FDA Approves Verzenio® (abemaciclib) as the First and Only CDK4/6 Inhibitor for Certain People with HR+ HER2- High Risk Early Breast Cancer

October 13, 2021

Adding Verzenio to endocrine therapy demonstrated a significant and clinically meaningful reduction in the risk of recurrence in patients with HR+ HER2-, node-positive, high risk early breast cancer and a Ki-67 score of ≥20%

Verzenio is the first addition to adjuvant endocrine therapy approved by the FDA in nearly two decades for the treatment of HR+ HER2- early breast cancer

Updated data supporting this new indication will be featured in the October 14 European Society for Medical Oncology (ESMO) Virtual Plenary

INDIANAPOLIS, Oct. 13, 2021 /PRNewswire/ -- The U.S. Food and Drug Administration (FDA) has approved Eli Lilly and Company's (NYSE: LLY) Verzenio® (abemaciclib), in combination with endocrine therapy (tamoxifen or an aromatase inhibitor), for the adjuvant treatment of adult patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), node-positive, early breast cancer (EBC) at high risk of recurrence and a Ki-67 score of ≥20% as determined by an FDA-approved test. Ki-67 is a marker of cellular proliferation. Verzenio is the first and only CDK4/6 inhibitor approved for this patient population.

"Over time, the collective results of the Verzenio clinical development program have demonstrated a differentiated CDK4/6 inhibitor profile, and the landmark data from the monarchE trial that supported this new indication in HR+ HER2- early breast cancer represent another important step forward for people who are in need of new treatment options," said Jacob Van Naarden, senior vice president, CEO of Loxo Oncology at Lilly and president, Lilly Oncology. "We are pleased with this initial approval in the adjuvant setting and as these data continue to mature, we look forward to further opportunities to work with health authorities to expand the use of Verzenio in this setting."

The Verzenio Phase 3 monarchE trial is a randomized (1:1), open-label, two cohort, multicenter study in adult women and men with HR+ HER2-, node-positive, resected EBC with clinical and pathological features consistent with a high risk of disease recurrence. In the trial, patients were randomized to receive two years of Verzenio 150 mg twice daily plus physician's choice of standard endocrine therapy, or standard endocrine therapy alone. Patients in both treatment arms were instructed to continue to receive adjuvant endocrine therapy for up to 5-10 years as recommended by their clinician. The primary endpoint of the study is invasive disease-free survival (IDFS) and was met at a pre-specified interim analysis in the intent-to-treat (ITT) population, with a statistically significant improvement in IDFS for patients treated with Verzenio plus ET compared to those treated with ET alone. Consistent with expert guidelines, IDFS was defined as the length of time before breast cancer comes back, any new cancer develops, or death.

Having achieved the study's primary endpoint in the entire enrolled population, a pre-specified analysis of IDFS was also conducted in patients with high-risk clinical and pathological factors and a Ki-67 score ≥20%. This subgroup analysis (N=2,003) included patients with ≥4 positive axillary lymph nodes (ALN), or 1-3 positive ALN with either Grade 3 disease and/or tumor size ≥5 cm, and whose tumors had a Ki-67 score of ≥20%. There was also a statistically significant improvement in IDFS for this pre-specified subgroup of patients receiving Verzenio plus ET compared to those who received ET alone (HR=0.643, 95% CI: 0.475, 0.872, p=0.0042).[1,3]

This approval is based on efficacy results from an analysis of this subgroup with additional follow-up, conducted post-hoc. In this analysis, Verzenio given in combination with ET continued to demonstrate a clinically meaningful benefit, with a 37 percent decrease in the risk of breast cancer recurrence or death compared to standard adjuvant ET alone for patients with high risk clinical and pathological features and a Ki-67 score ≥20% (HR: 0.626 [95% CI: 0.49-0.80]), and an absolute benefit in IDFS event rate of 7.1 percent at three years. The number of IDFS events at the time of this analysis was 104 with Verzenio plus ET compared to 158 with ET alone. Overall survival data were not mature and additional follow up is ongoing.

