Lilly Announces New Clinical Data from Verzenio and Oral SERD Programs at the American Society of Clinical Oncology Annual Meeting

June 4, 2021

New exploratory analysis of a pre-specified subgroup of patients with HR+, HER2- high risk early breast cancer who received neoadjuvant chemotherapy in the monarchE trial showed Verzenio plus endocrine therapy resulted in a 6.6% absolute difference in invasive disease-free survival versus endocrine therapy alone

First results from investigational oral selective estrogen receptor degrader (SERD) LY3484356 demonstrate pharmacokinetics, safety, and efficacy consistent with preclinical design

Two Phase 3 trials to be initiated in 2021: Verzenio eMonarcHER trial in HR+, HER2+ high risk early breast cancer and oral SERD EMBER-3 trial in ER+, HER2- advanced breast cancer

INDIANAPOLIS, June 4, 2021 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced new data for the investigational use of Verzenio® (abemaciclib) in high risk early breast cancer, and for its oral selective estrogen receptor degrader (SERD) LY3484356 at the 57th Annual Meeting of the American Society of Clinical Oncology (ASCO). Lilly is presenting an exploratory analysis from the positive Phase 3 monarchE trial evaluating Verzenio, a CDK4/6 inhibitor, in a subgroup of patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-) high risk early breast cancer (EBC) who had received neoadjuvant chemotherapy. Physicians often treat patients with HR+, HER2- breast cancer who they believe to be at the highest risk of recurrence with neoadjuvant chemotherapy prior to curative intent surgery. In addition, Loxo Oncology at Lilly is presenting interim clinical data from the ongoing Phase 1a trial evaluating the safety and efficacy of the oral SERD LY3484356 in patients with estrogen receptor-positive (ER+) advanced breast cancer and endometrial endometrioid cancer.

New Verzenio Data from monarchE Trial

In an exploratory analysis of a pre-specified subgroup of patients who received neoadjuvant chemotherapy (n=2,056), the addition of Verzenio to endocrine therapy (ET) resulted in a numerically greater effect size when compared to the intent-to-treat (ITT) population (n=5,637). This subgroup of patients made up more than 36 percent of the total trial population, had larger tumors at initial diagnosis and were more commonly premenopausal, representing one of the highest risk subgroups of patients in monarchE. Treatment with Verzenio in combination with standard adjuvant ET decreased the risk of breast cancer recurrence in these patients by 38.6 percent compared to ET alone (HR: 0.614; 95% CI: 0.473, 0.797). This corresponds to a 6.6 percent difference in the two-year rate of invasive disease-free survival (IDFS) between arms (87.2 percent in the Verzenio plus ET arm compared to 80.6 percent in the ET only control arm). The addition of Verzenio to ET also reduced the risk of developing metastatic disease by 39 percent (HR: 0.609; 95% CI: 0.459, 0.809). This corresponds to a 6.7 percent difference in two-year distant relapse-free survival (DRFS) rates – or time to developing breast cancer that has spread to other parts of the body – between the arms (89.5 percent in the Verzenio plus ET arm compared to 82.8 percent in the ET only control arm). This subgroup analysis was exploratory and not alpha-controlled for testing statistical significance. Safety data from the monarchE trial were consistent with the known safety profile of Verzenio and no new safety signals were observed.

"People who receive neoadjuvant chemotherapy typically represent a patient population with a substantial risk of breast cancer recurrence. The data from monarchE further confirm this higher risk based on the number of events that occurred in the control arm for this subset of patients," said Maura Dickler, M.D., distinguished medical fellow, Lilly Oncology. "Given the need for new treatments for high risk early breast cancer, especially in this neoadjuvant population, it's encouraging to see these impressive results with a 38 percent reduction in the risk of recurrence with the addition of Verzenio to standard endocrine therapy."

These data build on the results from the Phase 3 monarchE trial, which met its primary endpoint at the second interim efficacy analysis by showing a statistically significant improvement in IDFS. Verzenio, given in combination with ET, decreased the risk of breast cancer recurrence by 28.7 percent compared to ET alone (HR: 0.713; 95% CI: 0.583, 0.871; p=0.0009) with a 3 percent absolute difference in the two-year IDFS and DRFS rates in the ITT population. The monarchE trial is ongoing and patients will continue to be followed to assess safety, overall survival and patient reported outcomes, as well as other endpoints.

