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MEDIA UPDATE • MEDIA UPDATE • MEDIA UPDATE

Novartis Kisqali® data show superior overall survival compared to fulvestrant and consistent efficacy across advanced breast cancer patient subgroups in MONALEESA-3

- *MONALEESA-3 paper published today in* The New England Journal of Medicine *shows statistically significant overall survival results for Kisqali plus fulvestrant, reducing the risk of death by almost 30%*

- *Overall survival benefit for Kisqali plus fulvestrant was consistent regardless of line of therapy or response to prior endocrine treatment*

- *Kisqali is the only CDK4/6 inhibitor to demonstrate consistently superior overall survival in two Phase III trials, proven with multiple combination partners and in two distinct patient populations*

Basel, December 11, 2019 — MONALEESA-3 data published today in *The New England Journal of Medicine* (NEJM) shows Kisqali® (ribociclib) plus fulvestrant demonstrated a statistically significant improvement in overall survival, with an almost 30% reduction in risk of death compared to fulvestrant alone, in postmenopausal women with hormone-receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer[1]. MONALEESA-3 overall survival data were first presented at the European Society for Medical Oncology (ESMO) Congress in September 2019 (see media release). The *NEJM* publication includes new analyses confirming overall survival benefit across all patient sub-groups treated with Kisqali plus fulvestrant.

“These data show that treatment with Kisqali gives women with HR+/HER2- advanced breast cancer a chance for more life – whether they are treatment naïve or have had prior therapy,” said Jeff Engelman, MD, PhD, Global Head of Oncology Research, Novartis Institutes for BioMedical Research. “Pre-clinical data show that Kisqali is distinct from other CDK4/6 inhibitors in its ability to more selectively target and inhibit CDK4.”

The *NEJM* publication includes subgroup analyses according to line of therapy:
- At 42 months, estimated survival rates among patients who received first-line therapy were 66.9% (95% CI, 58.7 to 73.9) with Kisqali plus fulvestrant vs. 56.3% (95% CI, 44.2 to 66.8) with fulvestrant alone (hazard ratio 0.70; 95% CI, 0.48 to 1.02)
- Median overall survival among patients in the early-relapse and second-line subgroup was 40.2 months with Kisqali plus fulvestrant and 32.5 months with fulvestrant alone (hazard ratio, 0.73; 95% CI, 0.53 to 1.00)

A new post-hoc overall survival analysis based on prior endocrine therapy demonstrated that Kisqali plus fulvestrant had a:

- 36% reduction in risk of death in those who did not receive any previous endocrine therapy in any setting (HR= 0.64);
- 30% reduction in risk of death in those who were endocrine resistant, defined as progressive disease within the first 6 months of first-line endocrine therapy for advanced breast cancer while on endocrine therapy, or relapse within the first two years of (neo)adjuvant therapy (HR=0.70);
- 26% reduction in risk of death in those who were endocrine sensitive (HR=0.74).

No new safety signals were observed. The most common grade 3/4 adverse events of special interest observed 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%).

The publication of the full data results is available online.

About Kisqali® (ribociclib)

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)[2].

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

Kisqali® (ribociclib) 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/perimenopausal 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 severe or life-threatening inflammation of the lungs. Patients should tell their health care provider right away if they experience breathing problems or chest pains. 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.

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2. Novartis Data on File.

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