Adverse reactions from monarchE were consistent with the known safety profile for Verzenio.[2] Safety and tolerability were evaluated in 5,591 patients. The most common adverse reactions reported (≥10%) in the Verzenio plus ET (tamoxifen or an aromatase inhibitor) arm, and ≥2% higher than the ET arm alone, were diarrhea, infections, fatigue, nausea, headache, vomiting, stomatitis, decreased appetite, dizziness, rash, and alopecia.[3] The most common laboratory abnormalities (all grades ≥10%) were creatinine increased, white blood cell count decreased, neutrophil count decreased, anemia, lymphocyte count decreased, platelet count decreased, ALT increased, AST increased, and hypokalemia.

This FDA approval builds on the established body of evidence for Verzenio, which is already approved for the treatment of certain types of HR+ HER2- advanced or metastatic breast cancer. Concurrent with this approval, the FDA has expanded the use of Verzenio in all indications, when given in combination with endocrine therapy, to include men. Verzenio is available in tablet strengths of 200 mg, 150 mg, 100 mg, and 50 mg.

"The design and results of the monarchE study are practice-changing and represent the first advancement in adjuvant treatment of HR+ HER2- breast cancer in a very long time," said Sara M. Tolaney, MD, MPH, Harvard Medical School, Dana-Farber Cancer Institute, and investigator on the monarchE study. "This FDA approval for Verzenio in combination with endocrine therapy in the early breast cancer setting has the potential to become a new standard of care for this population. We are encouraged by the marked reduction in the risk of recurrence even beyond the two-year treatment period in these patients, and I'm grateful to be able to offer this as a treatment option to my patients."

"Women and men living with high risk HR+ HER2- early breast cancer want to do all they can to reduce the risk of the disease coming back, with the hope of living free of cancer. The approval of Verzenio provides a new treatment option to help them do just that," said Jean Sachs, chief executive officer, Living Beyond Breast Cancer. "This approval brings new optimism to the breast cancer community."

Data supporting this approval will be presented at the October 14 European Society for Medical Oncology (ESMO) Virtual Plenary.

The labelling for Verzenio contains warnings and precautions for diarrhea, neutropenia, interstitial lung disease (ILD/pneumonitis), hepatotoxicity, venous thromboembolism, and embryo-fetal toxicity. Instruct patients at the first sign of loose stools to initiate antidiarrheal therapy, increase oral fluids, and notify their healthcare provider. Perform complete blood counts and liver function tests prior to the start of Verzenio treatment, every two weeks for the first two months, monthly for the next two months and as clinically indicated. Based on results, Verzenio may require dose modification. Monitor patients for signs and symptoms of thrombosis and pulmonary embolism and treat as medically appropriate. Advise patients of potential risk to a fetus and to use effective contraception.

See Important Safety Information below and full Prescribing Information for additional information.

Click here to view the early breast cancer infographic.

Click here to view the monarchE clinical trial infographic.

Click to view the Verzenio product photos: 50 mg, 100 mg, 150 mg, 200 mg.

Click here to view the Verzenio logo.

About the monarchE Study
monarchE is a global, randomized, open-label, two cohort, multicenter Phase 3 study in adult women and men with HR+ HER2-, node-positive resected EBC with clinical and pathological features consistent with a high risk of disease recurrence. A total of 5,637 patients were randomized (1:1) to receive two years of Verzenio 150 mg twice daily plus physician's choice of standard endocrine therapy, or standard endocrine therapy alone. Patients in both treatment arms were instructed to continue to receive adjuvant endocrine therapy for up to 5-10 years as recommended by their clinician. Cohort 1 enrolled patients with ≥4 positive axillary lymph nodes (ALN), or 1-3 positive ALN and either Grade 3 disease or tumor size ≥5 cm. Cohort 2 enrolled patients with 1-3 positive ALN and centrally determined Ki-67 score of ≥20%. The primary endpoint was IDFS in the ITT population (Cohorts 1 & 2). Secondary endpoints were IDFS in patients with high Ki-67 score (in the ITT population and in the Cohort 1 population), DRFS, overall survival, and safety.[2,3]

