Landmark 5-Year monarchE Outcome Data Demonstrate Verzenio® (abemaciclib)'s Long-Term Impact on Cancer Recurrence in High-Risk Early Breast Cancer

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Impact of two years of adjuvant Verzenio treatment is observed well beyond the treatment period, reducing the risk of long-term recurrence by 32% and improving invasive disease-free survival by 7.6% at 5 years

These data reinforce two years of Verzenio plus endocrine therapy as the standard of care for these patients in this curative setting

Use of Verzenio as a treatment option in this setting is supported by an NCCN® Category 1 designation

INDIANAPOLIS, Oct. 20, 2023 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced five-year outcomes from a pre-planned analysis of the Phase 3 monarchE study evaluating two years of adjuvant Verzenio® (abemaciclib) in combination with endocrine therapy (ET) compared with ET alone in patients with HR+, HER2-, node-positive early breast cancer (EBC) at a high risk of recurrence. These data were shared in a late-breaking presentation at the 2023 European Society for Medical Oncology (ESMO) Congress.

"The five-year time period is an established landmark for adjuvant breast cancer clinical trials and is an important milestone for patients and physicians in this curative setting," said Nadia Harbeck, M.D., Ph.D, Director of the Breast Center and Chair for Conservative Oncology, Department of OB&GYN, LMU University Hospital (Munich, Germany), monarchE investigator, and presenter of the results at the 2023 ESMO Congress. "These five-year monarchE data clearly demonstrate a carryover effect beyond the completion of two years of abemaciclib treatment, with the IDFS and DRFS curves continuing to separate, reinforcing confidence in the role of abemaciclib added to endocrine therapy in the adjuvant setting for those with a high risk of recurrence."

The data presented include results from a pre-specified analysis reflecting a median follow-up of 4.5 years. All patients have completed the Verzenio treatment course, with more than 80% of patients having been followed for at least two years after completion. In the intent-to-treat (ITT) population, the risk of developing invasive disease was reduced by 32% (HR=0.680, 95% CI: 0.599, 0.772; nominal p<0.001). The absolute increase in invasive disease-free survival (IDFS) and distant relapse-free survival (DRFS) continued to deepen in magnitude at five years, to 7.6% and 6.7%, respectively, reflecting improvements from the two-, three-, and four-year rates. With the majority of the IDFS events being DRFS events, the DRFS benefit was also maintained with Verzenio reducing the risk of developing distant recurrence or death by 32.5% (HR=0.675, 95% CI: 0.588, 0.774; nominal p<0.001). In this five-year outcome analysis, the Kaplan-Meier curves continued to separate, confirming a sustained benefit beyond the two-year treatment period. IDFS and DRFS results for Cohort 1 were consistent with those for the ITT population. As reported previously, IDFS and DRFS benefit was seen across subgroups.

While overall survival (OS) data remain immature, fewer deaths were observed in the Verzenio arm (208 [7.4%] of 2,808 patients) compared to the control arm (234 [8.3%] of 2,829 patients) (HR=0.903, 95% CI: 0.749, 1.088; p = 0.284). Nearly twice as many patients receiving ET alone (n=269) developed and are living with metastatic disease compared to those receiving Verzenio (n=138).

There were no new safety findings, and overall results are consistent with the well-established safety profile for Verzenio. The most frequent adverse events (AEs) were diarrhea, neutropenia, and fatigue in the Verzenio-plus-ET arm, and arthralgia, hot flush, and fatigue in the ET-alone arm. The most common Grade 3-4 AEs were neutropenia, leucopenia, and diarrhea in the Verzenio arm and arthralgia, neutropenia, and ALT increased in the control arm.

Additionally, Lilly presented analyses showing that dose reductions did not compromise the efficacy of Verzenio in monarchE, which is consistent with published results of Verzenio in the metastatic setting. Dose reductions, when needed, can be an effective strategy in managing side effects and support the goal of maximizing treatment adherence for the two years of Verzenio treatment in high-risk early breast cancer.

"The mature recurrence efficacy benefit demonstrated in monarchE, achieved with a two-year treatment duration, reinforce Verzenio as the standard of care in this curative setting, where Verzenio is the only CDK4/6 inhibitor approved to treat people with HR+, HER2-, node-positive, high risk early breast cancer," said David Hyman, M.D., chief medical officer, Lilly. "Reaching the 5-year outcomes benchmark with adjuvant Verzenio should provide further confidence for those patients where treatment intensification is needed to help them achieve their goal of remaining cancer-free."

Updates from the Imlunestrant Clinical Development Program

In a separate mini oral presentation on Sunday, October 22, Lilly will share data from the Phase 1a/b EMBER study, evaluating imlunestrant – an investigational, oral selective estrogen receptor degrader (SERD) – as a monotherapy and in combination with everolimus or alpelisib for people with estrogen receptor positive (ER+), HER2- advanced breast cancer. These are the first clinical data on these combinations. Results demonstrated that single agent imlunestrant had a clinical benefit rate of 42% and this increased to 62% when given in combination with everolimus or alpelisib (both approved agents in the second-line setting). Side effects were mostly low grade for single agent imlunestrant, and the combination regimens had a similar side effect profile to everolimus or alpelisib given in combination with standard endocrine therapy.

