



## Lilly Announces Details of Presentations at ESMO Congress 2023

October 6, 2023

INDIANAPOLIS, Oct. 6, 2023 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced that data from studies of Verzenio® (abemaciclib; a CDK4/6 inhibitor), Retevmo® (selpercatinib; a *rearranged during transfection* [RET] inhibitor), and imlunestrant (an investigational oral selective estrogen receptor degrader [SERD]) will be presented at the 2023 European Society for Medical Oncology (ESMO) Congress taking place October 20-24 in Madrid.

### Presentation Highlights

#### *Verzenio (abemaciclib)*

In a late-breaking oral presentation, Lilly will share five-year results, an established benchmark for adjuvant breast cancer trials, from a preplanned interim analysis of the Phase 3 monarchE study. The trial is evaluating two years of adjuvant Verzenio treatment in combination with endocrine therapy (ET) compared with ET alone in patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), node-positive early breast cancer (EBC) at a high risk of recurrence. A separate poster presentation will provide data on the impact of dose reductions on efficacy for patients treated in monarchE.

#### *Retevmo (selpercatinib)*

In two late-breaking oral presentations that will be featured as part of the Presidential Symposium 1 on Saturday, October 21, Lilly will share interim analysis results from the Phase 3 LIBRETTO-431 and LIBRETTO-531 clinical studies. LIBRETTO-431 evaluated Retevmo versus platinum-based chemotherapy – with or without pembrolizumab – as an initial treatment for patients with *RET* fusion-positive non-small cell lung cancer (NSCLC). LIBRETTO-531 evaluated Retevmo versus multikinase inhibitors (cabozantinib or vandetanib) in patients with advanced *RET*-mutant medullary thyroid cancer (MTC).

#### *Imlunestrant (investigational oral SERD)*

In a mini oral presentation, Lilly will share clinical data on imlunestrant as a single agent and in combination therapy. These results include the first clinical data for imlunestrant in combination with everolimus or alpelisib and updated imlunestrant monotherapy data from the Phase 1 EMBER study in patients with estrogen receptor positive (ER+), HER2- advanced breast cancer.

Abstract titles and viewing details are listed below:

#### **Verzenio (abemaciclib):**

**Presentation Title:** Adjuvant abemaciclib plus endocrine therapy for high-risk, HR+, HER2-, early breast cancer: results from a preplanned monarchE overall survival interim analysis, including 5-year efficacy outcomes

**FPN #:** [LBA17](#)

**Presentation Date & Time:** Friday, October 20, 14:00 – 14:10 CEST

**Session:** Breast cancer, early stage

**Location:** Bilbao Auditorium - NCC

**Presenter:** Nadia Harbeck

**Presentation Title:** Impact of Dose Reductions on Efficacy of Adjuvant Abemaciclib for Patients with High-Risk Early Breast Cancer (EBC): Analyses from the monarchE Study

**FPN #:** [274P](#)

**Presentation Date & Time:** Saturday, October 21, 12:00 – 13:00 CEST

**Session:** Breast cancer, early stage

**Location:** Hall 8

**Presenter:** Joyce O'Shaughnessy

**Presentation Title:** Prognostic and predictive impact of estrogen/progesterone receptor (ER/PR), and Ki-67 expression: an exploratory analysis from the monarchE trial in patients with high-risk, HR+, HER2- early breast cancer (EBC)

**FPN #:** [240MO](#)

**Presentation Date & Time:** Monday, October 23, 17:00 – 17:05 CEST

**Session:** Breast cancer, early stage

**Location:** Bilbao Auditorium - NCC

**Presenter:** Matthew P. Goetz

**Presentation Title:** Evolution and Risk Stratification of Adjuvant Treatment Strategies for Early Breast Cancer: A Chinese Perspective Based on National Cancer Database

**FPN #:** [256P](#)

**Presentation Date & Time:** Saturday, October 21, 12:00 – 13:00 CEST

**Session:** Breast cancer, early stage

**Location:** Hall 8

**Presenter:** Ying Fan

#### **Retevmo (selpercatinib):**

**Presentation Title:** Randomized Phase 3 Study of First-line Selpercatinib versus Pembrolizumab and Chemotherapy in *RET* Fusion-positive NSCLC

(DV-011345)

