

**MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG****Novartis Kisqali® (ribociclib) receives positive CHMP opinion as first-line treatment for HR+/HER2- locally advanced or metastatic breast cancer in combination with any aromatase inhibitor**

- *CHMP opinion based on pivotal Phase III trial that showed Kisqali plus letrozole reduced risk of disease progression or death by 44% over letrozole alone among postmenopausal women with HR+/HER2- advanced breast cancer<sup>1</sup>*
- *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<sup>2</sup>*
- *Worldwide, an estimated 250,000 women will be diagnosed with advanced breast cancer each year<sup>3</sup>*

**Basel, June 23, 2017** – Novartis today announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending approval of 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. The CHMP recommendation of combining Kisqali with any aromatase inhibitor means that, if approved, oncologists could prescribe Kisqali with letrozole, anastrozole or exemestane, giving them the discretion to select the therapy they believe is most appropriate for each individual patient.

“This positive CHMP opinion brings us one step closer to improving the lives of women diagnosed with advanced or metastatic breast cancer throughout Europe,” said Bruno Strigini, CEO, Novartis Oncology. “There is currently no cure for advanced breast cancer, and approximately 30 percent of those affected by early-stage breast cancer will go on to develop advanced disease. We look forward to working with European health authorities to make Kisqali available to those who may benefit from it as quickly as possible.”

The positive CHMP opinion is based on superior efficacy and demonstrated safety of Kisqali plus letrozole versus letrozole alone in the pivotal Phase III MONALEESA-2 trial. The trial, which globally enrolled 668 postmenopausal women with HR+/HER2- advanced or metastatic breast cancer who received no prior systemic therapy for their advanced breast cancer, showed that Kisqali plus the aromatase inhibitor letrozole reduced the risk of progression or death by 44% over letrozole alone at interim analysis<sup>1</sup>. Most adverse events in the MONALEESA-2 trial were mild to moderate in severity, identified early through routine monitoring, and generally managed through dose interruption and/or reduction<sup>1</sup>.

A subsequent, pre-planned analysis of overall survival with an additional 11 months of follow-up demonstrated a median PFS of 25.3 months for Kisqali plus letrozole and 16.0 months for letrozole alone (HR=0.568 (95% CI: 0.457-0.704; p<0.0001))<sup>2</sup>. More than half of women with measurable disease taking Kisqali plus letrozole saw their tumor size shrink by at least 30% (overall response rate (ORR) in patients with measurable disease = 55% vs 39%, p=0.00025)<sup>2,4</sup>. Follow-up to measure overall survival is ongoing as data remain immature<sup>4</sup>.

The European Commission will review the CHMP recommendation and usually delivers its final decision within two months. The decision will be 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, Kisqali was approved by the US Food and Drug Administration (FDA) in combination with an aromatase inhibitor as initial endocrine-based therapy for treatment of postmenopausal women with HR+/HER2- advanced or metastatic breast cancer. Kisqali can be taken with or without food as a once-daily oral dose of 600 mg (three 200 mg film-coated tablets) for three weeks, followed by one week off treatment. Kisqali is taken in combination with four weeks of any aromatase inhibitor.

Globally, an estimated 250,000 women will be diagnosed with advanced breast cancer each year<sup>3</sup>. Up to one-third of patients with early-stage breast cancer will subsequently develop metastatic disease, for which there is currently no cure<sup>5,6</sup>.

#### **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. In the European Union, Kisqali is an investigational agent and has not been approved.

#### **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 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. 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.

### **Kisqali® (ribociclib) Important Safety Information FROM THE U.S. PRESCRIBING 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**

The foregoing release contains forward-looking statements that can be identified by words such as "positive CHMP opinion," "will," "positive opinion," "recommending," "CHMP recommendation," "could," "one step closer," "look forward," "ongoing," "within two months," "may," "investigational," "continuing to assess," "evaluating," "investigating," "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 market, 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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