# Lilly's Retevmo® (selpercatinib) Phase 3 Results in RET Fusion-Positive Non-Small Cell Lung Cancer and RET-Mutant Medullary Thyroid Cancer Both Published in The New England Journal of Medicine and Presented in a Presidential Symposium at ESMO Congress 2023

October 21, 2023

*- In the Phase 3 LIBRETTO-431 study, Retevmo more than doubled progression-free survival (PFS) compared to chemotherapy plus pembrolizumab in patients with advanced or metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC)*

*- In the Phase 3 LIBRETTO-531 study, Retevmo provided a 72% improvement in PFS compared to cabozantinib or vandetanib in patients with advanced or metastatic RET-mutant medullary thyroid cancer (MTC)*

INDIANAPOLIS, Oct. 21, 2023 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced results from both the LIBRETTO-431 Phase 3 study, which evaluated Retevmo® (selpercatinib) versus platinum-based chemotherapy — with or without pembrolizumab — as an initial treatment for patients with advanced or metastatic *rearranged during transfection* (*RET)* fusion-positive non-small cell lung cancer (NSCLC), and the LIBRETTO-531 Phase 3 study, which evaluated Retevmo versus multikinase inhibitors (MKIs) in patients with advanced or metastatic *RET*-mutant medullary thyroid cancer (MTC). In both clinical studies, results were based on pre-specified interim efficacy analyses conducted by independent data monitoring committees (IDMC). Results from the LIBRETTO-431 and LIBRETTO-531 Phase 3 trials were presented in a Presidential Symposium at the European Society for Medical Oncology (ESMO) Congress 2023 and simultaneously published in the *New England Journal of Medicine.*

"These results from LIBRETTO-431 and LIBRETTO-531 are striking and provide critical evidence supporting the importance of optimizing initial therapy for patients with *RET*-driven cancers," said David Hyman, M.D., chief medical officer, Lilly. "We are excited to be sharing these data with the clinical community in both *NEJM* and at ESMO. It is our hope that these data lead to further adoption of biomarker testing in the initial treatment journey for people with NSCLC and MTC and help make Retevmo a standard initial treatment option for all appropriate patients."

The labeling for Retevmo contains warnings and precautions for hepatotoxicity (evidence of liver dysfunction), interstitial lung disease (ILD)/pneumonitis, hypertension, QT interval prolongation, hemorrhagic events, hypersensitivity, tumor lysis syndrome, risk of impaired wound healing, hypothyroidism, and embryo-fetal toxicity.

***RET* Fusion-Positive NSCLC: Data from LIBRETTO-431**

LIBRETTO-431 is a Phase 3, randomized, open-label trial that evaluated Retevmo in patients with advanced or metastatic, treatment-naïve *RET* fusion-positive NSCLC. In the study, patients were randomly assigned to receive Retevmo, or pemetrexed and the investigator's choice of platinum-based chemotherapy (cisplatin or carboplatin) with or without pembrolizumab — which is a current first-line standard of care treatment option. LIBRETTO-431 is the first randomized trial that compared the safety and effectiveness of a targeted therapy to a PD-1 inhibitor plus chemotherapy in a biomarker-selected NSCLC patient population. The primary endpoint was tested first in patients stratified by intent-to-treat (ITT) with pembrolizumab if assigned to the control arm (ITT-pembrolizumab), then tested in the ITT population if deemed positive.

"These data provide clear evidence that Retevmo offers highly meaningful clinical impact for patients diagnosed with *RET* fusion-positive NSCLC and it should be considered as the first treatment option for these patients," said Caicun Zhou, M.D., Ph.D., director and professor at the Cancer Institute of Tongji University School of Medicine and Shanghai Pulmonary Hospital, and LIBRETTO-431 primary investigator. "While there is often urgency to treat, these results further highlight the importance of incorporating routine biomarker testing into a patient's care plan to direct early clinical decision-making towards the most effective therapies."