**Presentation Date & Time:** Saturday, October 21, 17:35 – 17:47 CEST

**FPN #:** [LBA4](#)

**Session:** [Presidential 1 \(ID 65\)](#) (Saturday, October 21, 16:30-18:15 CEST)

**Location:** Madrid Auditorium – Hall 6

**Presenter:** Herbert Ho Fung Loong

**Presentation Title:** Randomized Phase 3 Study of Selpercatinib versus Cabozantinib or Vandetanib in Advanced, Kinase Inhibitor-Naïve, *RET*-mutant Medullary Thyroid Cancer (DV-014219)

**FPN #:** [LBA3](#)

**Presentation Date & Time:** Saturday, October 21, 17:10 – 17:22 CEST

**Session:** [Presidential 1 \(ID 65\)](#) (Saturday, October 21, 16:30-18:15 CEST)

**Location:** Madrid Auditorium – Hall 6

**Presenter:** Julien Hadoux

**Presentation Title:** Patient-Reported Outcomes with Selpercatinib in Patients with *RET*-driven cancers in the Phase 1/2 LIBRETTO-001 Trial (DV-013416)

**FPN #:** [669P](#)

**Presentation Date & Time:** Monday, October 23, 12:00 – 13:00 CEST

**Session:** Developmental therapeutics

**Location:** Hall 8

**Presenter:** Hyunseok Kang

**Presentation Title:** Updated safety and efficacy of selpercatinib in patients (pts) with *RET*-activated thyroid cancer: Data from LIBRETTO-001 (DV-011352)

**FPN #:** [2229P](#)

**Presentation Date & Time:** Sunday, October 22, 12:00 – 13:00 CEST

**Session:** Thyroid cancer

**Location:** Hall 8

**Presenter:** Lori J. Wirth

#### **Imlunestrant (investigational oral SERD):**

**Presentation Title:** Imlunestrant with or without everolimus or alpelisib, in ER+, HER2- advanced breast cancer (aBC): Results from the Phase 1a/b EMBER study

**FPN #:** [383MO](#)

**Presentation Date & Time:** Sunday, October 22, 9:05 – 9:10 CEST

**Session:** Breast cancer, metastatic

**Location:** Bilbao Auditorium - NCC

**Presenter:** Komal Jhaveri

**Presentation Title:** A preoperative window-of-opportunity (WOO) study of imlunestrant in ER+, HER2- early breast cancer (EBC): Results from EMBER-2

**FPN #:** [273P](#)

**Presentation Date & Time:** Saturday, October 21, 12:00 – 13:00 CEST

**Session:** Breast cancer, early stage

**Location:** Hall 8

**Presenter:** Patrick Neven

#### **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.<sup>1</sup> 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.<sup>2</sup> NCCN® also includes Verzenio plus endocrine therapy as a preferred treatment option for metastatic breast cancer.<sup>2</sup>

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 specifically to investigate a CDK4/6 inhibitor in a high risk population.<sup>3</sup> In metastatic breast cancer, Verzenio has demonstrated statistically significant OS in the Phase 3 MONARCH 2 study.<sup>4</sup> 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 countries 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](http://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  $\leq$ 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  $\geq$ 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  $\geq$ 3 neutropenia ranged from 29 to 33 days, and the median duration of Grade  $\geq$ 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  $\geq$ 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  $\geq$ 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  $\geq$ 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,  $\geq$ 10%)** observed in monarchE for Verzenio plus tamoxifen or an aromatase inhibitor vs tamoxifen or an aromatase inhibitor, with a difference between arms of  $\geq$ 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** (CL<sub>Cr</sub> <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 (CL<sub>Cr</sub> ≥30-89 mL/min).

Please see full [Prescribing Information](#) and [Patient Information](#) for Verzenio.

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#### **About Retevmo<sup>®</sup> (selpercatinib, 40 mg & 80 mg capsules)**

Retevmo (selpercatinib, formerly known as LOXO-292) (pronounced reh-TEHV-moh) is a highly selective and potent RET kinase inhibitor with central nervous system (CNS) activity. Retevmo may affect both tumor cells and healthy cells, which can result in side effects. RET-driver alterations are

predominantly mutually exclusive from other oncogenic drivers. Retevmo is a U.S. FDA-approved oral prescription medicine, 120 mg or 160 mg dependent on weight (<50 kg or ≥50 kg, respectively), taken twice daily until disease progression or unacceptable toxicity.

