Novartis Kisqali® received FDA Breakthrough Therapy designation for initial endocrine-based treatment in premenopausal women with HR+/HER2- advanced breast cancer

Jan 03, 2018

- - Designation based on Phase III MONALEESA-7 results demonstrating superior efficacy of Kisqali in combination with oral endocrine therapy compared to oral endocrine therapy in pre- or perimenopausal women who received no prior endocrine therapy for advanced disease1
- - Treatment benefit with Kisqali combination therapy was consistent compared to the overall population regardless of treatment with tamoxifen or aromatase inhibitor endocrine partners, and across patient subgroups1
- - Premenopausal breast cancer is the leading cause of cancer death in women 20-59 years old underscoring the need for new treatment options2
- - This is the second Breakthrough Therapy designation granted to Kisqali for initial endocrine-based treatment in HR+/HER2- advanced or metastatic breast cancer

EAST HANOVER, N.J., Jan. 3, 2018 /PRNewswire/ -- Novartis today announced Kisqali® (ribociclib) received US Food and Drug Administration (FDA) Breakthrough Therapy designation for initial endocrine-based treatment of pre- or perimenopausal women with hormone-receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer in combination with tamoxifen or an aromatase inhibitor.

This Breakthrough Therapy designation is based on positive results of the Phase III MONALEESA-7 trial demonstrating Kisqali in combination with tamoxifen or an aromatase inhibitor as initial endocrine-based therapy significantly prolonged progression-free survival (PFS) compared to endocrine therapy alone (median PFS 23.8 (95% CI: 19.2 months-not reached) vs. 13.0 months (95% CI: 11.0-16.4 months); HR=0.553; 95% CI: 0.441-0.694; p<0.0001)[1]. A total of 672 women ranging from 25-58 years in age were enrolled and randomized in the trial[1]. All treatment combinations also included goserelin[1]. Treatment benefit with Kisqali combination therapy was consistent compared to the overall population regardless of treatment with tamoxifen or aromatase inhibitor endocrine partners, and across predefined patient subgroups[1].

"This Breakthrough Therapy designation reflects the significance and promise of the MONALEESA-7 data presented at SABCS last month," said Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. "Younger women often have distinct treatment goals and needs, and it is important for oncologists to offer effective and well-studied treatment options for their specific disease. We look forward to working with FDA to make this combination therapy available to premenopausal women living with HR+/HER2- advanced breast cancer in the US as soon as possible."

MONALEESA-7 was the first Phase III trial entirely dedicated to evaluating a CDK4/6 inhibitor in premenopausal women with HR+/HER2- advanced breast cancer. The trial evaluated Kisqali in combination with oral endocrine therapies (tamoxifen or an aromatase inhibitor) and goserelin compared to oral endocrine therapy and goserelin in this patient population. In subgroup analyses of median PFS by endocrine partner, Kisqali in combination with tamoxifen and goserelin demonstrated 22.1 months median PFS compared to 11.0 months for tamoxifen and

goserelin alone; Kisqali in combination with an aromatase inhibitor and goserelin demonstrated 27.5 months median PFS compared to 13.8 months for an aromatase inhibitor and goserelin alone[1].

No new safety signals were observed in the MONALEESA-7 trial; adverse events were generally consistent with those observed in MONALEESA-2, identified early and mostly managed through dose interruptions or reductions[1]. Combination treatment with Kisqali was well tolerated with a discontinuation rate due to adverse events of 3.6% compared to 3.0% in patients who received endocrine therapy alone[1]. The most common (≥5%) grade 3/4 adverse events in patients receiving Kisqali combination therapy compared to endocrine therapy alone were neutropenia (60.6% vs. 3.6%) and leukopenia (14.3% vs. 1.2%)[1].

Premenopausal breast cancer is a biologically distinct and more aggressive disease than postmenopausal breast cancer, and it is the leading cause of cancer death in women 20-59 years old[2,3].

According to FDA, Breakthrough Therapy designation is intended to expedite the development and review of potential new medicines that treat serious or life-threatening conditions, if the therapy has demonstrated substantial improvement over an available therapy on at least one clinically significant endpoint. The designation includes all of the Fast Track program features, as well as more intensive FDA guidance on an efficient drug development program[4].

This Breakthrough Therapy designation marks the second for Kisqali. The first Breakthrough Therapy designation for Kisqali was granted in August 2016 based on results of the Phase III MONALEESA-2 trial.

About MONALEESA-7
MONALEESA-7 is a Phase III randomized, double-blind, placebo-controlled trial investigating the efficacy and safety of Kisqali in combination with tamoxifen or a non-steroidal aromatase inhibitor plus goserelin versus tamoxifen or an aromatase inhibitor plus goserelin, in premenopausal or perimenopausal women with HR+/HER2- advanced breast cancer who had not previously received endocrine therapy for advanced disease. More than 670 women ranging from 25-58 years in age were randomized in the MONALEESA-7 trial.

About Kisqali® (ribociclib)
Kisqali is a selective cyclin-dependent kinase inhibitor, a class of drugs that help slow the progression of cancer by inhibiting two proteins called cyclin-dependent kinase 4 and 6 (CDK4/6). These proteins, when over-activated, can enable cancer cells to grow and divide too quickly. Targeting CDK4/6 with enhanced precision may play a role in ensuring that cancer cells do not continue to replicate uncontrollably.

Kisqali was approved by the US Food and Drug Administration (FDA) in March 2017, as a first-line treatment for postmenopausal women with HR+/HER2- advanced or metastatic breast cancer in combination with an aromatase inhibitor based on findings from the pivotal MONALEESA-2 trial. Kisqali is not currently approved for use in premenopausal women.

Kisqali is approved for use in 45 countries around the world, including the United States and European Union member states. Kisqali was developed by the Novartis Institutes for BioMedical Research (NIBR) under a research collaboration with Astex Pharmaceuticals.

About Novartis in Advanced Breast Cancer
For more than 25 years, Novartis has been at the forefront of driving scientific advancements for breast cancer patients and improving clinical practice in collaboration with the global community. With one of the most diverse breast cancer pipelines and the largest number of breast cancer compounds in development, Novartis leads the industry in discovery of new therapies and combinations, especially in HR+ advanced breast cancer, the most common form of the disease.

Kisqali® (ribociclib) Important US Safety Information

Kisqali® (ribociclib) is a prescription medicine used in combination with an aromatase inhibitor as the first hormonal-based therapy to treat women who have gone through menopause 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 a heart problem known as QT prolongation. This condition can cause an abnormal heartbeat and may lead to death. 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 pomegranate or pomegranate juice, and grapefruit or grapefruit juice while taking Kisqali. The most common side effects (incidence ≥20%) of Kisqali when used with letrozole include white blood cell count decreases, nausea, tiredness, diarrhea, hair thinning or hair loss, vomiting, constipation, headache, and back pain. The most common grade 3/4 side effects in the Kisqali + letrozole arm (incidence >2%) were low neutrophils, low leukocytes, abnormal liver function tests, low lymphocytes, 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; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; general economic and industry conditions, including the effects of the persistently weak economic and financial environment in many countries; safety, quality or manufacturing issues, 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
Located in East Hanover, NJ, Novartis Pharmaceuticals Corporation is an affiliate of Novartis which provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 121,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

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