About Early Breast Cancer and Risk of Recurrence
It is estimated that 90 percent of all breast cancers are detected at an early stage. Although the prognosis for HR+ HER2- EBC is generally positive, 20 percent of patients will experience recurrence potentially to incurable metastatic disease.[4] Risk of recurrence is greatest within the initial two to three years post-diagnosis, particularly in patients with node-positive, high risk EBC.[5] Factors associated with high risk of recurrence include: positive nodal status, large tumor size (≥5 cm), high tumor grade (Grade 3), and high rate of cellular proliferation [Ki-67 score (≥20%)].[3]

Node-positive means that cancer cells from the tumor in the breast have been found in the lymph nodes in the armpit area. Although the breast cancer is removed through surgery, the presence of cancer cells in the lymph nodes signifies that there is a higher chance of the cancer returning and spreading.

About Breast Cancer
Breast cancer has now surpassed lung cancer as the most commonly diagnosed cancer worldwide, according to GLOBOCAN. The estimated 2.3 million new cases indicate that 1 in every 8 cancers diagnosed in 2020 is breast cancer. With approximately 685,000 deaths in 2020, breast cancer is the fifth-leading cause of cancer death worldwide.[6] In the U.S., it is estimated that there will be 281,550 new cases of breast cancer in 2021.[7]

Approximately 70 percent of all breast cancers are of the HR+ HER2- subtype.[7]

About Verzenio® (abemaciclib)
Verzenio® abemaciclib is a targeted treatment known as a CDK4/6 inhibitor. Verzenio is a non-chemotherapy oral tablet.

Verzenio works inside the cell to block CDK4/6 activity and help stop the growth of cancer cells, so they may eventually die (based on preclinical studies).* Cyclin-dependent kinases (CDK)4/6 are activated by binding to D-cyclins. In estrogen receptor-positive (ER+) breast cancer cell lines, cyclin D1 and CDK4/6 promote phosphorylation of the retinoblastoma protein (Rb), cell cycle progression, and cell proliferation.

In vitro, continuous exposure to Verzenio inhibited Rb phosphorylation and blocked progression from G1 to S phase of the cell cycle, resulting in senescence and apoptosis (cell death). Preclinically, Verzenio dosed daily without interruption resulted in reduction of tumor size. Inhibiting CDK4/6 in healthy cells can result in side effects, some of which may be serious. Clinical evidence also suggests that Verzenio crosses the blood-brain barrier. In patients with advanced cancer, including breast cancer, concentrations of Verzenio and its active metabolites (M2 and M20) in cerebrospinal fluid are comparable to unbound plasma concentrations.

Verzenio is Lilly's first solid oral dosage form to be made using a faster, more efficient process known as continuous manufacturing. Continuous manufacturing is a new and advanced type of manufacturing within the pharmaceutical industry, and Lilly is one of the first companies to use this technology.

INDICATIONS FOR VERZENIO

Verzenio® (abemaciclib) in combination with endocrine therapy (ET) is indicated for the adjuvant treatment of adult patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), node-positive, early breast cancer (EBC) at high risk of recurrence and a Ki-67 score of ≥20% as determined by an FDA-approved test.

Verzenio is indicated for the treatment of HR+ HER2- advanced or metastatic breast cancer:

- in combination with an aromatase inhibitor for postmenopausal women, and men, as initial endocrine-based therapy
- in combination with fulvestrant for adult patients with disease progression following endocrine therapy
- as a single agent for adult patients with disease progression following endocrine therapy and prior chemotherapy in the

metastatic setting

IMPORTANT SAFETY INFORMATION FOR VERZENIO (abemaciclib)

Severe **diarrhea** associated with dehydration and infection occurred in patients treated with Verzenio. Across four clinical trials in 3691 patients**,** diarrhea occurred in 81 to 90% of patients who received Verzenio. Grade 3 diarrhea occurred in 8 to 20% of patients receiving Verzenio. Most patients experienced diarrhea during the first month of Verzenio treatment. The median time to onset of the first diarrhea event ranged from 6 to 8 days; and the median duration of Grade 2 and Grade 3 diarrhea ranged from 6 to 11 days and 5 to 8 days, respectively. Across trials, 19 to 26% of patients with diarrhea required a Verzenio dose interruption and 13 to 23% required a dose reduction.

