

# **Novartis Kisqali® is first and only CDK4/6 inhibitor to show superior median PFS compared to oral endocrine therapy as first-line treatment in a prospective, randomized Phase III trial dedicated to premenopausal women with HR+/HER2- advanced breast cancer**

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- - Kisqali plus an oral endocrine partner demonstrated significant efficacy with sustained benefit of nearly two years (median PFS 23.8 vs 13.0 months for endocrine therapy alone) and an early response with separation of the PFS curves as early as eight weeks[1]
- - MONALEESA-7 evaluated Kisqali in combination with oral hormonal therapies (tamoxifen or an aromatase inhibitor) and goserelin vs endocrine therapy and goserelin alone in this patient population[1]
- - Kisqali is the only CDK4/6 inhibitor to show efficacy in combination with tamoxifen (median PFS 22.1 vs 11.0 months); Kisqali plus aromatase inhibitor demonstrated additional 14 month PFS compared to aromatase inhibitor alone (median PFS 27.5 vs 13.8 months)[1]
- - Women taking Kisqali benefited for a longer time until health-related QoL deterioration and experienced a clinically meaningful improvement in pain, as early as eight weeks, that was sustained[1]
- - Pending approval in this indication, the clinical benefit demonstrated in the MONALEESA-7 trial expected to support the use of Kisqali as a standard of care for premenopausal women with HR+/HER2- advanced breast cancer

EAST HANOVER, N.J., Dec. 6, 2017 /PRNewswire/ -- Novartis today announced results from the Phase III MONALEESA-7 trial in premenopausal or perimenopausal women with hormone-receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer demonstrating Kisqali® (ribociclib) in combination with an aromatase inhibitor or tamoxifen and goserelin as initial endocrine-based therapy significantly prolonged progression-free survival (PFS) compared to endocrine therapy and goserelin alone<sup>1</sup>. These data will be presented today as a late-breaker oral presentation at the 2017 San Antonio Breast Cancer Symposium (SABCS) (Abstract #S2-05).

Kisqali in combination with tamoxifen or an aromatase inhibitor plus goserelin demonstrated a median PFS of 23.8 months (95% CI: 19.2 months-not reached) compared to 13.0 months (95% CI: 11.0-16.4 months) for tamoxifen or an aromatase inhibitor plus goserelin (HR=0.553; 95% CI: 0.441-0.694; p<0.0001)<sup>1</sup>. Premenopausal women treated with Kisqali combination therapy saw a response as early as eight weeks as demonstrated by separation of the PFS curves compared to endocrine therapy alone<sup>1</sup>.

"The strength of the MONALEESA-7 data is impressive and will give oncologists an important option if ribociclib is approved as treatment for this patient population as well as greater flexibility in the choice of endocrine therapy given with this agent," said Dr. Debu Tripathy, chair of Breast Medical Oncology, The University of Texas MD Anderson Cancer Center. "Women who are premenopausal at the time of their breast

cancer diagnosis tend to have more aggressive disease with poorer prognosis along with unique needs and experiences, so it is critical we determine which treatments will be most effective while also well tolerated."

MONALEESA-7 trial evaluated Kisqali in combination with tamoxifen and an aromatase inhibitor. This is the only Phase III study to evaluate a CDK4/6 inhibitor in combination with tamoxifen and establishes the safety and efficacy of Kisqali in this combination as first-line treatment for advanced breast cancer (median PFS of 22.1 vs 11.0 months; HR=0.585; 95% CI: 0.387-0.884)<sup>1</sup>. Kisqali in combination with an aromatase inhibitor demonstrated an additional 14 months progression-free survival over endocrine therapy alone (median PFS of 27.5 vs 13.8 months; HR=0.569; 95% CI: 0.436-0.743)<sup>1</sup>.

Premenopausal women taking Kisqali benefited for a longer time until health-related quality of life (QoL) deterioration compared to those taking endocrine therapy alone<sup>1</sup>. Women taking Kisqali also had a clinically meaningful improvement in pain symptoms as early as eight weeks; this improvement was sustained<sup>1</sup>.

No new safety signals were observed in the MONALEESA-7 trial; adverse events were generally consistent with those observed in MONALEESA-2, identified early and mostly managed through dose interruptions or reductions<sup>1</sup>. Combination treatment with Kisqali was well tolerated with a discontinuation rate due to adverse events of 3.6% compared to 3.0% in patients who received endocrine therapy alone<sup>1</sup>. The most common (≥5%) grade 3/4 adverse events in patients receiving Kisqali combination therapy compared to endocrine therapy alone were neutropenia (60.6% vs 3.6%) and leukopenia (14.3% vs 1.2%)<sup>1</sup>.

"We are pleased to see Kisqali combination therapy provide strong efficacy and prolonged quality of life with pain reduction in younger women, and look forward to working with health authorities to bring a new treatment option to premenopausal or perimenopausal women," said Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. "Research in premenopausal advanced breast cancer is extremely limited as these women traditionally have been excluded from clinical trials or reduced to a subgroup in trials designed for their postmenopausal counterparts. We designed the robust MONALEESA clinical trial program to be inclusive of all women and men with HR+/HER2- advanced breast cancer."

Premenopausal breast cancer is a biologically distinct and more aggressive disease than postmenopausal breast cancer, and it is the leading cause of cancer death in women 20-59 years old<sup>3,4</sup>.

Novartis plans to discuss MONALEESA-7 data with global health authorities worldwide.

#### About MONALEESA-7

MONALEESA-7 is a Phase III randomized, double-blind, placebo-controlled trial investigating the efficacy and safety of Kisqali in combination with tamoxifen or a non-steroidal aromatase inhibitor plus goserelin versus tamoxifen or an aromatase inhibitor plus goserelin, 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 23-58 years in age were randomized in the MONALEESA-7 trial. The first patient assessment occurred at eight weeks; separation of the PFS curves at this time was not a pre-specified endpoint of the study.

#### About Kisqali<sup>®</sup> (ribociclib)

Kisqali 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 approved by the U.S. Food and Drug Administration (FDA) in March 2017, as a first-line treatment

for postmenopausal women with HR+/HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor based on findings from the pivotal MONALEESA-2 trial. Kisqali is not currently approved for use in premenopausal patients.

Kisqali is approved for use in 44 countries around the world, including the United States and European Union member states. 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<sup>1</sup>.

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-2 is a Phase III global registration trial evaluating Kisqali in combination with letrozole compared to letrozole alone in postmenopausal women with HR+/HER2- advanced breast cancer who received no prior therapy for their advanced breast cancer.

MONALEESA-3 is a Phase III study evaluating Kisqali in combination with fulvestrant compared to fulvestrant alone in postmenopausal women or men with HR+/HER2- advanced breast cancer who have received no or a maximum of one prior endocrine therapy. MONALEESA-3 is fully enrolled.

CompLEEment-1 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. CompLEEment-1 is enrolling.

The safety and efficacy of Kisqali with endocrine therapy as adjuvant therapy in premenopausal and postmenopausal women who have not previously received treatment with a CDK4/6 inhibitor is also being evaluated in the EarLEE-1 study, which is enrolling.

More information about these studies can be found at [www.ClinicalTrials.gov](http://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.

#### 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  $\geq 20\%$ ) 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.

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

Located in East Hanover, NJ, Novartis Pharmaceuticals Corporation is an affiliate of Novartis which 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

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2. Kisqali (ribociclib) Prescribing information. East Hanover, New Jersey, USA: Novartis Pharmaceuticals Corporation; March 2017.
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