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Novartis receives positive CHMP opinion to expand Kisqali® combination therapy to all women with HR+/HER2- locally advanced or metastatic breast cancer

- *Kisqali is the CDK4/6 inhibitor with the largest body of first-line evidence demonstrating consistent, superior and sustained efficacy vs. endocrine therapy alone*[1]

- *CHMP opinion is supported by two pivotal Phase III trials showing clinical benefit of Kisqali-based regimens, regardless of combination partner or menopausal status, as first or second-line treatment*[1]

- *Kisqali plus fulvestrant demonstrated superior efficacy in patients with* de novo *advanced breast cancer, and in those who had not received adjuvant therapy in more than a year vs. fulvestrant alone in large Phase III trial population*[1]

- *Breast cancer is the leading cause of cancer death in women 20-59 years old*[2]*; Kisqali is the only CDK4/6 inhibitor with a dedicated Phase III clinical trial in pre- and perimenopausal women with HR+/HER2- advanced breast cancer*[1]

Basel, November 16, 2018 – Novartis today announced the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending an expanded indication for Kisqali® (ribociclib), the CDK4/6 inhibitor with the largest body of first-line clinical trial evidence demonstrating consistent, superior and sustained efficacy compared to endocrine therapy alone. CHMP recommended Kisqali for the treatment of women with hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) locally advanced or metastatic breast cancer in combination with fulvestrant as initial endocrine-based therapy and in women who have received prior endocrine therapy. The positive opinion also recommended approval of Kisqali in combination with endocrine therapy and a luteinising hormone-release hormone agonist (LHRH) for pre- and perimenopausal women.

“Today’s CHMP opinion brings us one step closer to providing more women with HR+/HER2- advanced breast cancer in Europe with a treatment option,” said Liz Barrett, CEO, Novartis Oncology. “The MONALEESA Phase III program enrolled more than 2,000 women, giving Kisqali by far the most extensive first-line evidence in clinical trials among any of the CDK4/6 inhibitors. This is another testament to how we are reimagining cancer.”

This positive CHMP opinion is based on data from the Phase III MONALEESA-7 and MONALEESA-3 trials. These trials demonstrated prolonged progression-free survival (PFS) for Kisqali-based regimens compared to endocrine therapy alone and showed improvements as early as eight weeks after start of treatment with Kisqali combination therapy.

In MONALEESA-7, Kisqali plus an aromatase inhibitor and goserelin nearly doubled the median PFS compared to an aromatase inhibitor and goserelin alone in pre- or perimenopausal women (27.5 months compared to 13.8 months; HR=0.569; 95% CI: 0.436-

0.743)[3]. In MONALEESA-3, Kisqali plus fulvestrant demonstrated a median PFS of 20.5 months compared to 12.8 months for fulvestrant alone (HR=0.593; 95% CI: 0.480-0.732) across the overall population of first-line and second-line postmenopausal women[4]. Across the two trials, the most common adverse reactions (incidence ≥20%) were neutropenia, nausea, infections, fatigue, diarrhea, leukopenia, vomiting, alopecia, headache, constipation, rash and cough[3,4].

Globally, an estimated 267,000 women will be diagnosed with advanced breast cancer each year and up to one-third of patients with early-stage breast cancer will subsequently develop advanced disease[5,6]. One in five women diagnosed with breast cancer in Europe are younger than 50 years old[7]. 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[1,8]. These young women face specific challenges, including induction of premature menopause, emotional distress and strain on their professional and personal lives[9,10,11].

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.

About Kisqali® (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[1].

Kisqali was initially approved by the US Food and Drug Administration (FDA) in March 2017 and by the European Commission in August 2017, as initial endocrine-based therapy for postmenopausal women with HR+/HER2- locally advanced or metastatic breast cancer in combination with an aromatase inhibitor based on findings from the pivotal MONALEESA-2 trial[12]. In July 2018, Kisqali was approved by the FDA for the treatment of pre-, peri- or postmenopausal women in the US, and indicated for use in combination with fulvestrant as both first- or second-line therapy in postmenopausal women[1].

Kisqali is approved for use in more than 70 countries around the world, including the United States and European Union member states. Kisqali is not currently approved for use in combination with fulvestrant or in premenopausal women in Europe. Kisqali was developed by the Novartis Institutes for BioMedical Research (NIBR) under a research collaboration with Astex Pharmaceuticals[12].

About Novartis in Advanced Breast Cancer
For more than 30 years, Novartis has been tackling breast cancer with superior science, great collaboration and a passion for transforming patient care. With one of the most diverse breast cancer pipelines and one of the largest numbers 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
KISQALI® (ribociclib) is a prescription medicine approved in combination with an aromatase inhibitor or fulvestrant as initial endocrine – based therapy or following disease progression on endocrine therapy in women 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 or adolescents. KISQALI can cause a heart problem known as QT prolongation. This condition can cause an abnormal heartbeat and may lead to

death. KISQALI is not indicated for concomitant use with tamoxifen due to an increased risk of QT prolongation. 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 highly 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 grapefruit or grapefruit juice while taking KISQALI. The most common side effects (incidence ≥20%) include infections, white blood cell count decreases, headache, cough, nausea, tiredness, diarrhea, vomiting, constipation, hair loss and rash. The most common Grade 3/4 side effects (incidence >5%) were infections, low neutrophils, low leukocytes, low red blood cells, abnormal liver function tests, low lymphocytes, low phosphate levels and vomiting. Abnormalities were observed in hematology and clinical chemistry laboratory tests.

Please see full Prescribing Information for KISQALI, available at www.kisqali.com.

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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; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political and economic conditions; safety, quality or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, 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 is reimagining medicine to improve and extend people's lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world's top companies investing in research and development. Novartis products reach nearly 1 billion people globally and we are finding innovative ways to expand access to our latest treatments. About 125 000 people of more than 140 nationalities work at Novartis around the world. Find out more at www.novartis.com.

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