Instruct patients to start antidiarrheal therapy, such as loperamide, at the first sign of loose stools, increase oral fluids, and notify their healthcare provider for further instructions and appropriate follow-up. For Grade 3 or 4 diarrhea, or diarrhea that requires hospitalization, discontinue Verzenio until toxicity resolves to ≤Grade 1, and then resume Verzenio at the next lower dose.

Neutropenia, including febrile neutropenia and fatal neutropenic sepsis, occurred in patients treated with Verzenio. Across four clinical trials in 3691 patients, neutropenia occurred in 37 to 46% of patients receiving Verzenio. A Grade ≥3 decrease in neutrophil count (based on laboratory findings) occurred in 19 to 32% of patients receiving Verzenio. Across trials, the median time to first episode of Grade ≥3 neutropenia ranged from 29 to 33 days, and the median duration of Grade ≥3 neutropenia ranged from 11 to 16 days. Febrile neutropenia has been reported in <1% of patients exposed to Verzenio across trials. Two deaths due to neutropenic sepsis were observed in MONARCH 2. Inform patients to promptly report any episodes of fever to their healthcare provider.

Monitor complete blood counts prior to the start of Verzenio therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

Severe, life-threatening, or fatal **interstitial lung disease (ILD) or pneumonitis** can occur in patients treated with Verzenio and other CDK4/6 inhibitors. In Verzenio-treated patients in EBC (monarchE), 3% of patients experienced ILD or pneumonitis of any grade: 0.4% were Grade 3 or 4 and there was one fatality (0.1%). In Verzenio-treated patients in MBC (MONARCH 1, MONARCH 2, MONARCH 3), 3.3% of Verzenio-treated patients had ILD or pneumonitis of any grade: 0.6% had Grade 3 or 4, and 0.4% had fatal outcomes. Additional cases of ILD or pneumonitis have been observed in the postmarketing setting, with fatalities reported.

Monitor patients for pulmonary symptoms indicative of ILD or pneumonitis. Symptoms may include hypoxia, cough, dyspnea, or interstitial infiltrates on radiologic exams. Infectious, neoplastic, and other causes for such symptoms should be excluded by means of appropriate investigations. Dose interruption or dose reduction is recommended in patients who develop persistent or recurrent Grade 2 ILD or pneumonitis. Permanently discontinue Verzenio in all patients with Grade 3 or 4 ILD or pneumonitis.

Grade ≥3 increases in alanine aminotransferase (ALT) (2 to 6%) and **aspartate aminotransferase (AST)** (2 to 3%) were reported in patients receiving Verzenio. Across three clinical trials in 3559 patients (monarchE, MONARCH 2, MONARCH 3), the median time to onset of Grade ≥3 ALT increases ranged from 57 to 87 days and the median time to resolution to Grade <3 was 13 to 14 days. The median time to onset of Grade ≥3 AST increases ranged from 71 to 185 days and the median time to resolution to Grade <3 ranged from 11 to 15 days.

Monitor liver function tests (LFTs) prior to the start of Verzenio therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Dose interruption, dose reduction, dose discontinuation, or delay in starting treatment cycles is recommended for patients who develop persistent or recurrent Grade 2, or any Grade 3 or 4 hepatic transaminase elevation.

Venous thromboembolic events (VTE) were reported in 2 to 5% of patients across three clinical trials in 3559 patients treated with Verzenio (monarchE, MONARCH 2, MONARCH 3). VTE included deep vein thrombosis, pulmonary embolism, pelvic venous thrombosis, cerebral venous sinus thrombosis, subclavian and axillary vein thrombosis, and inferior vena cava thrombosis. In clinical trials, deaths due to VTE have been reported in patients treated with Verzenio.

Verzenio has not been studied in patients with early breast cancer who had a history of VTE. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate. Dose interruption is recommended for EBC patients with any grade VTE and for MBC patients with a Grade 3 or 4 VTE.