## INDICATIONS FOR RETEVMO®

Retevmo® is kinase inhibitor indicated for the treatment of:

- Adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a *rearranged during transfection (RET)* gene fusion, as detected by an FDA-approved test.
- Adult and pediatric patients 12 years of age and older with advanced or metastatic medullary thyroid cancer (MTC) with a *RET* mutation, as detected by an FDA-approved test, who require systemic therapy.<sup>1</sup>
- Adult and pediatric patients 12 years of age and older with advanced or metastatic thyroid cancer with a *RET* gene fusion, as detected by an FDA-approved test, who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate).<sup>1</sup>
- Adult patients with locally advanced or metastatic solid tumors with a *RET* gene fusion that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options.<sup>1</sup>

<sup>1</sup>This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

## IMPORTANT SAFETY INFORMATION FOR RETEVMO® (selpercatinib)

**Hepatotoxicity:** Serious hepatic adverse reactions occurred in 3% of patients treated with Retevmo. Increased aspartate aminotransferase (AST) occurred in 59% of patients, including Grade 3 or 4 events in 11% and increased alanine aminotransferase (ALT) occurred in 55% of patients, including Grade 3 or 4 events in 12%. Monitor ALT and AST prior to initiating Retevmo, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose, or permanently discontinue Retevmo based on the severity.

Severe, life-threatening, and fatal **interstitial lung disease (ILD)/pneumonitis** can occur in patients treated with Retevmo. ILD/pneumonitis occurred in 1.8% of patients who received Retevmo, including 0.3% with Grade 3 or 4 events, and 0.3% with fatal reactions. Monitor for pulmonary symptoms indicative of ILD/pneumonitis. Withhold Retevmo and promptly investigate for ILD in any patient who presents with acute or worsening of respiratory symptoms which may be indicative of ILD (e.g., dyspnea, cough, and fever). Withhold, reduce dose, or permanently discontinue Retevmo based on severity of confirmed ILD.

**Hypertension** occurred in 41% of patients, including Grade 3 hypertension in 20% and Grade 4 in one (0.1%) patient. Overall, 6.3% had their dose interrupted and 1.3% had their dose reduced for hypertension. Treatment-emergent hypertension was most commonly managed with anti-hypertension medications. Do not initiate Retevmo in patients with uncontrolled hypertension. Optimize blood pressure prior to initiating Retevmo. Monitor blood pressure after 1 week, at least monthly thereafter, and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue Retevmo based on the severity.

Retevmo can cause concentration-dependent **QT interval prolongation**. An increase in QTcF interval to >500 ms was measured in 7% of patients and an increase in the QTcF interval of at least 60 ms over baseline was measured in 20% of patients. Retevmo has not been studied in patients with clinically significant active cardiovascular disease or recent myocardial infarction. Monitor patients who are at significant risk of developing QTc prolongation, including patients with known long QT syndromes, clinically significant bradyarrhythmias, and severe or uncontrolled heart failure. Assess QT interval, electrolytes, and thyroid-stimulating hormone (TSH) at baseline and periodically during treatment, adjusting frequency based upon risk factors including diarrhea. Correct hypokalemia, hypomagnesemia, and hypocalcemia prior to initiating Retevmo and during treatment. Monitor the QT interval more frequently when Retevmo is concomitantly administered with strong and moderate CYP3A inhibitors or drugs known to prolong QTc interval. Withhold and dose reduce or permanently discontinue Retevmo based on the severity.

Serious, including fatal, **hemorrhagic events** can occur with Retevmo. Grade ≥3 hemorrhagic events occurred in 3.1% of patients treated with Retevmo including 4 (0.5%) patients with fatal hemorrhagic events, including cerebral hemorrhage (n=2), tracheostomy site hemorrhage (n=1), and hemoptysis (n=1). Permanently discontinue Retevmo in patients with severe or life-threatening hemorrhage.

**Hypersensitivity** occurred in 6% of patients receiving Retevmo, including Grade 3 hypersensitivity in 1.9%. The median time to onset was 1.9 weeks (range: 5 days to 2 years). Signs and symptoms of hypersensitivity included fever, rash and arthralgias or myalgias with concurrent decreased platelets or transaminitis. If hypersensitivity occurs, withhold Retevmo and begin corticosteroids at a dose of 1 mg/kg prednisone (or equivalent). Upon resolution of the event, resume Retevmo at a reduced dose and increase the dose of Retevmo by 1 dose level each week as tolerated until reaching the dose taken prior to onset of hypersensitivity. Continue steroids until patient reaches target dose and then taper. Permanently discontinue Retevmo for recurrent hypersensitivity.