A total of 256 patients received at least one dose of study treatment (Retevmo, 158; control arm, 98). Of the 261 patients in the ITT population, 159 were randomly assigned to Retevmo and 102 to the control arm. Of the 212 patients in the ITT-pembrolizumab population, 129 were randomly assigned to Retevmo and 83 to pembrolizumab with chemotherapy. Patients randomized to the control arm who had disease progression confirmed by blinded independent central review (BICR) were eligible for optional crossover to Retevmo.

In the ITT-pembrolizumab population, the median PFS by BICR was 24.8 months (95% CI: 16.9, not estimable [NE]) with Retevmo versus 11.2 months (95% CI: 8.8, 16.8) in the control arm, corresponding to a hazard ratio (HR) of 0.465 (95% CI: 0.309, 0.699; p<0.001). PFS was longer with Retevmo than in the control arm across all pre-specified subgroups. The overall response rate (ORR) by BICR with Retevmo was 83.7% (95% CI: 76.2, 89.6) compared to 65.1% (95% CI: 53.8, 75.2) in the control arm. Similar results were observed in the ITT population in both BICR and investigator-assessed endpoints and across all pre-specified subgroups. Retevmo demonstrated superior PFS with an HR of 0.482 (95% CI: 0.331, 0.700; p<0.001) and an increase of more than 13 months in median PFS by BICR, showing 24.8 months (95% CI: 17.3, NE) with Retevmo versus 11.2 months (95% CI: 8.8, 16.8) with control. Overall survival (OS) results remain immature with a censoring rate of approximately 80% (HR 0.961, 95% CI: 0.503, 1.835) in the ITT-pembrolizumab arm.

Intracranial baseline assessments were available for evaluation by neuroradiologic BICR for 192 patients in the central nervous system (CNS)-pembrolizumab population (Retevmo, 120; control arm, 72). Time to CNS progression was longer with Retevmo than in the control arm (cause-specific HR: 0.28; 95% CI: 0.12, 0.68), with eight patients (6.7%) on Retevmo having a first event of CNS progression compared to 13 patients (18.1%) in the control arm. Forty-two of the 192 patients (21.9%) were confirmed to have brain metastases at baseline, of which 29 were measurable (Retevmo, 17; control arm, 12). In the patients with measurable baseline brain metastases, the intracranial response rate for those who received Retevmo was 82.4% (95% CI: 56.6, 96.2) versus 58.3% (95% CI: 27.7, 84.8) in the control arm. Complete responses were observed in 35.3% of patients with Retevmo versus 16.7% in the control arm. Median intracranial response duration was not yet mature, but at 12 months, 76.0% of patients remained in response with Retevmo versus 62.5% in the control arm.

**_RET_-Mutant MTC: Data from LIBRETTO-531**
LIBRETTO-531 is a Phase 3, randomized, open-label trial that evaluated Retevmo versus physician's choice of MKIs cabozantinib or vandetanib, which are currently approved first-line options for patients with advanced or metastatic, kinase inhibitor-naïve *RET*-mutant MTC. It is the first randomized trial that compared the safety and effectiveness of a highly selective *RET*-kinase inhibitor versus MKIs in this population.

"The magnitude of benefit observed in patients treated with Retevmo makes clear that it should become the standard of care for the initial systemic treatment of patients with progressive advanced *RET*-mutant MTC," said Julien Hadoux, M.D., Ph.D., medical oncologist at the Gustave Roussy Cancer Center and LIBRETTO-531 investigator. "These data should prove to be practice-changing for clinicians caring for patients with MTC and lead to routine biomarker testing."

A total of 291 patients with progressive *RET*-mutant MTC and no prior history of MKI therapy for advanced or metastatic disease were randomized in the study. One hundred and ninety-three patients were randomized to the Retevmo arm and 98 to the control arm to receive investigator's choice of cabozantinib (73) or vandetanib (25). Patients randomized to the control arm who experienced disease progression confirmed by BICR were eligible to cross over to Retevmo.