Verzenio can cause **fetal harm** when administered to a pregnant woman, based on findings from animal studies and the mechanism of action. In animal reproduction studies, administration of abemaciclib to pregnant rats during the period of organogenesis caused teratogenicity and decreased fetal weight at maternal exposures that were similar to the human clinical exposure based on area under the curve (AUC) at the maximum recommended human dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Verzenio and for 3 weeks after the last dose. Based on findings in animals, Verzenio may impair fertility in males of reproductive potential. There are no data on the presence of Verzenio in human milk or its effects on the breastfed child or on milk production. Advise lactating women not to breastfeed during Verzenio treatment and for at least 3 weeks after the last dose because of the potential for serious adverse reactions in breastfed infants.

The **most common adverse reactions (all grades**, **≥10%)** observed in **monarchE for Verzenio plus tamoxifen or an aromatase inhibitor vs tamoxifen or an aromatase inhibitor**, **with a difference between arms of ≥2%,** were diarrhea (84% vs 9%), infections (51% vs 39%), neutropenia (46% vs 6%), fatigue (41% vs 18%), leukopenia (38% vs 7%), nausea (30% vs 9%), anemia (24% vs 4%), headache (20% vs 15%), vomiting (18% vs 4.6%), stomatitis (14% vs 5%), lymphopenia (14% vs 3%), thrombocytopenia (13% vs 2%), decreased appetite (12% vs 2.4%), ALT increased (12% vs 6%), AST increased (12% vs 5%), dizziness (11% vs 7%), rash (11% vs 4.5%), and alopecia (11% vs 2.7 %).

The **most frequently reported ≥5% Grade 3 or 4 adverse reaction** that occurred in the Verzenio arm vs the tamoxifen or an aromatase inhibitor arm of monarchE were neutropenia (19.6% vs 1%), leukopenia (11% vs <1%), diarrhea (8% vs 0.2%), and lymphopenia (5% vs <1%).

Lab abnormalities (all grades; Grade 3 or 4) for **monarchE in ≥10% for Verzenio plus tamoxifen or an aromatase inhibitor with a difference between arms of ≥2%** were increased serum creatinine (99% vs 91%; .5% vs <.1%), decreased white blood cells (89% vs 28%; 19.1% vs 1.1%), decreased neutrophil count (84% vs 23%; 18.7% vs 1.9%), anemia (68% vs 17%; 1% vs .1%), decreased lymphocyte count (59% vs 24%; 13.2 % vs

2.5%), decreased platelet count (37% vs 10%; .9% vs .2%), increased ALT (37% vs 24%; 2.6% vs 1.2%), increased AST (31% vs 18%; 1.6% vs .9%), and hypokalemia (11% vs 3.8%; 1.3% vs 0.2%).

The **most common adverse reactions (all grades**, **≥10%)** observed in **MONARCH 3 for Verzenio plus anastrozole or letrozole vs anastrozole or letrozole, with a difference between arms of ≥2%,** were diarrhea (81% vs 30%), fatigue (40% vs 32%), neutropenia (41% vs 2%), infections (39% vs 29%), nausea (39% vs 20%), abdominal pain (29% vs 12%), vomiting (28% vs 12%), anemia (28% vs 5%), alopecia (27% vs 11%), decreased appetite (24% vs 9%), leukopenia (21% vs 2%), creatinine increased (19% vs 4%), constipation (16% vs 12%), ALT increased (16% vs 7%), AST increased (15% vs 7%), rash (14% vs 5%), pruritus (13% vs 9%), cough (13% vs 9%), dyspnea (12% vs 6%), dizziness (11% vs 9%), weight decreased (10% vs 3.1%), influenza-like illness (10% vs 8%), and thrombocytopenia (10% vs 2%).

The **most frequently reported ≥5% Grade 3 or 4 adverse reactions** that occurred in the Verzenio arm vs the placebo arm of **MONARCH 3** were neutropenia (22% vs 1%), diarrhea (9% vs 1.2%), leukopenia (7% vs <1%)), increased ALT (6% vs 2%), and anemia (6% vs 1%).