New Verzenio Phase 3 Trial

Lilly recently initiated a new Phase 3 trial, eMonarcHER, which will evaluate the safety and efficacy of Verzenio in combination with standard adjuvant ET in patients with HR+, HER2+, node-positive, high risk early breast cancer receiving adjuvant ET after completing surgery and neoadjuvant and/or adjuvant HER2 targeted therapy. Despite several advancements for the neoadjuvant and adjuvant treatment of HER2+ breast cancer, research has primarily involved HER2 targeting agents; however, not all HER2+ breast cancers are successfully treated with HER2 targeted therapy. This new Phase 3 study introduces the novel strategy of CDK4/6 inhibition to improve outcomes with adjuvant hormonal therapy in patients with HR+/HER2+ breast cancer at high risk of recurrence after completion of HER2 targeted therapy. Lilly shared the trial design of eMonarcHER at ASCO.

Oral SERD (LY3484356) Phase 1a Data

The first clinical data from the ongoing Phase 1 EMBER trial of LY3484356 were also presented at ASCO. As of April 7, 2021, 65 patients were enrolled in the trial, including 58 with ER+ advanced breast cancer and seven with ER+ endometrial endometrioid cancer (EEC). All patients received LY3484356 monotherapy. Advanced breast cancer patients had received a median of two prior lines of therapy with 60 percent receiving prior fulvestrant, 83 percent a CDK4/6 inhibitor, and 26 percent chemotherapy. Of 54 patients with available circulating tumor DNA (ctDNA) data, ESR1 mutations were detected in 37 percent.

Pharmacokinetic analyses during the dose escalation phase demonstrated dose-proportional increases in LY3484356 exposure across all evaluated doses (200 mg once daily [QD] to 1200 mg QD). At all doses, steady state LY3484356 plasma concentrations in patients exceeded the EC80 range associated with efficacy in preclinical studies, as well as steady state fulvestrant peak serum concentration.

No dose limiting toxicities were observed and no maximum tolerated dose was established. Most treatment-emergent adverse events were grade 1 or 2 in severity. The treatment-related adverse events observed most commonly were nausea (19 [29%]), diarrhea (11 [17%]), and fatigue (8 [12%]). Grade 3 treatment-emergent adverse events occurred in six (9%) patients, which were treatment-related in two (3%) patients (diarrhea [n=1] and decreased neutrophil count [n=1]). Serious adverse events occurred in three (5%) patients, only one of which, grade 3 diarrhea, was treatment-related. No cardiac safety signal was seen. Dose reductions due to adverse events occurred in two (3%) patients, one of which was the treatment-related grade 3 diarrhea. No patient discontinued due to an adverse event and 400 mg QD has been selected as the recommended Phase 2 dose.

The efficacy data presented were based on investigator assessment. Patients were considered efficacy-evaluable for objective response rate (ORR) if they had RECIST measurable disease at baseline and at least one post-baseline tumor assessment or discontinued treatment prior to their first post-baseline assessment and for clinical benefit rate (CBR) if they were enrolled at least 24 weeks prior to the data cut-off date. In advanced breast cancer, two confirmed partial responses were observed in 35 efficacy-evaluable patients, both occurring after 24 weeks of therapy at the 400 mg dose and in patients who had received at least three prior regimens for metastatic disease. One of the observed partial responses was seen in a patient with fulvestrant, CDK4/6, and chemotherapy-refractory disease. The other partial response occurred in a patient with three lines of prior endocrine therapy, including an mTOR inhibitor. The CBR across all dose levels was 48 percent (13/27). In EEC, no objective responses were observed among the six efficacy-evaluable patients and the CBR was 50 percent (2/4). In patients with available serial ctDNA data, 86 percent (18/21) had early (cycle 2 day 1) declines in overall ctDNA and the degree of decline was generally deeper in patients who experienced clinical benefit versus those who did not. As of the data cut-off, 35 patients remained on treatment, including both patients with partial responses, and 79 percent (31/39) of those with stable disease or partial responses.

"When we began clinical development of our oral SERD, we hoped to see pharmacokinetic exposures that exceeded fulvestrant, a safety profile amenable to chronic use and combination, and evidence of single agent efficacy. To date, LY3484356 has delivered on these objectives," said David Hyman, M.D., chief medical officer, oncology at Lilly. "We look forward to continuing to explore the profile of LY3484356 in the ongoing dose expansion portion of the EMBER study and through the Phase 3 EMBER-3 trial in metastatic ER+, HER2- breast cancer, set to begin later this year."

