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Novartis Kisqali® now first and only CDK4/6 inhibitor indicated in US as first-line therapy specifically for premenopausal women; and as initial therapy with fulvestrant in postmenopausal women

- *Kisqali is now the only CDK4/6 inhibitor indicated in combination with an aromatase inhibitor as first-line treatment for pre-, peri- or postmenopausal women with HR+/HER2- advanced breast cancer in the US*[1]
- *Kisqali is the only CDK4/6 inhibitor that is indicated with fulvestrant as both initial or second-line treatment for postmenopausal women with HR+/HER2- advanced breast cancer*[1]
- *FDA approval is based on MONALEESA-3 and MONALEESA-7 clinical trials, which demonstrated robust efficacy of Kisqali combination therapy in multiple treatment partners and settings*[1]
- *First FDA approval using the Real-Time Oncology Review and Assessment Aid pilot programs; application approved in less than one month*

Basel, July 18, 2018 – Novartis today announced a new approval for Kisqali® (ribociclib) from the US Food and Drug Administration (FDA) for women with hormone-receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer. Kisqali is now the only CDK4/6 inhibitor indicated for use with an aromatase inhibitor for the treatment of pre-, peri- or postmenopausal women in the US, and also is indicated for use in combination with fulvestrant as both first- or second-line therapy in postmenopausal women[1]. FDA reviewed this supplemental New Drug Application (sNDA) under its Real-Time Oncology Review and Assessment Aid pilot programs and approved the application in less than one month after submission.

“Compelling data for Kisqali have led to the broadest first-line indications of any CDK4/6 inhibitor,” said Liz Barrett, CEO, Novartis Oncology. “With this new approval Kisqali has the potential to help even more people in the US live a longer life without progression of disease from this incurable form of breast cancer.”

This approval is based on the pivotal MONALEESA-7 and MONALEESA-3 Phase III clinical trials that demonstrated prolonged progression-free survival (PFS) and improvements as early as eight weeks for Kisqali-based regimens compared to endocrine therapy alone[1]. In MONALEESA-7, Kisqali plus an aromatase inhibitor and goserelin nearly doubled the median PFS compared to an aromatase inhibitor and goserelin alone (27.5 months compared to 13.8 months; HR=0.569; 95% CI: 0.436-0.743) in pre- or perimenopausal women[1]. 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[1].

“These MONALEESA clinical trial program data add to the body of evidence that CDK 4/6 inhibition, in the case of these studies with ribociclib, gives women diagnosed with HR+/HER2- advanced breast cancer an important first-line treatment option,” said Dennis J.

Slamon, MD, Director of Clinical/Translational Research, University of California, Los Angeles Jonsson Comprehensive Cancer Center. “Based on Phase III trial results that consistently showed clinical benefit, physicians should be encouraged to re-evaluate treatment for advanced breast cancer in the first-line setting.”

Approximately 155,000 people in the US are living with metastatic breast cancer[2]. Up to one-third of patients with early-stage breast cancer will subsequently develop advanced disease, for which there is currently no cure[3]. Advanced breast cancer in premenopausal women is a biologically distinct and more aggressive disease, and it is the leading cause of cancer death in women 20-59 years old[4,5].

“Premenopausal women diagnosed with advanced breast cancer often face unique social challenges and a poorer prognosis. For the first time in nearly 20 years, we have results from a dedicated clinical trial among these women,” said Jennifer Merschdorf, CEO, Young Survival Coalition. “With this approval, some younger women now have a new therapy indicated specifically for them that may help extend their lives without progression of disease.”

Novartis is committed to providing patients with access to medicines, as well as resources and support to address a range of needs. The Kisqali patient support program is available to help guide eligible patients through the various aspects of getting started on treatment, from providing educational information to helping them understand their insurance coverage and identify potential financial assistance options. For more information, patients and healthcare professionals can call 1-800-282-7630.

Discussions with global health authorities regarding the MONALEESA-3 and MONALEESA-7 data are ongoing.