Lab abnormalities (all grades; Grade 3 or 4) for **MONARCH 3 in ≥10% for Verzenio plus anastrozole or letrozole with a difference between arms of ≥2%** were increased serum creatinine (98% vs 84%; 2.2% vs 0%), decreased white blood cells (82% vs 27%; 13% vs 0.6%), anemia (82% vs 28%; 1.6% vs 0%), decreased neutrophil count (80% vs 21%; 21.9% vs 2.6%), decreased lymphocyte count (53% vs 26%; 7.6% vs 1.9%), decreased platelet count (36% vs 12%; 1.9% vs 0.6%), increased ALT (48% vs 25%; 6.6% vs 1.9%), and increased AST (37% vs 23%; 3.8% vs 0.6%).

The **most common adverse reactions (all grades, ≥10%)** observed in **MONARCH 2 for Verzenio plus fulvestrant vs fulvestrant, with a difference between arms of ≥2%,** were diarrhea (86% vs 25%), neutropenia (46% vs 4%), fatigue (46% vs 32%), nausea (45% vs 23%), infections (43% vs 25%), abdominal pain (35% vs 16%), anemia (29% vs 4%), leukopenia (28% vs 2%), decreased appetite (27% vs 12%), vomiting (26% vs 10%), headache (20% vs 15%), dysgeusia (18% vs 2.7%), thrombocytopenia (16% vs 3%), alopecia (16% vs 1.8%), stomatitis (15% vs 10%), ALT increased (13% vs 5%), pruritus (13% vs 6%), cough (13% vs 11%), dizziness (12% vs 6%), AST increased (12% vs 7%), peripheral edema (12% vs 7%), creatinine increased (12% vs <1%), rash (11% vs 4.5%), pyrexia (11% vs 6%), and weight decreased (10% vs 2.2%).

The **most frequently reported ≥5% Grade 3 or 4 adverse reactions** that occurred in the Verzenio arm vs the placebo arm of **MONARCH 2** were neutropenia (25% vs 1%), diarrhea (13% vs 0.4%), leukopenia (9% vs 0%), anemia (7% vs 1%), and infections (5.7% vs 3.5%).

Lab abnormalities (all grades; Grade 3 or 4) for **MONARCH 2 in ≥10% for Verzenio plus fulvestrant with a difference between arms of ≥2%** were increased serum creatinine (98% vs 74%; 1.2% vs 0%), decreased white blood cells (90% vs 33%; 23.7% vs .9%), decreased neutrophil count (87% vs 30%; 32.5% vs 4.2%), anemia (84% vs 34%; 2.6% vs .5%), decreased lymphocyte count (63% vs 32%; 12.2% vs 1.8%), decreased platelet count (53% vs 15%; 2.1% vs 0%), increased ALT (41% vs 32%; 4.6% vs 1.4%), and increased AST (37% vs 25%; 3.9% vs 4.2%).

The **most common adverse reactions (all grades**, **≥10%)** observed in **MONARCH 1** with Verzenio were diarrhea (90%), fatigue (65%), nausea (64%), decreased appetite (45%), abdominal pain (39%), neutropenia (37%), vomiting (35%), infections (31%), anemia (25%), thrombocytopenia (20%), headache (20%), cough (19%), constipation (17%), leukopenia (17%), arthralgia (15%), dry mouth (14%), weight decreased (14%), stomatitis (14%), creatinine increased (13%), alopecia (12%), dysgeusia (12%), pyrexia (11%), dizziness (11%), and dehydration (10%).

The **most frequently reported ≥5% Grade 3 or 4 adverse reactions** from **MONARCH 1** with Verzenio were diarrhea (20%), neutropenia (24%), fatigue (13%), and leukopenia (5%).

Lab abnormalities (all grades; Grade 3 or 4) for MONARCH 1 with Verzenio were increased serum creatinine (99%; .8%), decreased white blood cells (91%; 28%), decreased neutrophil count (88%; 26.6%), anemia (69%; 0%), decreased lymphocyte count (42%; 13.8%), decreased platelet count (41%; 2.3%), increased ALT (31%; 3.1%), and increased AST (30%; 3.8%).

