Novartis Kisqali® prolonged PFS benefit for pre- and perimenopausal patients with aggressive HR+/HER2– metastatic breast cancer compared to chemotherapy

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- RIGHT Choice Phase II trial is the first randomized study in patients with aggressive HR+/HER2– metastatic breast cancer (MBC), including visceral crisis, comparing a CDK4/6 inhibitor (CDK4/6i) plus endocrine therapy (ET) versus combination chemotherapy (CT)[1]
- Kisqali plus ET demonstrated a statistically significant progression-free survival (PFS) benefit of one year compared to combination CT; data to be presented at SABCS 2022[1]
- Kisqali is a unique CDK4/6i that has consistently shown statistically significant overall survival benefit while preserving or improving quality of life across three Phase III trials in MBC, including in patients with aggressive disease[1-13]

EAST HANOVER, N.J., Dec. 6, 2022 -- Novartis today announced results from the RIGHT Choice Phase II trial evaluating Kisqali® (ribociclib) plus endocrine therapy (ET) against combination chemotherapy (CT) in the first-line setting for pre- and perimenopausal patients with aggressive forms of hormone receptor-positive, human epidermal growth factor receptor-2 negative (HR+/HER2–) metastatic breast cancer (MBC), including patients with visceral crisis. CT has remained the preferred option for patients with rapidly progressing disease and visceral crisis, despite the widespread adoption of CDK4/6 inhibitors (CDK4/6i) plus ET as first-line treatment for HR+/HER2- MBC. Kisqali demonstrated a nearly one-year progression-free survival (PFS) benefit in the study, supporting the superiority of Kisqali plus ET for this hard-to-treat patient population. RIGHT Choice is the first randomized study comparing a CDK4/6i plus ET vs. combination CT in aggressive HR+/HER2– MBC; data from this open-label, multi-national trial will be presented as a late-breaker oral presentation at the 2022 San Antonio Breast Cancer Symposium (SABCS) and included in the SABCS press program.

"Younger patients with aggressive disease often show resistance to treatment, resulting in worse prognoses – so it is encouraging to see RIGHT Choice data demonstrating a significant one-year benefit for this patient population when using ribociclib plus endocrine therapy compared to combination chemotherapy. Patients on the ribociclib arm had also lower rates of adverse events, such as diarrhea and fatigue, compared to chemotherapy, which could potentially impact quality of life," said Dr. Yen-Shen Lu, Division Chief of Medical Oncology at Department of Oncology, National Taiwan University Hospital. "With these improvements in outcomes and tolerability, oncologists should consider ribociclib plus ET as a treatment option for patients with aggressive forms of HR+/HER2– MBC, including patients with visceral crisis."

The study enrolled 222 patients with aggressive forms of HR+/HER2– MBC (i.e., with symptomatic visceral metastases, rapid disease progression or markedly symptomatic non-visceral metastases), including more than 50% of patients with visceral crisis as determined by investigators; Kisqali plus ET doubled the median PFS vs. combination CT at 24.0 months compared to 12.3 months (HR=0.54; 95% CI: 0.36-0.79; p=.0007) in

the first-line setting. Median time to treatment failure with Kisqali plus ET was 18.6 months compared to 8.5 months with combination CT (HR=0.45; 95% CI: 0.32-0.63). Furthermore, patients in the Kisqali plus ET arm of the trial reported lower rates of treatment-related serious adverse events (AEs) and lower rates of discontinuation due to treatment-related AEs, compared to patients in the combination CT trial arm. Overall, the Kisqali safety profile was consistent with previously reported data[1].

"Kisqali is a unique CDK4/6 inhibitor with the most robust evidence demonstrating overall survival and quality of life benefits for a wide spectrum of patients, including those with aggressive disease," said Jeff Legos, Executive Vice President, Global Head of Oncology and Hematology at Novartis. "RIGHT Choice adds to the breadth of data that supports Kisqali as the first-line treatment of choice for patients with MBC, including those with visceral crisis."

About Kisqali® (ribociclib)
Kisqali is the only CDK4/6 inhibitor with proven overall survival benefit across all three pivotal Phase III advanced breast cancer trials[2-13] and is recognized by the National Comprehensive Cancer Network (NCCN) guidelines as the only CDK4/6i with overall survival benefit in first-line HR+/HER2- advanced breast cancer[14]. Additionally, Kisqali has the highest rating of any CDK4/6i on the ESMO Magnitude of Clinical Benefit Scale, achieving a score of five out of five for first-line premenopausal patients with HR+/HER2- advanced breast cancer[15]. Further, Kisqali in combination with either letrozole or fulvestrant has uniquely, among other CDK4/6i, received a score of four out of five for postmenopausal patients with HR+/HER2- advanced breast cancer treated in the first line[16].

Kisqali has been approved in more than 95 countries worldwide, including by the United States Food and Drug Administration (FDA) and the European Commission, for the treatment of women with HR+/HER2- advanced or metastatic breast cancer in combination either with an aromatase inhibitor or with fulvestrant as initial endocrine-based therapy or following disease progression on endocrine therapy. Kisqali in combination with fulvestrant is approved as initial endocrine-based therapy or following disease progression on endocrine therapy in men by the FDA[17].