**Tumor lysis syndrome (TLS)** occurred in 0.6% of patients with medullary thyroid carcinoma receiving Retevmo. Patients may be at risk of TLS if they have rapidly growing tumors, a high tumor burden, renal dysfunction, or dehydration. Closely monitor patients at risk, consider appropriate prophylaxis including hydration, and treat as clinically indicated.

**Impaired wound healing** can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Therefore, Retevmo has the potential to adversely affect wound healing. Withhold Retevmo for at least 7 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of Retevmo after resolution of wound healing complications has not been established.

Retevmo can cause **hypothyroidism**. Hypothyroidism occurred in 13% of patients treated with Retevmo; all reactions were Grade 1 or 2. Hypothyroidism occurred in 13% of patients (50/373) with thyroid cancer and 13% of patients (53/423) with other solid tumors including NSCLC. Monitor thyroid function before treatment with Retevmo and periodically during treatment. Treat with thyroid hormone replacement as clinically indicated. Withhold Retevmo until clinically stable or permanently discontinue Retevmo based on severity.

Based on data from animal reproduction studies and its mechanism of action, Retevmo can cause **fetal harm** when administered to a pregnant woman. Administration of selpercatinib to pregnant rats during organogenesis at maternal exposures that were approximately equal to those observed at the recommended human dose of 160 mg twice daily resulted in embryoletality and malformations. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Retevmo and for 1 week after the last dose. There are no data on the presence of selpercatinib or its metabolites in human milk or on their effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with Retevmo and for 1 week after the last dose.

**Severe adverse reactions (Grade 3-4) occurring in  $\geq 20\%$  of patients who received Retevmo in LIBRETTO-001**, were hypertension (20%), diarrhea (5%), prolonged QT interval (4.8%), dyspnea (3.1%), fatigue (3.1%), hemorrhage (2.6%), abdominal pain (2.5%), vomiting (1.8%), headache (1.4%), nausea (1.1%), constipation (0.8%), edema (0.8%), rash (0.6%), and arthralgia (0.3%).

**Serious adverse reactions occurred in 44% of patients** who received Retevmo. The most frequently reported serious adverse reactions (in  $\geq 2\%$  of patients) were pneumonia, pleural effusion, abdominal pain, hemorrhage, hypersensitivity, dyspnea, and hyponatremia.

**Fatal adverse reactions occurred in 3% of patients**; fatal adverse reactions included sepsis (n=6), respiratory failure (n=5), hemorrhage (n=4), pneumonia (n=3), pneumonitis (n=2), cardiac arrest (n=2), sudden death (n=1), and cardiac failure (n=1).

**Common adverse reactions (all grades) occurring in  $\geq 20\%$  of patients who received Retevmo in LIBRETTO-001**, were edema (49%), diarrhea (47%), fatigue (46%), dry mouth (43%), hypertension (41%), abdominal pain (34%), rash (33%), constipation (33%), nausea (31%), headache (28%), cough (24%), vomiting (22%), dyspnea (22%), hemorrhage (22%), arthralgia (21%), and prolonged QT interval (21%).

**Laboratory abnormalities (all grades  $\geq 20\%$ ; Grade 3-4) worsening from baseline in patients who received Retevmo in LIBRETTO-001**, were increased AST (59%; 11%), decreased calcium (59%; 5.7%), increased ALT (56%; 12%), decreased albumin (56%; 2.3%), increased glucose (53%; 2.8%), decreased lymphocytes (52%; 20%), increased creatinine (47%; 2.4%), decreased sodium (42%; 11%), increased alkaline phosphatase (40%; 3.4%), decreased platelets (37%; 3.2%), increased total cholesterol (35%; 1.7%), increased potassium (34%; 2.7%), decreased glucose (34%; 1.0%), decreased magnesium (33%; 0.6%), increased bilirubin (30%; 2.8%), decreased hemoglobin (28%; 3.5%), and decreased neutrophils (25%; 3.2%).

Concomitant use of **acid-reducing agents** decreases selpercatinib plasma concentrations which may reduce Retevmo antitumor activity. Avoid concomitant use of proton-pump inhibitors (PPIs), histamine-2 (H2) receptor antagonists, and locally-acting antacids with Retevmo. If coadministration cannot be avoided, take Retevmo with food (with a PPI) or modify its administration time (with a H2 receptor antagonist or a locally-acting antacid).