Strong and moderate CYP3A inhibitors increased the exposure of abemaciclib plus its active metabolites to a clinically meaningful extent and may lead to increased toxicity. Avoid concomitant use of ketoconazole. Ketoconazole is predicted to increase the AUC of abemaciclib by up to 16-fold. In patients with recommended starting doses of 200 mg twice daily or 150 mg twice daily, reduce the Verzenio dose to 100 mg twice daily with concomitant use of strong CYP3A inhibitors other than ketoconazole. In patients who have had a dose reduction to 100 mg twice daily due to adverse reactions, further reduce the Verzenio dose to 50 mg twice daily with concomitant use of strong CYP3A inhibitors. If a patient taking Verzenio discontinues a strong CYP3A inhibitor, increase the Verzenio dose (after 3 to 5 half-lives of the inhibitor) to the dose that was used before starting the inhibitor. With concomitant use of moderate CYP3A inhibitors, monitor for adverse reactions and consider reducing the Verzenio dose in 50 mg decrements. Patients should avoid grapefruit products.

Avoid concomitant use of strong or moderate CYP3A inducers and consider alternative agents. Coadministration of strong or moderate CYP3A inducers decreased the plasma concentrations of abemaciclib plus its active metabolites and may lead to reduced activity.

With severe hepatic impairment (Child-Pugh C), reduce the Verzenio dosing frequency to once daily. The pharmacokinetics of Verzenio in patients with **severe renal impairment** (CLcr <30 mL/min), end stage renal disease, or in patients on dialysis **is unknown.** No dosage adjustments are necessary in patients with mild or moderate hepatic (Child-Pugh A or B) and/or renal impairment (CLcr ≥30-89 mL/min).

Please see full Prescribing Information for Verzenio.

AL HCP ISI 12OCT2021

About Lilly Oncology
For more than 50 years, Lilly has been dedicated to delivering life-changing medicines and support to people living with cancer and those who care for them. Lilly is determined to build on this heritage and continue making life better for all those affected by cancer around the world. To learn more about Lilly's commitment to people with cancer, please visit www.LillyOncology.com.

About Eli Lilly and Company
Lilly is a global health care leader that unites caring with discovery to create medicines that make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at lilly.com and lilly.com/newsroom. P-LLY

© Lilly USA, LLC 2021. ALL RIGHTS RESERVED.

Verzenio® is a trademark owned by or licensed to Eli Lilly and Company, its subsidiaries, or affiliates.

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Verzenio (abemaciclib) as a treatment for patients with early breast cancer and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date or that Verzenio will receive additional regulatory approvals or be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

[1] Harbeck et al. High Ki-67 as a Biomarker for Identifying Patients with High Risk Early Breast Cancer Treated in monarchE PD2-01, SABCS 2020

[2] Johnston SRD, Harbeck N, Hegg R, et al; monarchE Committee Members and Investigators. Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR+, HER2-, node-positive, high-risk, early breast cancer (monarchE) [published online ahead of print, September 20, 2020]. *J Clin Oncol*. doi:10.1200/JCO.20.02514.

[3] Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company.

[4] Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005;365(9472):1687-1717. doi:10.1016/S0140-6736(05)66544-0.

[5] Cheng L, Swartz MD, Zhao H, et al. Hazard of recurrence among women after primary breast cancer treatment--a 10-year follow-up using data from SEER-Medicare. *Cancer Epidemiol Biomarkers Prev*. 2012;21:800-809.

[6] Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71(3):209-249

[7] National Cancer Institute, SEER. Cancer Stat Facts: Female Breast Cancer. https://seer.cancer.gov/statfacts/html/breast.html. Accessed September 14, 2021.

Refer to:Tracy Henrikson, tracy.henrikson@lilly.com; 609-454-7116 (Lilly): media
Kevin Hern, hern_kevin_r@lilly.com; 317-277-1838 (Lilly): investors

View original content to download multimedia:https://www.prnewswire.com/news-releases/fda-approves-verzenio-abemaciclib-as-the-first-and-only-cdk46-inhibitor-for-certain-people-with-hr-her2--high-risk-early-breast-cancer-301398910.html

SOURCE Eli Lilly and Company