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MEDIA & INVESTOR RELEASE

Novartis Kisqali® data demonstrate superior benefit across main intrinsic subtypes in metastatic breast cancer

- *Findings presented at SABCS from largest intrinsic subtype analysis show Kisqali is unique among CDK4/6 inhibitors, delivers consistent efficacy across main HR+/HER2- intrinsic subtypes*[1]

- *Benefit seen even in patients with the endocrine-resistant HER2-enriched subtype, who face poor prognosis with endocrine therapy alone, reinforces Kisqali as first line treatment choice for all patients*[2]

- *Data presented at SABCS also show Kisqali more selectively inhibits CDK4, the active target in breast cancer and a pivotal driver of disease progression, compared to palbociclib*[3]

- *Kisqali remains the CDK4/6 inhibitor with longest reported overall survival, proven in two Phase III trials to help people with metastatic breast cancer live longer regardless of menopausal status, endocrine sensitivity or endocrine partner*[4-6]

Basel, December 9, 2020 — Novartis today announced new Kisqali® (ribociclib) data demonstrating consistent efficacy benefit with Kisqali plus endocrine therapy across the main intrinsic subtypes of hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) metastatic breast cancer. The largest biomarker analysis of efficacy in intrinsic subtypes evaluated whether there was a correlation between these subtypes and efficacy outcomes in patients treated with Kisqali across the three Phase III MONALEESA trials[1]. The findings will be presented in an oral presentation at the 2020 San Antonio Breast Cancer Virtual Symposium.

This broad ad hoc exploratory analysis showed that Kisqali plus endocrine therapy consistently provided significant progression-free survival (PFS) benefit across three of four subtypes of HR+/HER2- metastatic breast cancer (LumA HR=0.63; p<.001, LumB HR=0.52; p<.001, HER2-enriched HR=0.39; p<.001, Basal-like HR=1.15; p=.7672)[1]. The largest PFS benefit was seen in patients with the HER2-enriched subtype – a non-luminal subtype associated with endocrine resistance and poor prognosis[1]. In contrast, benefit was not observed with palbociclib in the HER2-enriched subtype in a retrospective analysis of the PALOMA-2 trial presented at the 2017 San Antonio Breast Cancer Symposium [7].

“The significant benefit seen with ribociclib in the endocrine-resistant HER2-enriched subtype is a unique and important finding, differentiating it from the other CDK4/6 inhibitors. The underlying hypothesis is that ribociclib induces hormone-sensitivity in this group of tumors beyond inhibition of the cell-cycle,” said Aleix Prat, Head, Department of Medical Oncology,

Hospital Clinic, Barcelona, Spain. “The body of preclinical data showing that ribociclib has the ability to more selectively target and inhibit CDK4, which is a key driver of disease progression in breast cancer, may help us understand why ribociclib provides consistent benefit, especially in patients with more aggressive disease.”

The four intrinsic subtypes of breast cancer (Luminal A, Luminal B, HER2-enriched and basal-like) have revealed critical differences in terms of incidence, survival and response to treatment[8-12]. Additionally, the insights provided by intrinsic subtypes complement and expand upon the information provided by standard clinical parameters and pathological markers. The observed benefit with Kisqali provides reassurance about it as a treatment choice for the majority of people with metastatic breast cancer without the need for additional testing.

Preclinical CDK4/6 Study
Additional data to be presented at SABCS include a poster presentation of a preclinical analysis in which cellular models were used to examine the effects of CDK4/6 inhibitors on either CDK4 or CDK6. The preclinical *in vivo* study confirmed previously published biochemical *in vitro* and proliferation data, demonstrating that Kisqali selectively inhibits CDK4, whereas palbociclib has similar activity against both CDK4 and CDK6 in cells[3]. Kisqali inhibited CDK4 at 11-fold and 9-fold lower drug concentrations than CDK6, whereas palbociclib inhibited CDK4 at 2-fold lower drug concentrations than CDK6 in both cell lines[3].

“The data presented at SABCS show that Kisqali offers a superior benefit for metastatic breast cancer patients, even in those with the HER2-enriched subtype, who face a very poor prognosis. These data build on previous findings showing Kisqali provides a benefit regardless of type of metastases, endocrine partner or menopausal status. The totality of evidence to date gives us incredible confidence that Kisqali is unique among CDK4/6 inhibitors, and we believe doctors should consider Kisqali for their patients,” said Susanne Schaffert, PhD, President of Novartis Oncology.

About Kisqali® (ribociclib)
Kisqali is the CDK4/6 inhibitor with the largest body of first-line clinical trial evidence demonstrating consistent and sustained efficacy compared to endocrine therapy alone. Kisqali is the only CDK4/6 inhibitor to achieve statistically significant OS in two Phase III trials with two distinct patient populations[4-6]. The substantial OS benefit and improved quality of life observed in MONALEESA-7 support the ESMO Magnitude of Clinical Benefit Scale (MCBS) perfect five out of five rating for Kisqali plus endocrine therapy in premenopausal HR+/HER2- MBC[13]. Kisqali also received an ESMO-MCBS score of four out of five, the highest score achieved by any CDK 4/6 inhibitor in combination with fulvestrant, for first-line postmenopausal patients based on the statistically significant OS benefit observed in MONALEESA-3 and maintained quality of life[13]. Overall survival follow-up is ongoing for the Phase III MONALEESA-2 trial.

Kisqali was initially approved by the US Food and Drug Administration (FDA) in March 2017 and by the European Commission (EC) 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. Kisqali in combination with an aromatase inhibitor was approved for the treatment of pre-, peri- or postmenopausal women as initial endocrine based therapy, and also indicated for use in combination with fulvestrant as both first- or second-line therapy in postmenopausal women by the FDA in July 2018 and by the EC in December 2018. Regulatory filings are underway with other health authorities worldwide.

Novartis is continuing to reimagine cancer by investigating Kisqali in early breast cancer. The NATALEE study is a Phase III clinical trial of Kisqali with endocrine therapy in the adjuvant treatment of HR+/HER2- early breast cancer being conducted in collaboration with Translational Research In Oncology (TRIO).

Kisqali was developed by the Novartis Institutes for BioMedical Research (NIBR) under a research collaboration with Astex Pharmaceuticals.

Important Safety Information from the Kisqali EU SmPC
Kisqali® (ribociclib) is a prescription medicine approved in combination with an aromatase inhibitor as initial endocrine - based therapy in women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer or fulvestrant as initial endocrine - based therapy or following disease progression on endocrine 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 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.

About Novartis in Advanced Breast Cancer
Novartis tackles breast cancer with superior science, collaboration and a passion for transforming patient care. We've taken a bold approach to our research by including patient populations often neglected in clinical trials, identifying new pathways or mutations that may play a role in disease progression and developing therapies that not only maintain, but also improve, quality of life for patients. Our priority over the past 30 years and today is to deliver treatments proven to improve and extend lives for those diagnosed with advanced breast cancer.

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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,” “may,” “could,” “would,” “expect,” “anticipate,” “seek,” “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

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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 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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