Phase 3 EMBER-3 Trial of LY3484356
Lilly is preparing to initiate a randomized, open-label, Phase 3 study of LY3484356 in patients with ER+, HER2- locally advanced or metastatic breast cancer previously treated with endocrine therapy. Patients will be randomized to receive LY3484356 monotherapy or investigator's choice of monotherapy endocrine therapy (fulvestrant or exemestane). The trial, EMBER-3, is expected to begin enrollment in the third quarter of 2021.

Please refer to Lilly's press release from May 19, 2021 for a full list of presentations at the meeting.

About the monarchE Trial
monarchE is a Phase 3, multicenter, randomized, open-label trial that enrolled 5,637 patients with HR+, HER2-, node-positive, high risk early breast cancer. Patients were randomized 1:1 to Verzenio (150 mg twice daily) plus standard adjuvant ET or standard adjuvant ET alone. Patients were treated for two years (treatment period) or until meeting criteria for discontinuation. Patients in both arms will receive 5-10 years of ET as clinically indicated (2 years on study followed by a further 3-8 years in long-term follow-up). The primary objective is invasive disease-free survival (IDFS) defined according to the Standard Definitions for Efficacy Endpoints (STEEP) criteria. In adjuvant breast cancer trials, this includes the length of time before any cancer comes back, a new cancer develops or death. Secondary objectives include distant relapse-free survival, overall survival, safety, pharmacokinetics and health outcomes.

High risk was specifically defined as women (any menopausal status) and men with resected HR+, HER2- invasive early breast cancer with either ≥4 pathologically positive axillary lymph nodes (ALNs) or 1 to 3 positive ALNs and at least one of the following high-risk features: primary invasive tumor size ≥5 cm, histological grade 3 tumor, or central Ki-67 index ≥20%. If applicable, patients must have also completed adjuvant chemotherapy and radiotherapy prior to enrolling and have recovered from all acute side effects.

About Verzenio® (abemaciclib)
Verzenio (abemaciclib) is an inhibitor of cyclin-dependent kinases (CDK)4/6, which 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.

About the EMBER Trial
This global, first-in-human, open-label Phase 1a/b trial evaluates LY3484356 alone or in combination with other anticancer therapies in participants with ER+ advanced breast cancer or endometrioid endometrial cancer. The trial includes a Phase 1a dose escalation phase and a Phase 1b dose expansion phase. The Phase 1a dose escalation enrolls patients with ER+/HER2- advanced breast cancer who have received up to three prior treatment regimens and ER+ EEC who have progressed after prior platinum-based therapy. The dose escalation phase followed an i3+3 design with LY3484356 administered orally in 28-day cycles. As dose cohorts were cleared, additional patient enrollment to cleared dose levels was permitted. The primary objective of the Phase 1a portion is to determine the recommended Phase 2 dose. Secondary objectives include assessments of safety, pharmacokinetics, and anti-tumor activity (objective response rate (ORR) and clinical benefit rate (CBR), as assessed per Response Evaluation Criteria in Solid Tumors (RECIST v1.1).

About LY3484356
LY3484356 is an investigational, oral selective estrogen receptor degrader (SERD) with pure antagonistic properties. 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. LY3484356 was specifically designed to deliver continuous estrogen receptor target inhibition throughout the dosing period and regardless of ESR1 mutational status.

LY3484356 is currently being studied in the first-in-human, multi-center Phase 1a/1b EMBER trial in patients with estrogen receptor-positive locally advanced or metastatic breast cancer and other select non-breast cancers and in the Phase 1 EMBER-2 trial in preoperative, postmenopausal women

with stage I-III, ER+/HER2- breast cancer. For additional information about LY3484356 clinical trials, please refer to www.clinicaltrials.gov. Interested patients and physicians can contact the Loxo Oncology at Lilly clinical trial team by e-mailing clinicaltrials@loxooncology.com.

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

- in combination with an aromatase inhibitor for postmenopausal women as initial endocrine-based therapy
- in combination with fulvestrant for women 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)

Diarrhea occurred in 81% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 86% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and 90% of patients receiving Verzenio alone in MONARCH 1. Grade 3 diarrhea occurred in 9% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 13% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and in 20% of patients receiving Verzenio alone in MONARCH 1. Episodes of diarrhea have been associated with dehydration and infection.

