Novartis International AG
Novartis Global Communications
CH-4002 Basel
Switzerland

http://www.novartis.com

MEDIA RELEASE • COMMUNIQUE AUX MEDIAS • MEDIENMITTEILUNG

Novartis Kisqali® delivers consistently superior overall survival – MONALEESA-3 trial demonstrates more life for postmenopausal HR+/HER2- advanced breast cancer patients

- *In MONALEESA-3, Kisqali plus fulvestrant achieved statistically significant overall survival benefit vs. fulvestrant alone in postmenopausal women (HR=0.724; p=0.00455)*[1]

- *Kisqali is the only CDK4/6 inhibitor to demonstrate positive overall survival in two pivotal Phase III trials -- consistently demonstrating approximately 30% reduction in the risk of death*

- *Overall survival benefit proven with multiple combination partners and the largest number of patients in MONALEESA-3 plus MONALEESA-7 make Kisqali the CDK4/6 inhibitor with unparalleled overall survival evidence*

- *MONALEESA-3 data to be presented in ESMO Congress 2019 Presidential Symposium*

Basel, September 29, 2019 – Novartis today announced results from the MONALEESA-3 trial, which showed Kisqali® (ribociclib) achieved statistically significant improvement in overall survival (OS). This is the second Phase III trial in which Kisqali combination therapy met the secondary endpoint of overall survival at the pre-planned interim analysis. MONALEESA-3 evaluated efficacy and safety of Kisqali plus fulvestrant in postmenopausal women with hormone-receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer. These data will be presented as a late-breaker oral presentation in the Presidential Symposium at the European Society for Medical Oncology (ESMO) Congress 2019.

“Seen now in two Phase III trials, ribociclib consistently and significantly prolongs life among premenopausal and postmenopausal women, and in combination with an aromatase inhibitor and fulvestrant. These results arm oncologists with more evidence to make a confident treatment choice for their hormone receptor-positive metastatic breast cancer patients,” said Dennis J. Slamon, MD, Director of Clinical/Translational Research, University of California, Los Angeles Jonsson Comprehensive Cancer Center.

Kisqali in combination with fulvestrant met its secondary endpoint of overall survival, demonstrating a statistically significant improvement in survival with a 28% reduction in risk of death (median OS not reached vs. 40.0 months; HR=0.724; 95% CI: 0.568-0.924; p=0.00455). The significant extension in survival met the early efficacy stopping criteria at a pre-specified interim analysis. At 42 months, estimated rates of survival were 58% for Kisqali combination treatment and 46% for fulvestrant alone. Results in the first-line and second-line subgroups, including in patients who relapsed within 12 months of adjuvant treatment, were consistent with the overall MONALEESA-3 patient population.

Median PFS in the first-line was also reached at this analysis and demonstrated that Kisqali in combination with fulvestrant has a median PFS of 33.6 months compared to 19.2 months in the placebo arm (HR=0.546; 95% CI: 0.415-0.718). Additionally, the need for chemotherapy was delayed in all patients who were prescribed Kisqali plus fulvestrant (HR=0.696; 95% CI: 0.551-0.879).

“The remarkable results from MONALEESA-3 and MONALEESA-7 make Kisqali the CDK4/6 inhibitor with consistently superior overall survival,” said Susanne Schaffert, PhD, President, Novartis Oncology. “In nearly 25 years, the five-year survival rates in HR+ metastatic breast cancer have improved by less than 5%. We are committed to helping give these women more life and are reimagining a world where metastatic breast cancer becomes a curable disease.”

MONALEESA-3 is the largest trial to evaluate a CDK4/6 inhibitor plus fulvestrant as initial therapy in postmenopausal women (N=726). The trial included women with no prior endocrine therapy, including those diagnosed *de novo,* women who relapsed within 12 months of adjuvant therapy and women who progressed on endocrine therapy for advanced disease. The most common grade 3/4 adverse events of special interest observed in this analysis in patients who received Kisqali plus fulvestrant compared to fulvestrant alone were neutropenia (57.1% vs 0.8%), hepatobiliary toxicity (13.7% vs 5.8%), QTc prolongation (3.1% vs 1.2%), respiratory disorders (2.3% vs 3.3%) and interstitial lung disease (0.2% vs 0%).

“Pre-clinical data show that Kisqali is distinct from other CDK4/6 inhibitors in its ability to more selectively target and inhibit CDK4,” said Jeff Engelman, MD, PhD Global Head of Oncology Research, Novartis Institutes for BioMedical Research. “CDK4 is a major driver of breast cancer progression and inhibiting it has been shown to block the growth of breast cancer cells.”

There currently remains no cure for advanced breast cancer. Breast cancer is the number one cause of cancer death in European women, claiming the lives of more than 150,000 women in 2018.[3]

About Kisqali® (ribociclib)
Kisqali® (ribociclib) 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[1]. Kisqali is the only CDK4/6 inhibitor to achieve statistically significant overall survival in two Phase III trials with two distinct patient populations[1]. Overall survival results from MONALEESA-7 were presented at ASCO 2019, demonstrating Kisqali plus endocrine therapy significantly extends life in premenopausal women with HR+/HER2- advanced breast cancer. Overall survival follow-up is ongoing for the Phase III MONALEESA-2 trial.

Kisqali is approved for use in more than 75 countries around the world, including the United States and European Union member states. 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[1].

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)[1].

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,” “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 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 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 more than 750 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 www.novartis.com.

Novartis is on Twitter. Sign up to follow @Novartis at http://twitter.com/novartis, follow @NovartisNews for the latest News & Media Updates at https://twitter.com/novartisnews and follow @NovartisCancer at https://twitter.com/NovartisCancer
For Novartis multimedia content, please visit www.novartis.com/news/media-library
For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Slamon, DJ, et al. Overall survival (OS) results of the Phase III MONALEESA-3 trial of postmenopausal patients (pts) with hormone receptor–positive (HR+), human epidermal growth factor 2–negative (HER2−) advanced breast cancer (ABC) treated with fulvestrant (FUL) ± ribociclib (RIB). Presented at the European Society of Medical Oncology (ESMO) Congress, September 29, 2019, Barcelona, Spain (LBA7).
2. Slamon DJ, et al. Ribociclib (RIB) + fulvestrant (FUL) in postmenopausal women with hormone receptor-positive (HR+), HER2-negative (HER2-) advanced breast cancer (ABC): Results from MONALEESA-3. Journal of Clinical Oncology 2018.
3. Ferlay, J, et al. Global Cancer Observatory: Cancer Today. International Agency for Research on Cancer. Available at: https://gco.iarc.fr/today/home, accessed September 10, 2019.

# # #

Novartis Global External Communications
E-mail: media.relations@novartis.com

Antonio Ligi
Novartis External Communications
+41 61 324 13 74
antonio.ligi@novartis.com

Julie Masow
Novartis Oncology Media Relations
+1 862 579 8456
julie.masow@novartis.com

Eric Althoff
Novartis US External Communications
+1 646 438 4335
eric.althoff@novartis.com

Novartis Investor Relations
Central investor relations line: +41 61 324 7944
E-mail: investor.relations@novartis.com

Central		North America	
Samir Shah	+41 61 324 7944	Sloan Simpson	+1 862 778 5052
Pierre-Michel Bringer	+41 61 324 1065	Cory Twining	+1 862 778 3258
Thomas Hungerbuehler	+41 61 324 8425		
Isabella Zinck	+41 61 324 7188		