0 months for letrozole alone.
- Patients on Kisqali plus letrozole maintained overall health-related quality of life compared to those treated with letrozole alone, and no new safety concerns have been identified.
- Novartis continues to evaluate Kisqali in multiple trials, in combination with different hormonal therapies, across a broad range of patients.

Basel, June 2, 2017 – Novartis announced today updated findings from the Phase III MONALEESA-2 study that reinforce the efficacy and safety of Kisqali® (ribociclib) plus letrozole in postmenopausal women with hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer. After an additional 11 months of follow-up, a median progression-free survival (PFS) of 25.3 months (95% CI: 23.0-30.3) for Kisqali plus letrozole and 16.0 months (95% CI: 13.4-18.2) for letrozole alone was observed (HR=0.568 (95% CI: 0.457-0.704; p<0.0001)). These data will be presented on Sunday, June 4, 2017 at the 53rd Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago (Abstract #1038).

These updated results further support that Kisqali plus letrozole improves PFS as a first-line treatment across all patient subgroups. After two years of treatment, the progression-free survival rate was 54.7% in the Kisqali plus letrozole arm compared to 35.9% in patients treated with letrozole alone. In a cohort of 213 US patients treated as part of MONALEESA-2, the median PFS was 27.6 months with Kisqali plus letrozole and 15.0 months with letrozole alone (HR=0.527 (95% CI: 0.351–0.793)).

Treatment benefit remained consistent across all patient subgroups regardless of demographics or disease characteristics, including women with visceral disease and those diagnosed de novo. In women with measurable disease at baseline, 55% saw their tumor size shrink by at least 30% (overall response rate (ORR)) compared to 39% with letrozole plus placebo. Follow-up to measure overall survival is ongoing as data remain immature.

“This new look at the MONALEESA-2 data, after an additional year of follow-up, demonstrates the continued efficacy of ribociclib plus letrozole,” said Gabriel N. Hortobagyi, MD, Professor of Medicine, Department of Breast Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center and MONALEESA-2 Principal Investigator. “With more than two years of follow-up, the PFS data confirm the inclusion of ribociclib plus an aromatase inhibitor as a strong option among first-line treatments for HR-positive, HER2-negative advanced breast cancer.”
A separate analysis of patient-reported, health-related quality of life (HRQoL) outcomes from the MONALEESA-2 trial presented at ASCO (Abstract #1020) showed no significant difference in quality of life for women taking Kisqali plus letrozole compared to those taking letrozole alone\\(^2\). This suggests that adverse events did not significantly impact HRQoL\\(^2\).

Updated safety data from the MONALEESA-2 trial show the safety profile of Kisqali plus letrozole remained consistent and the incidence of laboratory and electrocardiogram (ECG) irregularities is similar to that observed at the first interim analysis\\(^1\). At the time of this updated analysis, the most common (≥10%) grade 3/4 laboratory abnormalities were as follows for Kisqali plus letrozole compared to letrozole alone: decreased neutrophils (62.6% vs 1.5%), decreased leukocytes (36.8% vs 1.5%), decreased lymphocytes (16.2% vs 3.9%) and elevated alanine aminotransferase (11.4% vs 1.2%)\\(^1\).

“Updated MONALEESA-2 results validate the sustained efficacy and established safety profile of Kisqali plus letrozole in patients with HR+/HER2- metastatic breast cancer and confirm the data that supported its recent FDA approval,” said Vas Narasimhan, MD, Head, Global Drug Development and Chief Medical Officer, Novartis. “We are excited about the potential of Kisqali, and are continuing to evaluate its activity in several Phase III trials with multiple hormonal therapy combinations across a broad range of patient populations, including in the adjuvant setting. We look forward to sharing new results with the scientific community in the coming months and years.”

The MONALEESA clinical trial program includes two additional Phase III trials in advanced breast cancer, MONALEESA-3 and MONALEESA-7, which are evaluating the efficacy and safety of Kisqali in combination with other endocrine partners. Novartis also is enrolling patients in a study to further evaluate Kisqali in men and pre- or postmenopausal women (CompLEEment-1) and initiating Phase III trials evaluating Kisqali in the adjuvant therapy setting (EarLEE-1 and EarLEE-2).

Kisqali was approved by the US Food and Drug Administration (FDA) on March 13, 2017, as a first-line treatment for HR+/HER2- metastatic breast cancer in combination with any aromatase inhibitor.