At the interim analysis, the study had met the criteria for positive PFS. At a median follow-up of approximately 12 months, the BICR-assessed median PFS in the Retevmo arm was not reached and remained inestimable (95% CI, NE to NE), whereas the BICR-assessed median PFS in the control arm was 16.8 months (95% CI: 12.2, 25.1). This corresponded to a HR of 0.280 (95% CI: 0.165, 0.475; p<0.0001). Investigator-assessed PFS yielded similar results with an HR of 0.187 (95% CI: 0.109, 0.321; p<0.0001). Both BICR and investigator-assessed PFS were longer with Retevmo across all pre-planned subgroups.

Treatment with Retevmo resulted in a significant improvement in treatment failure-free survival (TFFS) with an HR of 0.254 (95% CI: 0.153, 0.423; p<0.001). The ORR with Retevmo was 69.4% (95% CI: 62.4, 75.8) compared to 38.8% (95% CI: 29.1, 49.2) in the control arm (95% CI: 2.2, 6.3). OS results remain immature with a censoring rate of more than 90%, although a favorable trend was observed (HR 0.374, 95% CI: 0.147, 0.949).

The safety profile observed for Retevmo in both studies was generally consistent with those identified across the previously reported Retevmo development program (LIBRETTO-001, LIBRETTO-121, LIBRETTO-321).

**About _RET_-Driven Cancers**
Genomic alterations in the *RET* kinase, which include fusions and activating point mutations, lead to overactive *RET* signaling and uncontrolled cell growth. *RET* fusions have been identified in approximately 1% to 2% of all NSCLC cases. NSCLC accounts for about 85% of all lung cancer diagnoses in the U.S., of which approximately 50% have actionable biomarkers.

MTC accounts for 1% to 2% of thyroid cancers in the U.S. *RET* mutations are found in up to 50% of sporadic MTC and over 90% of hereditary MTC.

**About LIBRETTO-431**
LIBRETTO-431 is a randomized Phase 3 clinical trial of patients with advanced or metastatic, treatment-naïve *RET* fusion-positive NSCLC. The trial enrolled 261 patients with advanced or metastatic *RET* fusion-positive NSCLC who had received no prior systemic therapy for metastatic disease. Enrolled trial participants were randomized 2:1 to receive either selpercatinib or platinum-based chemotherapy (carboplatin or cisplatin) and pemetrexed therapy with or without pembrolizumab as initial treatment of their advanced or metastatic *RET* fusion-positive NSCLC. *RET* fusions may be identified using local testing. This trial's primary endpoint is PFS, and secondary endpoints include OS, ORR, duration of response (DOR), and intracranial ORR. For patients randomized to the control arm, crossover was allowed at progression.

**About LIBRETTO-531**
LIBRETTO-531 is a randomized Phase 3 clinical trial of patients with progressive, advanced or metastatic, kinase inhibitor-naïve *RET*-mutant MTC. The trial enrolled 291 patients, and participants were randomized 2:1 to receive either selpercatinib or physician's choice of cabozantinib or vandetanib as initial treatment of their advanced or metastatic *RET*-mutant MTC. *RET* mutations may be identified using local testing. This trial's primary endpoint is PFS, and secondary endpoints include TFFS, ORR, DOR, and OS. For patients randomized to the control arm, crossover was allowed at progression.

**About Retevmo® (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 a 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.[1]
- 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).[1]
- 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. [1]

[1] 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 embryolethality 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 ≥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 ≥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 ≥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 ≥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] ≥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 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, Twitter and LinkedIn. P-LLY

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**Lilly 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 Retevmo® (selpercatinib) as a potential treatment for people with locally advanced and metastatic *RET* fusion-positive NSCLC and *RET*-mutant MTC 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 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.

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