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Novartis Kisqali® (ribociclib) receives EU approval as first-line treatment for HR+/HER2- locally advanced or metastatic breast cancer in combination with any aromatase inhibitor

- *Approval is based on pivotal MONALEESA-2 trial, which showed Kisqali plus letrozole reduced risk of disease progression or death by 43% versus letrozole alone[1]*
- *Kisqali plus letrozole demonstrated a median progression-free survival (PFS) of 25.3 months versus 16.0 months of patients who received letrozole alone[1]*
- *Kisqali plus letrozole demonstrated rapid clinical improvement in patients with measurable disease, with 76% seeing a reduction in tumor size after only eight weeks versus 67% with letrozole alone[2]*
- *Up to one-third of patients with early-stage breast cancer will subsequently develop advanced disease[3]; globally an estimated 250,000 women are diagnosed with advanced breast cancer each year[4]*

Basel, August 24, 2017 – Novartis announced that the European Commission (EC) approved Kisqali® (ribociclib) in combination with an aromatase inhibitor for treatment of postmenopausal women with hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) locally advanced or metastatic breast cancer as initial endocrine-based therapy. Kisqali is the first CDK4/6 inhibitor approved in Europe based on a first-line Phase III trial that met its primary endpoint of progression-free survival (PFS) at interim analysis.

“This approval of Kisqali reinforces our recognized leadership in cancer research and our commitment to innovative targeted therapies,” said Bruno Strigini, CEO, Novartis Oncology. “We are proud of our collaboration with study investigators and patients, which provides the medical community with an important new treatment option for women with advanced or metastatic breast cancer.”

EU approval follows a positive opinion granted in June by the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA), which was based on superior efficacy and demonstrated safety of Kisqali plus letrozole versus letrozole alone in the pivotal Phase III MONALEESA-2 trial. The opinion included a recommendation that allows oncologists the flexibility to prescribe Kisqali with any aromatase inhibitor (i.e., letrozole, anastrozole or exemestane) they deem most appropriate for their patient.

“Advanced breast cancer remains incurable, so it’s important to start with a powerful treatment option at initial diagnosis,” said Wolfgang Janni, MD, PhD, University of Ulm, MONALEESA-2 investigator. “I am encouraged that women in Europe living with HR+/HER2- advanced breast cancer may be treated in first-line with ribociclib in combination with letrozole, which demonstrated strong progression-free survival of more than two years in the pivotal MONALEESA-2 trial.”

MONALEESA-2 enrolled 668 postmenopausal women with HR+/HER2- advanced or metastatic breast cancer who received no prior systemic therapy for their advanced breast cancer and showed that Kisqali plus letrozole, an aromatase inhibitor, reduced the risk of progression or death by 43% over letrozole alone (median PFS=25.3 months (95% CI: 23.0-30.3) vs. 16.0 months (95% CI: 13.4-18.2); HR=0.568 (95% CI: 0.457-0.704; p<0.0001)[1]. More than half of patients (55%) with measurable disease taking Kisqali plus letrozole experienced a tumor reduction of at least 30 percent[1].

Up to one-third of patients with early-stage breast cancer will subsequently develop advanced disease, for which there is currently no cure[3]. Globally approximately 250,000 women are diagnosed with advanced breast cancer each year[4].

Kisqali can be taken orally once-daily with or without food at a suggested starting dose of 600 mg (three 200 mg tablets) for three weeks, followed by one week off treatment. Kisqali is taken in combination with continuous use of any aromatase inhibitor.

This decision is applicable to all 28 European Union member states plus Iceland, Norway and Liechtenstein. Additional regulatory filings are underway with other health authorities worldwide.

In March 2017, the US Food and Drug Administration (FDA) approved Kisqali, in combination with any aromatase inhibitor, as a treatment for metastatic breast cancer. Ribociclib in combination with letrozole was added to the National Comprehensive Cancer Network® Clinical Practice Guidelines in Oncology (NCCN Guidelines®) as a category 1 option for HR+/HER2- postmenopausal metastatic breast cancer patients[5].

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
Novartis is continuing to assess Kisqali through the robust MONALEESA clinical trial program, which includes two additional Phase III trials, MONALEESA-3 and MONALEESA-7 that are evaluating Kisqali in combination with multiple endocrine therapy partners across a broad range of patients, including premenopausal women. 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 is initiating two multi-center, 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 or aromatase inhibitors. EarLEE-1 aims to 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-1 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. The open-label, multicenter, Phase IIIb CompLEEment-1 trial is currently enrolling participants.

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.

Disclaimer
This press release contains forward-looking statements, including “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 119,000 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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