Diarrhea incidence was greatest during the first month of Verzenio dosing. In MONARCH 3, the median time to onset of the first diarrhea event was 8 days, and the median duration of diarrhea for Grades 2 and 3 were 11 and 8 days, respectively. In MONARCH 2, the median time to onset of the first diarrhea event was 6 days, and the median duration of diarrhea for Grades 2 and 3 were 9 days and 6 days, respectively. In MONARCH 3, 19% of patients with diarrhea required a dose omission and 13% required a dose reduction. In MONARCH 2, 22% of patients with diarrhea required a dose omission and 22% required a dose reduction. The time to onset and resolution for diarrhea were similar across MONARCH 3, MONARCH 2, and MONARCH 1.

Instruct patients that at the first sign of loose stools, they should start antidiarrheal therapy such as loperamide, 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 occurred in 41% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 46% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and 37% of patients receiving Verzenio alone in MONARCH 1. A Grade ≥3 decrease in neutrophil count (based on laboratory findings) occurred in 22% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 32% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and in 27% of patients receiving Verzenio alone in MONARCH 1. In MONARCH 3, the median time to first episode of Grade ≥3 neutropenia was 33 days, and in MONARCH 2 and MONARCH 1, was 29 days. In MONARCH 3, median duration of Grade ≥3 neutropenia was 11 days, and for MONARCH 2 and MONARCH 1 was 15 days.

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.

Febrile neutropenia has been reported in <1% of patients exposed to Verzenio in the MONARCH studies. Two deaths due to neutropenic sepsis were observed in MONARCH 2. Inform patients to promptly report any episodes of fever to their healthcare provider.

Severe, life-threatening, or fatal **interstitial lung disease (ILD) and/or pneumonitis** can occur in patients treated with Verzenio and other CDK4/6 inhibitors. Across clinical trials (MONARCH 1, MONARCH 2, MONARCH 3), 3.3% of Verzenio-treated patients had ILD/pneumonitis of any grade, 0.6% had Grade 3 or 4, and 0.4% had fatal outcomes. Additional cases of ILD/pneumonitis have been observed in the post-marketing setting, with fatalities reported.

Monitor patients for pulmonary symptoms indicative of ILD/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/pneumonitis. Permanently discontinue Verzenio in all patients with grade 3 or 4 ILD/pneumonitis.

Grade ≥3 increases in **alanine aminotransferase (ALT)** (6% versus 2%) and **aspartate aminotransferase (AST)** (3% versus 1%) were reported in the Verzenio and placebo arms, respectively, in MONARCH 3. Grade ≥3 increases in ALT (4% versus 2%) and AST (2% versus 3%) were reported in the Verzenio and placebo arms respectively, in MONARCH 2.

In MONARCH 3, for patients receiving Verzenio plus an aromatase inhibitor with Grade ≥3 increases in ALT or AST, median time to onset was 61 and 71 days, respectively, and median time to resolution to Grade <3 was 14 and 15 days, respectively. In MONARCH 2, for patients receiving Verzenio plus fulvestrant with Grade ≥3 increases in ALT or AST, median time to onset was 57 and 185 days, respectively, and median time to resolution to Grade <3 was 14 and 13 days, respectively.

For assessment of potential **hepatotoxicity**, 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 Grade 3 or 4, hepatic transaminase elevation.

Venous thromboembolic events were reported in 5% of patients treated with Verzenio plus an aromatase inhibitor as compared to 0.6% of patients treated with an aromatase inhibitor plus placebo in MONARCH 3. Venous thromboembolic events were reported in 5% of patients treated with Verzenio plus fulvestrant in MONARCH 2 as compared to 0.9% of patients treated with fulvestrant plus placebo. Venous thromboembolic events included deep vein thrombosis, pulmonary embolism, pelvic venous thrombosis, cerebral venous sinus thrombosis, subclavian and axillary vein thrombosis, and inferior vena cava thrombosis. Across the clinical development program, deaths due to venous thromboembolism have been reported. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate.

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 at least 3 weeks after the last dose. 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. Based on findings in animals, Verzenio may impair fertility in males of reproductive potential.

