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MEDIA & INVESTOR RELEASE

New Kisqali® data shows consistent overall survival benefit across genomic and clinical subtypes of interest in HR+/HER2- metastatic breast cancer

- *Data from the MONALEESA Phase III program provide further evidence of the unique profile of Kisqali, the CDK4/6 inhibitor with the longest reported median overall survival (OS) in HR+/HER2- metastatic breast cancer (over 5 years) and proven OS benefit across patient subgroups*[1-5]

- *Kisqali pooled data at the San Antonio Breast Cancer Symposium confirms OS benefit across most common genomic intrinsic subtypes of HR+/HER2- metastatic breast cancer, including the aggressive, ET-resistant HER2-enriched subtype*[6]

- *Data supports rationale for HARMONIA, the first prospective, head-to-head Phase III trial seeking to identify the best therapeutic option between Kisqali and Ibrance®* for patients with the HER2-enriched subtype*

- *Kisqali remains the only CDK4/6i with consistent OS benefit across the entire MONALEESA program, regardless of site and number of metastases, prior treatment, endocrine partner, line of therapy or menopausal status*[1-5,7-8]

Basel, December 8, 2021 — Novartis today announced new Kisqali® (ribociclib) data demonstrating a consistent overall survival (OS) benefit with Kisqali plus endocrine therapy (ET) across genomic subtypes of hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer (mBC), similarly in the indolent as well as in the aggressive, endocrine therapy (ET)-resistant subtypes[6]. The findings will be presented as a late-breaking oral presentation at the 2021 San Antonio Breast Cancer Symposium (SABCS).

“The overall survival benefit seen even in HER2-enriched adds to the body of evidence supporting the need to test the hypothesis that ribociclib may alter tumor biology, resulting in a better response to ET across common HR+/HER2- subtypes,” said Aleix Prat, President of SOLTI, Head of the Medical Oncology Department at Hospital Clínic of Barcelona, Head of the Translational Genomics Group and Targeted Therapies in Solid Tumors at IDIBAPS and Professor of Medicine at the University of Barcelona. “One of the most interesting aspects of these ribociclib data is the overall survival benefit seen across the spectrum of indolent, less proliferative disease compared to the aggressive and ET-resistant disease, assuring the overall survival benefit of ribociclib in patients regardless of their baseline prognosis.”

A broad ad hoc exploratory analysis of nearly 1,000 tumor samples showed that Kisqali in combination with ET consistently provided significant OS benefit compared to ET alone across main intrinsic subtypes (Luminal A: n=542; HR=0.75; 95% CI: 0.58-0.96; p=.021; Luminal B: n=278; HR=0.69; 95% CI: 0.50-0.95; p=.023; and HER2-enriched: n=147; HR=0.60; 95% CI: 0.40-0.92; p=.018)[6]. Patients with the HER2-enriched subtype associated with endocrine resistance and poor prognosis in HR+/HER2- breast cancer, achieved a significant improvement in median OS of 40.3 months compared to 29.4 months for ET alone[6]. The longest survival benefit from Kisqali plus ET was seen in patients with the luminal A subtype, who achieved a median OS of 68.0 months compared to 54.6 months on ET alone[6]. Patients with basal-like subtype, which is known to behave more like triple-negative breast cancer, had poorer OS outcomes in both the Kisqali combination and ET alone groups with a median OS of 19.4 months and 21.2 months, respectively (n=30; HR=1.89; 95% CI: 0.80-4.47; p=.148)[6]. These data follow the biomarker analysis of the MONALEESA trials presented at SABCS 2020 and published in *Journal of Clinical Oncology*, in which Kisqali demonstrated progression free survival (PFS) benefit across the most common intrinsic subtypes in metastatic breast cancer[9-10].

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[11-15]. Additionally, the insights provided by genomic intrinsic subtypes complement and expand upon the information provided by standard clinical parameters and pathological markers.

“The consistent overall survival data presented at SABCS again show the unique profile of Kisqali, reinforcing the scientific rationale for initiating HARMONIA, the first Phase III, head-to-head trial evaluating Kisqali versus Ibrance® in HR+/HER2- metastatic breast cancer,” said Susanne Schaffert, PhD, President of Novartis Oncology. “We know that for people living with metastatic breast cancer, quality of life in addition to extending life is so important to them, so we are excited to share meaningful outcomes from a global quality of life assessment.”

Additional research of interest to be presented at SABCS includes the following:

Abstract Title	Abstract Number/ Presentation Details
Genomic profiling of PAM50-based intrinsic subtypes in HR+/HER2- advanced breast cancer across the MONALEESA studies[17]	PD2-05 Wednesday, December 8 7:00am CT
Analysis of first-line patients with de novo disease vs late relapse and all pts with vs without prior chemotherapy in the MONALEESA-3 trial[18]	P1-18-11 Wednesday, December 8, 7:00am CT
Overall survival subgroup analysis by metastatic site from the Phase III MONALEESA-2 study of first-line ribociclib + letrozole in postmenopausal patients with HR+/HER2− advanced breast cancer[8]	GS2-01 Wednesday, December 8 8:45am CT
Circulating tumor DNA (ctDNA) dynamics in patients with hormone receptor positive HR+/HER2- advanced breast cancer treated in first line with ribociclib and letrozole in the BioItaLEE trial[19]	GS3-07 Thursday, December 9 10:15am CT
Assessment of quality of life in patients with advanced breast cancer in clinical practice: a real-world multi-country survey[16]	P4-12-03 Thursday, December 9 5:00pm – 6:30pm CT

Visit https://www.hcp.novartis.com/virtual-congress/sabcs-2021/ for the latest information from Novartis, including our commitment to the Oncology community, and access to our SABCS Virtual Scientific Program data presentations (for registered participants).

About Kisqali® (ribociclib)
Kisqali is the CDK4/6 inhibitor with the largest body of clinical trial evidence demonstrating consistent and superior overall survival benefit compared to endocrine therapy alone. Overall survival results were presented previously: MONALEESA-7 (ASCO 2019) and MONALEESA-3 (ESMO 2019) and MONALEESA-2 (ESMO 2021); MONALEESA-7 and MONALEESA-3 were published in the *New England Journal of Medicine*, with updated exploratory analyses presented at SABCS 2020 and ASCO 2021, demonstrating Kisqali plus endocrine therapy significantly extends life in pre/perimenopausal or postmenopausal women with HR+/HER2- advanced breast cancer[1-5].

Kisqali is approved by the US Food and Drug Administration (FDA) and by the European Commission (EC) as initial endocrine-based therapy for postmenopausal women with HR+/HER2- locally advanced or metastatic breast cancer in combination with an aromatase inhibitor. Kisqali in combination with an aromatase inhibitor is 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 and by the EC[20]. Kisqali is approved in over 95 countries[21].

Novartis is continuing to reimagine cancer with additional trials of Kisqali. NATALEE is a large confirmatory 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)[22]. Novartis is collaborating with the Akershus University Hospital in Norway on the NEOLETRIB-trial, a neoadjuvant phase II trial studying the effects of Kisqali in HR+/HER2- early breast cancer including effects on the gut microbiota and senescence[21]. Novartis is also collaborating with SOLTI, who is leading the Phase III HARMONIA clinical trial evaluating Kisqali compared to palbociclib in patients with HR+/HER2- advanced breast cancer with aggressive tumor biology, defined as HER2-enriched[21].

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

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.

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.

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,” “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 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 and requirements for increased pricing transparency; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; safety, quality, data integrity 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 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 108,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com.

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