About the monarchE Study

monarchE was a global, randomized, open-label, two cohort, multicenter Phase 3 clinical trial that enrolled 5,637 adults with HR+, HER2-, node-positive EBC at high risk of recurrence. The study enrolled patients across more than 600 sites in 38 countries and is the only adjuvant study designed to investigate a CDK4/6 inhibitor specifically in a node-positive, high risk EBC population. To be enrolled in Cohort 1 (n=5,120), which is the FDA-approved population, patients had to have 4+ positive nodes or 1-3 positive nodes and at least one of the following: tumors that were ≥5 cm or Grade 3. Patients enrolled in Cohort 2 could not have met the eligibility criteria for Cohort 1. To be enrolled in Cohort 2 (n=517), patients had to have

1-3 positive nodes and Ki-67 score ≥20%. Patients in each cohort were randomized 1:1 to receive either Verzenio 150 mg twice daily plus standard-of-care adjuvant ET (Cohort 1, n=2,555; Cohort 2, n=253) or standard-of-care adjuvant ET alone (Cohort 1, n=2,565; Cohort 2, n=264) for 2 years. ET continued for at least 5 years if deemed medically appropriate. The primary endpoint was IDFS. Consistent with expert guidelines, IDFS was defined as the length of time before breast cancer comes back, any new cancer develops, or death.

About Early Breast Cancer and Risk of Recurrence

It is estimated that 90% of all breast cancers are detected at an early stage.[1] Approximately 70% of all breast cancer cases are the HR+, HER2- subtype.[2] Although the prognosis for HR+, HER2- EBC is generally favorable, high risk patients are three times more likely than those with low risk characteristics to experience recurrence – with the majority being incurable metastatic disease.[3] These patients have an increased risk of recurrence during the first two years of endocrine therapy.

Factors associated with high risk of recurrence in HR+, HER2- early breast cancer include: positive nodal status, the number of positive nodes, large tumor size (≥5 cm), and high tumor grade (Grade 3). Node-positive means that cancer cells from the tumor in the breast have been found in the lymph nodes near the breast. Although breast cancer is removed through surgery, the presence of cancer cells in the lymph nodes signifies that there is a higher chance of developing recurrence and distant metastatic disease.

About Breast Cancer

Breast cancer has 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.[4] In the U.S., it is estimated that there will be more than 300,000 new cases of breast cancer diagnosed in 2023. Breast cancer is the second leading cause of cancer death in women in the U.S.[5]

About Verzenio® (abemaciclib)

Verzenio® (abemaciclib) is approved to treat people with certain HR+, HER2- breast cancers in the adjuvant and advanced or metastatic setting. Verzenio is the first and only CDK4/6 inhibitor approved to treat node-positive, high risk early breast cancer (EBC) patients.[6] The National Comprehensive Cancer Network® (NCCN®) recommends consideration of two years of abemaciclib (Verzenio) added to endocrine therapy as a Category 1 treatment option in the adjuvant setting.[7] NCCN® also includes Verzenio plus endocrine therapy as a preferred treatment option for metastatic breast cancer.[7]

The collective results of Lilly's clinical development program continue to differentiate Verzenio as a CDK4/6 inhibitor. In high risk EBC, Verzenio has shown a persistent and deepening benefit beyond the two-year treatment period in the monarchE trial, the only adjuvant study designed to investigate a CDK4/6 inhibitor specifically in a node-positive, high risk EBC population.[8] In metastatic breast cancer, Verzenio has demonstrated statistically significant overall survival in the Phase 3 MONARCH 2 study.[9] Verzenio has shown a consistent and generally manageable safety profile across clinical trials. In addition to breast cancer, Lilly is studying Verzenio in different forms of difficult-to-treat prostate cancer.

Verzenio is an oral tablet taken twice daily and available in strengths of 50 mg, 100 mg, 150 mg, and 200 mg. Discovered and developed by Lilly researchers, Verzenio was first approved in 2017 and is currently authorized for use in more than 90 counties around the world. For full details on indicated uses of Verzenio in HR+, HER2- breast cancer, please see full Prescribing Information, available at www.Verzenio.com.

INDICATIONS FOR VERZENIO®

VERZENIO® is a kinase inhibitor indicated:

- in combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence.
- in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.
- in combination with fulvestrant for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease progression following endocrine therapy.
- as monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer 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 and Patient Information for Verzenio.

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About Imlunestrant
Imlunestrant (LY3484356) is an investigational, next-generation oral selective estrogen receptor degrader (SERD) designed to deliver continuous ER target inhibition, including ESR1-mutant breast cancer. The estrogen receptor (ER) is the key therapeutic target for patients with ER+, HER2- breast cancer. Novel degraders of ER may overcome endocrine therapy resistance while providing consistent oral pharmacology and convenience of administration. Imlunestrant was specifically designed to deliver continuous estrogen receptor target inhibition throughout the dosing period and regardless of ESR1 mutational status. Imlunestrant is currently being studied in several clinical studies.

About Lilly
Lilly unites caring with discovery to create medicines that make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 51 million people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges, redefining diabetes care, treating obesity and curtailing its most devastating long-term effects, advancing the fight against Alzheimer's disease, providing solutions to some of the most debilitating immune system disorders, and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/news or follow us on Facebook, Instagram and LinkedIn. P-LLY

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Cautionary Statement Regarding Forward-Looking Statements
This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Verzenio as a treatment for people with certain types of early breast cancer and imlunestrant as a potential treatment for people with certain types of breast

cancer and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date, that Verzenio will receive additional regulatory approvals, or that imlunestrant will prove to be a safe and effective treatment for certain types of breast cancer or receive regulatory approval. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's 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.

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Refer to: Tracy Henrikson; tracy.henrikson@lilly.com; 609-454-7116 – media
Joe Fletcher; jfletcher@lilly.com; (317) 296-2884 – investors

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