Novartis is committed to continuing to study Kisqali in breast cancer. NATALEE is a large Phase III clinical trial of Kisqali plus endocrine therapy in the adjuvant treatment of HR+/HER2- early breast cancer being conducted in collaboration with Translational Research In Oncology (TRIO)[18]. Additionally, Novartis is collaborating with SOLTI, who is leading HARMONIA, to test whether Kisqali changes tumor biology to enable a better response to endocrine-based therapy compared to Ibrance®* for patients with advanced HR+/HER2-, HER2-enriched subtype[19], and 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 to discover the potentially unique underlying mechanism of action[20].

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

Indications

KISQALI® (ribociclib) is a prescription medicine used to treat adults with hormone receptor-positive, human epidermal growth factor receptor 2-negative (HR+/HER2–) breast cancer that has gotten worse or has spread to other parts of the body (metastatic), in combination with:

- an aromatase inhibitor as the first endocrine-based therapy; or
- fulvestrant as the first endocrine-based therapy or following disease progression on endocrine therapy in

postmenopausal women or in men.

It is not known if KISQALI is safe and effective in children.

Important Safety Information

What is the most important information I should know about KISQALI?

KISQALI may cause serious side effects, including:

Lung problems. KISQALI may cause severe or life-threatening inflammation of the lungs during treatment that may lead to death. Tell your health care provider right away if you have any new or worsening symptoms, including:

- trouble breathing or shortness of breath
- cough with or without mucus
- chest pain

Severe skin reactions. Tell your health care provider or get medical help right away if you get severe rash or rash that keeps getting worse; reddened skin; flu-like symptoms; skin pain/burning; blistering of the lips, eyes, or mouth; or blisters on the skin or skin peeling, with or without fever.

Heart rhythm problems (QT prolongation). KISQALI can cause a heart problem known as QT prolongation. This condition can cause an abnormal heartbeat and may lead to death. Your health care provider should check your heart and do blood tests before and during treatment with KISQALI. Tell your health care provider right away if you have a change in your heartbeat (a fast or irregular heartbeat), or if you feel dizzy or faint.

Liver problems (hepatobiliary toxicity). KISQALI can cause serious liver problems. Your health care provider should do blood tests to check your liver before and during treatment with KISQALI. Tell your health care provider right away if you get any of the following signs and symptoms of liver problems:

- yellowing of your skin or the whites of your eyes (jaundice)
- dark or brown (tea-colored) urine
- feeling very tired
- loss of appetite
- pain on the right side of your stomach area (abdomen)
- bleeding or bruising more easily than normal

Low white blood cell counts (neutropenia). Low white blood cell counts are very common during treatment with KISQALI and may result in infections that may be severe. Your health care provider should check your white blood cell counts before and during treatment with KISQALI. Tell your health care provider right away if you have signs and symptoms of low white blood cell counts or infections such as fever and chills.

Your health care provider may tell you to decrease your dose, temporarily stop, or completely stop taking KISQALI if you develop certain serious side effects during treatment with KISQALI.

What should I tell my health care provider before taking KISQALI?
Before you take KISQALI, tell your health care provider if you:

- have any heart problems, including heart failure, irregular heartbeats, and QT prolongation
- have ever had a heart attack
- have a slow heartbeat (bradycardia)
- have problems with the amount of potassium, calcium, phosphorus, or magnesium in your blood

- have fever, chills, or any other signs or symptoms of infection
- have liver problems
- have any other medical conditions
- are pregnant, or plan to become pregnant. KISQALI can harm your unborn baby
- - If you are able to become pregnant, your health care provider should do a pregnancy test before you start treatment with KISQALI.
  - 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.
  - Talk to your health care provider about birth control methods that may be right for you during this time.
  - If you become pregnant or think you are pregnant, tell your health care provider right away.
- are breastfeeding or plan to breastfeed. It is not known if KISQALI passes into your breast milk. Do not breastfeed during treatment with KISQALI and for at least 3 weeks after the last dose of KISQALI

Tell your health care provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. KISQALI and other medicines may affect each other, causing side effects. Know the medicines you take. Keep a list of them to show your health care provider or pharmacist when you get a new medicine.

What should I avoid while taking KISQALI?
Avoid eating grapefruit and avoid drinking grapefruit juice during treatment with KISQALI since these may increase the amount of KISQALI in your blood.

The most common side effects of KISQALI include:

- decreased white blood cell counts
- decreased red blood cell counts
- abnormal liver function tests
- infections
- nausea
- increased kidney function test
- tiredness
- decreased platelet counts
- diarrhea
- vomiting
- headache
- constipation
- hair loss
- cough
- rash
- back pain
- low blood sugar level

KISQALI may cause fertility problems if you are male and take KISQALI. This may affect your ability to father a child. Talk to your health care provider if this is a concern for you.

Tell your health care provider if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of KISQALI. For more information, ask your health care provider or pharmacist. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see accompanying full Prescribing Information including Patient Information.

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 metastatic breast cancer.

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About Novartis

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation – an affiliate of 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 employs nearly 14,500 people in the United States. For more information, please visit https://www.novartis.us.

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