Concomitant use of **strong and moderate CYP3A inhibitors** increases selpercatinib plasma concentrations which may increase the risk of Retevmo adverse reactions including QTc interval prolongation. Avoid concomitant use of strong and moderate CYP3A inhibitors with Retevmo. If concomitant use of a strong or moderate CYP3A inhibitor cannot be avoided, reduce the Retevmo dosage as recommended and monitor the QT interval with ECGs more frequently.

Concomitant use of **strong and moderate CYP3A inducers** decreases selpercatinib plasma concentrations which may reduce Retevmo anti-tumor activity. Avoid coadministration of Retevmo with strong and moderate CYP3A inducers.

Concomitant use of Retevmo with **CYP2C8 and CYP3A substrates** increases their plasma concentrations which may increase the risk of adverse reactions related to these substrates. Avoid coadministration of Retevmo with CYP2C8 and CYP3A substrates where minimal concentration changes may lead to increased adverse reactions. If coadministration cannot be avoided, follow recommendations for CYP2C8 and CYP3A substrates provided in their approved product labeling.

Retevmo is a P-glycoprotein (P-gp) inhibitor. Concomitant use of Retevmo with **P-gp substrates** increases their plasma concentrations, which may increase the risk of adverse reactions related to these substrates. Avoid coadministration of Retevmo with P-gp substrates where minimal concentration changes may lead to increased adverse reactions. If coadministration cannot be avoided, follow recommendations for P-gp substrates provided in their approved product labeling.

The safety and effectiveness of Retevmo have not been established in **pediatric patients less than 12 years of age**. The safety and effectiveness of Retevmo have been established in pediatric patients aged 12 years and older for medullary thyroid cancer (MTC) who require systemic therapy and for advanced *RET* fusion-positive thyroid cancer who require systemic therapy and are radioactive iodine-refractory (if radioactive iodine is appropriate). Use of Retevmo for these indications is supported by evidence from adequate and well-controlled studies in adults with additional pharmacokinetic and safety data in pediatric patients aged 12 years and older. Monitor open growth plates in **adolescent patients**. Consider interrupting or discontinuing Retevmo if abnormalities occur.

No dosage modification is recommended for patients with **mild to severe renal impairment** (estimated Glomerular Filtration Rate [eGFR]  $\geq 15$  to 89 mL/min, estimated by Modification of Diet in Renal Disease [MDRD] equation). A recommended dosage has not been established for patients with end-stage renal disease.

Reduce the dose when administering Retevmo to patients with **severe hepatic impairment** (total bilirubin greater than 3 to 10 times upper limit of normal [ULN] and any AST). No dosage modification is recommended for patients with mild or moderate hepatic impairment. Monitor for Retevmo-related adverse reactions in patients with hepatic impairment.

**Please see full [Prescribing Information](#) for Retevmo.**

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#### **About Imlunestrant**

Imlunestrant (LY3484356) is an investigational, next-generation 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. 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](https://www.lilly.com) and [Lilly.com/news](https://www.lilly.com/news) or follow us on [Facebook](https://www.facebook.com/lilly), [Instagram](https://www.instagram.com/lilly), [Twitter](https://twitter.com/lilly) and [LinkedIn](https://www.linkedin.com/company/lilly). 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® (abemaciclib) as a potential treatment for people with certain types of early breast cancer and Retevmo® (selpercatinib) as a potential treatment for people with locally advanced and metastatic *RET* fusion-positive NSCLC, *RET*-mutant MTC, and *RET*-activated thyroid 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, or that Verzenio, imlunestrant, or Retevmo will receive additional regulatory approvals, or that they will be commercially successful. 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.

<sup>1</sup> Verzenio. Prescribing information. Lilly USA, LLC.

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<sup>3</sup> Johnston SRD, Toi M, O'Shaughnessy J, Rastogi P, et al. Abemaciclib plus endocrine therapy for hormone receptor-positive, HER2-negative, node-positive, high-risk early breast cancer (monarchE): results from a preplanned interim analysis of a randomised, open-label, phase 3 trial. *Lancet Oncol.* 2023 Jan;24(1):77-90.

<sup>4</sup> Sledge GW Jr, Toi M, Neven P, et al. The effect of abemaciclib plus fulvestrant on overall survival in hormone receptor-positive, ERBB2-negative breast cancer that progressed on endocrine therapy—MONARCH 2: a randomized clinical trial. *JAMA Oncol.* 2020;6(1):116-124. doi:10.1001/jamaoncol. 2019.4782.

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