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

**About the Kisqali Clinical Trial Program**

MONALEESA-3 is evaluating Kisqali in combination with fulvestrant compared to fulvestrant alone in postmenopausal women with HR+/HER2- advanced breast cancer who have received no or a maximum of one prior endocrine therapy. MONALEESA-7 is investigating Kisqali in combination with endocrine therapy and goserelin compared to endocrine therapy and goserelin alone in premenopausal women with HR+/HER2- advanced breast cancer who have not previously received endocrine therapy. These trials are fully enrolled.
Novartis will initiate two multicenter, randomized, double-blind Phase III clinical trials, EarLEE-1 and EarLEE-2, to evaluate the safety and efficacy of Kisqali with endocrine therapy as adjuvant therapy in pre- and postmenopausal women who have not previously received treatment with CDK4/6. EarLEE-1 will assess Kisqali with adjuvant endocrine therapy compared to adjuvant endocrine therapy alone in women with HR+/HER2- high-risk early breast cancer. EarLEE-2 will investigate Kisqali with adjuvant endocrine therapy compared to adjuvant endocrine therapy alone in women with HR+/HER2- intermediate-risk early breast cancer.

The CompLEEment study is evaluating the safety and efficacy of Kisqali plus letrozole in men and pre- or postmenopausal women with HR+/HER2- advanced breast cancer with no prior hormonal therapy for advanced disease. This open-label, multicenter, Phase IIIb CompLEEment-1 trial is currently enrolling participants.

More information about these studies can be found at ClinicalTrials.gov.

About Novartis in Advanced Breast Cancer
For more than 25 years, Novartis has been at the forefront of driving scientific advancements for breast cancer patients and improving clinical practice in collaboration with the global community. With one of the most diverse breast cancer pipelines and the largest number of breast cancer compounds in development, Novartis leads the industry in discovery of new therapies and combinations, especially in HR+ advanced breast cancer, the most common form of the disease.

Kisqali® (ribociclib) Important US Safety Information
Kisqali® (ribociclib) is a prescription medicine used in combination with an aromatase inhibitor as the first hormonal-based therapy to treat women who have gone through menopause with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer. It is not known if Kisqali is safe and effective in children. Kisqali can cause a heart problem known as QT prolongation. This condition can cause an abnormal heartbeat and may lead to death. Patients should tell their health care provider right away if they have a change in their heartbeat (a fast or irregular heartbeat), or if they feel dizzy or faint. Kisqali can cause serious liver problems. Patients should tell their health care provider right away if they get any of the following signs and symptoms of liver problems: yellowing of the skin or the whites of the eyes (jaundice), dark or brown (tea-colored) urine, feeling very tired, loss of appetite, pain on the upper right side of the stomach area (abdomen), and bleeding or bruising more easily than normal. Low white blood cell counts are very common when taking Kisqali and may result in infections that may be severe. Patients should tell their health care provider right away if they have signs and symptoms of low white blood cell counts or infections such as fever and chills. Before taking Kisqali, patients should tell their health care provider if they are pregnant, or plan to become pregnant as Kisqali can harm an unborn baby. Females who are able to become pregnant and who take Kisqali should use effective birth control during treatment and for at least 3 weeks after the last dose of Kisqali. Do not breastfeed during treatment with Kisqali and for at least 3 weeks after the last dose of Kisqali. Patients should tell their health care provider about all of the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements since they may interact with Kisqali. Patients should avoid pomegranate or pomegranate juice, and grapefruit or grapefruit juice while taking Kisqali. The most common side effects (incidence ≥20%) of Kisqali when used with letrozole include white blood cell count decreases, nausea, tiredness, diarrhea, hair thinning or hair loss, vomiting, constipation, headache, and back pain. The most common grade 3/4 side effects in the Kisqali + letrozole arm (incidence >2%) were low neutrophils, low leukocytes, abnormal liver function tests, low lymphocytes, and vomiting. Abnormalities were observed in hematology and clinical chemistry laboratory tests.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as "continues," "recommended," "will," "support," "ongoing," "suggests," "excited," "potential," "continuing to evaluate," "look forward," "in the coming months and years," "may," "evaluating," "investigating," "investigate," "pipelines," "in development," or similar terms, or by express or implied discussions regarding potential new indications or labeling for Kisqali or any of the other products in the Novartis breast cancer pipeline, regarding potential marketing approvals for Kisqali or any of the other products in the Novartis breast cancer pipeline, or regarding potential future revenues from Kisqali and the other products in the Novartis breast cancer pipeline. 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 Kisqali or any of the other products in the Novartis breast cancer pipeline will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Neither can there be any guarantee that Kisqali will be submitted or approved for sale in any additional markets, or at any particular time. Nor can there be any guarantee that any of the other products in the Novartis breast cancer pipeline will be submitted or approved for sale in any market, or at any particular time. Neither can there be any guarantee that Kisqali or any of the other products in the Novartis breast cancer pipeline will be commercially successful in the future. In particular, management’s expectations regarding Kisqali and the other products in the Novartis breast cancer pipeline 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; the company’s ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward healthcare cost containment, including ongoing pricing and reimbursement pressures; safety, quality or manufacturing issues, 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 provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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