About Kisqali Clinical Trial Programs
With more than 2,000 patients enrolled in current trials, the MONALEESA program is the largest industry sponsored Phase III clinical program researching a CDK4/6 inhibitor in HR+/HER2- advanced breast cancer:

- MONALEESA-7 is the only Phase III global registration trial investigating the efficacy and safety of a CDK4/6 inhibitor, Kisqali, in combination with an aromatase inhibitor plus goserelin versus an aromatase inhibitor plus goserelin, in pre- or perimenopausal women with HR+/HER2- advanced breast cancer who had not previously received endocrine therapy for advanced disease. Results from the pre-specified NSAI-only subgroup of 495 pre- or perimenopausal women with HR+/HER2- advanced breast cancer who received no prior endocrine therapy for advanced disease showed an estimated median progression-free survival (PFS, RECIST 1.1) of 27.5 months for patients on the Kisqali arm compared with 13.8 months for those on the placebo arm (HR 0.569; 95% CI: 0.436, 0.743). Kisqali is not indicated for concomitant use with tamoxifen[6].
- MONALEESA-3 is a Phase III global registration trial 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. Nearly 70% of patients in MONALEESA-3 receiving Kisqali plus fulvestrant as initial therapy were estimated to remain progression-free at the median follow-up of 16.5 months (median PFS not reached vs.18.3 months; HR=0.577; 95% CI: 0.415-0.802)[1].
- 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 advanced breast cancer that led to the initial FDA approval. MONALEESA-2 is ongoing to evaluate overall survival[1].

Across the pivotal trials (M2, M3, and M7), the most common adverse reactions (incidence ≥20%) were neutropenia, nausea, infections, fatigue, diarrhea, leukopenia, vomiting, alopecia, headache, constipation, rash and cough[1].

CompLEEment-1 is an open-label, multicenter, Phase IIIb study evaluating the safety and efficacy of Kisqali plus letrozole in pre- or postmenopausal women and men with HR+/HER2- advanced breast cancer who have not received prior hormonal therapy for advanced disease[6].

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

Novartis is continuing the development of Kisqali in early breast cancer (EBC) through a collaboration with Translational Research In Oncology (TRIO). The NATALEE study is a Phase III clinical trial of Kisqali with endocrine therapy in the adjuvant treatment of HR+/HER2- EBC[6].

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[6].

Kisqali was initially approved by the US Food and Drug Administration 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[6].

Kisqali is approved for use in more than 60 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[6].

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
KISQALI® (ribociclib) is a prescription medicine used in combination with an aromatase inhibitor as the first hormonal-based therapy to treat pre/peri- and postmenopausal women and in combination with fulvestrant as the first hormonal-based therapy or following disease progression on hormonal therapy in postmenopausal 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. 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 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 white blood cell count decreases, nausea, infections, tiredness, diarrhea, vomiting, hair loss, headache, constipation, rash, and cough. The most common Grade 3/4 side effects (incidence >5%) were low neutrophils, low leukocytes, abnormal liver function tests, and low lymphocytes. Abnormalities were observed in hematology and clinical chemistry laboratory tests.
Please see full Prescribing Information for KISQALI, available at 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,” “option,” “should,” “encouraged,” “will,” “may,” “committed,” “ongoing,” “investigating,” “evaluating,” “continuing,” “can,” “may,” “pipelines,” or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for Kisqali or the other 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 Kisqali or the other 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 Kisqali or the other investigational or approved products described in this press release 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. 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 2017, the Group achieved net sales of USD 49.1 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 125,000 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. Kisqali (ribociclib) Prescribing information. East Hanover, New Jersey, USA: Novartis Pharmaceuticals Corporation; July 2018.
2. Mariotto, Angela B., et al. "Estimation of the Number of Women Living with Metastatic Breast Cancer in the United States." *Cancer Epidemiology and Prevention Biomarkers* 26.6 (2017): 809-815.
3. Redig AJ, et al. Breast cancer as a systemic disease: a view of metastasis. *J Intern Med.* 2013; 274: 113-126.
4. Benz CC. Impact of aging on the biology of breast cancer. *Crit Rev Oncol Hematol*. 2008;66:65-74.
5. World Health Organization. Women's health fact sheet. September 2013. Available at http://www.who.int/mediacentre/factsheets/fs334/en/. Accessed July 2018.
6. Novartis Data on File.

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