Novartis reports positive results from Phase III trial of Kisqali® (ribociclib) combination therapy in premenopausal women with HR+/HER2- advanced or metastatic breast cancer

- **MONALEESA-7** met primary endpoint of progression-free survival, demonstrating superior efficacy of Kisqali combination therapy vs. endocrine treatment alone in first-line treatment of premenopausal women with HR+/HER2- advanced breast cancer

- Kisqali is the first CDK4/6 inhibitor to be studied in a Phase III global trial exclusively focusing on premenopausal women with HR+/HER2- advanced breast cancer

- Premenopausal breast cancer is a biologically distinct and more aggressive disease than postmenopausal breast cancer and is the leading cause of cancer death in women 20-59 years old

- Results will be presented at San Antonio Breast Cancer Symposium (SABCS) in December; Novartis plans to initiate discussions with regulatory authorities

**Basel, November 8, 2017** – Novartis today announced positive topline results from the global **MONALEESA-7** trial, the second Phase III trial of Kisqali® (ribociclib) in advanced or metastatic breast cancer. The **MONALEESA-7** trial met its primary endpoint of progression-free survival (PFS) in premenopausal women with hormone-receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced breast cancer.

**MONALEESA-7** is the first prospective global Phase III trial in more than 20 years, designed specifically for premenopausal women diagnosed with advanced breast cancer, to demonstrate superiority of any CDK4/6 inhibitor in combination with oral hormonal therapies and goserelin versus endocrine treatment alone in this patient population.

“There remains a significant unmet treatment need in younger women diagnosed with premenopausal advanced breast cancer, as the disease tends to be more aggressive with a poorer prognosis,” said Samit Hirawat, Executive Vice President and Head, Global Drug Development at Novartis Oncology. “The **MONALEESA-7** trial is the first CDK 4/6 inhibitor Phase III trial designed specifically for this patient population, and we are excited that the study met its primary endpoint, which may allow us to expand the population of patients who can benefit from treatment with Kisqali. We look forward to presenting **MONALEESA-7** study data at SABCS next month and discussing these results with regulatory agencies worldwide.”

**MONALEESA-7** is a Phase III randomized, double-blind, placebo-controlled trial investigating the efficacy and safety of Kisqali in combination with oral hormonal therapies and goserelin versus endocrine treatment alone in premenopausal or perimenopausal women with HR+/HER2- advanced breast cancer who had not previously received endocrine therapy for advanced
disease. More than 670 women ranging from 25-58 years in age were randomized in the MONALEESA-7 trial\(^1\).

No additional safety signal was identified in the MONALEESA-7 study\(^1\). Results of MONALEESA-7 trial will be presented at the 40\(^{th}\) annual San Antonio Breast Cancer Symposium (SABCS) in December. Novartis plans to begin discussions with global health authorities worldwide.

**About Kisqali\(^\text{®}\) (ribociclib)**
Kisqali (ribociclib) is the only CDK4/6 inhibitor approved based on a first-line, Phase III trial that met its primary endpoint early. It 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 is not approved for use in premenopausal patients.

Kisqali is approved for use in 42 countries around the world, including the United States, European Union. Kisqali was developed by the Novartis Institutes for BioMedical Research (NIBR) under a research collaboration with Astex Pharmaceuticals.

**About the Kisqali Clinical Trial Program**
With more than 2,000 patients, the MONALEESA program is the largest Phase III clinical program researching use of a CDK4/6 inhibitor in advanced breast cancer\(^1\).

The MONALEESA-7 findings add to the body of evidence from MONALEESA-2 supporting the benefit of Kisqali plus hormone therapy in first-line treatment of HR+/HER2- advanced or metastatic breast cancer. Novartis is continuing to evaluate Kisqali in combination with multiple hormonal therapies across a broad range of patients, including in the adjuvant setting.

MONALEESA-3 is a Phase III study 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.

CompLEEment is an open-label, multicenter, Phase IIIb study evaluating the safety and efficacy of Kisqali plus letrozole in men and pre- or postmenopausal women with HR+/HER2- advanced breast cancer who have not received prior hormonal therapy for advanced disease.

EarLEE-1 and EarLEE-2 are multi-center, randomized, double-blind Phase III clinical trials that will 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 a CDK4/6 inhibitor. EarLEE-1 will assess Kisqali plus adjuvant endocrine therapy compared to adjuvant endocrine therapy alone in women with HR+/HER2- high-risk early breast cancer and EarLEE-2 will enroll women with HR+/HER2- intermediate-risk early breast cancer.

More information about these studies can be found at www.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.

**Important Safety Information from the Kisqali EU SmPC**

The most common ADRs and the most common grade 3/4 ADRs (reported at a frequency ≥20% and ≥2% respectively) for which the frequency for Kisqali plus letrozole exceeds the frequency for placebo plus letrozole were blood and lymphatic system disorders (including abnormally low neutrophil and white blood cell count), headache, back pain, nausea, fatigue, diarrhea, vomiting, constipation, hair loss and rash and abnormally low levels of neutrophils or white blood cells, abnormal liver function tests (increased alanine and aspartate aminotransferase), abnormally low lymphocyte count, low levels of phosphate, vomiting, nausea, fatigue and back pain, respectively. Low levels of neutrophils was the most commonly seen severe adverse event; fever in addition to a low neutrophil count was reported in 1.5% of patients.

Kisqali can cause serious side effects such as a significant decrease in neutrophil count, abnormal liver function tests and may have an effect on the electrical activity of the heart known as QT/QTc interval prolongation, which could lead to disturbances in heart rhythm. As a precaution, patients should have complete blood counts, liver function, and serum electrolyte levels measured prior to starting treatment as well as during treatment with Kisqali. Patients should also have their heart activity checked before and monitored during treatment.

The efficacy and safety of ribociclib have not been studied in patients with critical visceral disease.

The use of Kisqali with medicinal products known to prolong QTc interval or strong CYP3A4 inhibitors should be avoided as this may lead to prolongation of the QT/QTc interval. If treatment with a strong CYP3A4 inhibitor cannot be avoided, the Kisqali dose should be reduced. Concomitant administration with other medicines that could affect cardiac repolarization or prolong the QT/QTc interval should be taken into account prior to and during treatment with Kisqali. Patients taking sensitive CYP3A4 substrates with narrow therapeutic index should use caution because of the increased risk of adverse events that may occur if these medications are co-administered with Kisqali.

Kisqali contains soya lecithin and therefore it should not be taken by patients who are allergic to peanut or soya.

Animal studies suggest that Kisqali may cause fetal harm in pregnant women. Therefore, as a precaution, women of childbearing potential should use effective contraception while receiving Kisqali during treatment and up to 21 days after stopping treatment. Women should not breast feed for at least 21 days after the last dose of Kisqali. Kisqali may affect fertility in males.

Please see full Prescribing Information for Kisqali, available at [www.kisqali.com](http://www.kisqali.com).

**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,” “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; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; general economic and industry conditions, including the effects of the persistently weak economic and financial environment in many countries; 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 121,000 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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References
1. Novartis Data on File

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