The **most common adverse reactions (all grades, ≥10%)** observed in **MONARCH 3 for Verzenio plus anastrozole or letrozole** and **≥2% higher than placebo plus anastrozole or letrozole vs placebo plus anastrozole or letrozole** were diarrhea (81% vs 30%), neutropenia (41% vs 2%), fatigue (40% vs 32%), 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%), influenza-like illness (10% vs 8%), and thrombocytopenia (10% vs 2%).

The **most common adverse reactions (all grades, ≥10%)** observed in **MONARCH 2 for Verzenio plus fulvestrant and ≥2% higher than placebo plus fulvestrant vs placebo plus fulvestrant** 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 3%), thrombocytopenia (16% vs 3%), alopecia (16% vs 2%), 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%), pyrexia (11% vs 6%), and weight decreased (10% vs 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%), leukopenia (17%), constipation (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** that occurred in the Verzenio arm vs the placebo arm of **MONARCH 3** were neutropenia (22% vs 2%), diarrhea (9% vs 1%), leukopenia (8% vs <1%), ALT increased (7% vs 2%), and anemia (6% vs 1%).

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 (27% vs 2%), diarrhea (13% vs <1%), leukopenia (9% vs 0%), anemia (7% vs 1%), and infections (6% vs 3%).

The **most frequently reported ≥5% Grade 3 or 4 adverse reactions** from **MONARCH 1** with Verzenio were neutropenia (24%), diarrhea (20%), fatigue (13%), infections (7%), leukopenia (6%), anemia (5%), and nausea (5%).

Lab abnormalities (all grades; Grade 3 or 4) for **MONARCH 3 in ≥10% for Verzenio plus anastrozole or letrozole and ≥2% higher than placebo plus anastrozole or letrozole vs placebo plus anastrozole or letrozole** were increased serum creatinine (98% vs 84%; 2% vs 0%), decreased white blood cells (82% vs 27%; 13% vs <1%), anemia (82% vs 28%; 2% vs 0%), decreased neutrophil count (80% vs 21%; 22% vs 3%), decreased lymphocyte count (53% vs 26%; 8% vs 2%), decreased platelet count (36% vs 12%; 2% vs <1%), increased ALT (48% vs 25%; 7% vs 2%), and increased AST (37% vs 23%; 4% vs <1%).

Lab abnormalities (all grades; Grade 3 or 4) for **MONARCH 2 in ≥10% for Verzenio plus fulvestrant and ≥2% higher than placebo plus fulvestrant vs placebo plus fulvestrant** were increased serum creatinine (98% vs 74%; 1% vs 0%), decreased white blood cells (90% vs 33%; 23% vs 1%), decreased neutrophil count (87% vs 30%; 33% vs 4%), anemia (84% vs 33%; 3% vs <1%), decreased lymphocyte count (63% vs 32%; 12% vs 2%), decreased platelet count (53% vs 15%; 2% vs 0%), increased ALT (41% vs 32%; 5% vs 1%), and increased AST (37% vs 25%; 4% vs 4%).

Lab abnormalities (all grades; Grade 3 or 4) for MONARCH 1 were increased serum creatinine (98%; <1%), decreased white blood cells (91%; 28%), decreased neutrophil count (88%; 27%), anemia (68%; 0%), decreased lymphocyte count (42%; 14%), decreased platelet count (41%; 2%), increased ALT (31%; 3%), and increased AST (30%; 4%).

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 the strong CYP3A inhibitor 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 Class 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).

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Please see full Prescribing Information for Verzenio.

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 LillyOncology.com.

About Loxo Oncology at Lilly
Loxo Oncology at Lilly was created in December 2019, combining the Lilly Research Laboratories oncology organization and Loxo Oncology, which was acquired by Lilly in early 2019. Loxo Oncology at Lilly brings together the focus and spirit of a biotech with the scale and resources of large pharma, with the goal of rapidly delivering impactful new medicines for people with cancer. Our approach centers on creating new oncology medicines that unequivocally work early in clinical development and will matter to patients.

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

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Lilly Forward-Looking Statement
This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Lilly's oncology portfolio and pipeline, including Verzenio (abemaciclib) and LY3484356 as treatments for patients with 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 research, development, regulatory approval, and commercialization. Among other things, there can be no guarantee that future studies will be completed as planned, that future study results will be consistent with the results to date, or that Verzenio or LY3484356 will receive (or 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.

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