Lilly's Retevmo (selpercatinib) delivers substantial event-free survival benefit as an adjuvant therapy in early-stage RET fusion-positive lung cancer

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Selpercatinib demonstrated a highly statistically significant and clinically meaningful improvement in reducing the risk of disease recurrence or death

Results from the LIBRETTO-432 trial build on previous results for selpercatinib in advanced NSCLC and reinforce the value of genomic testing at diagnosis and across all stages of disease

INDIANAPOLIS, Feb. 16, 2026 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced positive topline results from the Phase 3 LIBRETTO-432 clinical trial of Retevmo (selpercatinib) as adjuvant therapy versus placebo. The study met its primary endpoint, demonstrating a highly statistically significant and clinically meaningful improvement in investigator-assessed event-free survival (EFS) in patients with early-stage (II-IIIA) *rearranged during transfection (RET)* fusion-positive non-small cell lung cancer (NSCLC).

Overall survival results trended in favor of selpercatinib, but were immature at the time of this analysis with few events observed. The overall safety profile of selpercatinib in LIBRETTO-432 was generally consistent with previously reported trials in the selpercatinib development program.

Detailed results will be presented at an upcoming medical congress, submitted to a peer-reviewed journal, and discussed with health authorities globally.

"We have consistently observed that cancer medicines can deliver their greatest impact when administered early in the course of a patient's treatment journey. The LIBRETTO-432 results support this observation, demonstrating an effect size in line with the most striking data for targeted adjuvant therapy in lung cancer," said Jacob Van Naarden, executive vice president and president of Lilly Oncology. "Building on the adoption of targeted therapies for early-stage patients with EGFR- and ALK-driven lung cancer, we hope these results further accelerate the use of genomic testing for all people diagnosed with early-stage disease."

LIBRETTO-432 is the first and only randomized Phase 3 study to evaluate the safety and efficacy of a selective RET kinase inhibitor as adjuvant therapy in this population.

NSCLC accounts for about 85 percent of all lung cancer diagnoses in the U.S., and around 30 percent of patients with NSCLC present with stage IB-IIIA disease.[1,2] Approximately 50 percent of people with NSCLC have actionable biomarkers, and *RET* fusions have been identified in one to two percent of all NSCLC cases.[3,4]

For more information on the LIBRETTO Phase 3 clinical trial program, please visit clinicaltrials.gov.

About LIBRETTO-432
LIBRETTO-432 is a Phase 3, global, multicenter, randomized, double-blind, controlled clinical trial of selpercatinib versus placebo in patients with *RET* fusion-positive NSCLC following completion of definitive radiotherapy or surgery with curative intent, and other adjuvant therapy, if indicated. The trial enrolled 151 patients who were randomized 1:1 to receive either selpercatinib or placebo as adjuvant therapy for *RET* fusion-positive NSCLC. The primary endpoint is EFS as assessed by investigator in the primary analysis population, which was comprised of patients with stage II-IIIA *RET* fusion-positive NSCLC. Secondary endpoints include EFS as assessed by investigator in the overall population, overall survival (OS), EFS as assessed by blinded independent central review (BICR), time to distant disease recurrence in the central nervous system (CNS) as assessed by investigator and BICR, progression-free survival on the next line of treatment (PFS2), positive predictive value (PPV) of *RET* tests from investigator-identified laboratories with respect to the Lilly-designated *RET* test, safety and tolerability.

About Retevmo
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.[5]

INDICATIONS FOR RETEVMO (selpercatinib)

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

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 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 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.

Retevmo can cause **hypersensitivity**, including severe skin reactions such as Stevens-Johnson Syndrome. All grade hypersensitivity occurred in 6% of patients receiving Retevmo, including Grade 3 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. Stevens-Johnson Syndrome has been observed in the post-marketing setting. Discontinue Retevmo in patients with Stevens-Johnson Syndrome. 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%).

Severe adverse reactions (Grade 3-4) occurring in ≥15% of patients who received Retevmo or chemotherapy with or without pembrolizumab in LIBRETTO-431 were hypertension (20% vs 3.1%), electrocardiogram QT prolonged (9% vs 0%), fatigue (3.2% vs 5%), edema (2.5% vs 0%), rash (1.9% vs 1.0%), diarrhea (1.3% vs 2.0%), abdominal pain (0.6% vs 2.0%), pyrexia (0.6% vs 0%), COVID19 infection (0.6% vs 0%), constipation (0% vs 1.0%), nausea (0% vs 1.0%), vomiting (0% vs 1.0%), and decreased appetite (0% vs 2.0%).

Serious adverse reactions occurred in 44% of patients who received Retevmo in LIBRETTO-001. 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 in LIBRETTO-001**; 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).

Serious adverse reactions occurred in 35% of patients who received Retevmo in LIBRETTO-431. The most frequently reported serious adverse reactions (≥2% of patients) were pleural effusion and abnormal hepatic function. **Fatal adverse reactions occurred in 4.4% of patients who received Retevmo in LIBRETTO-431**; fatal adverse reactions included myocardial infarction (n=2), respiratory failure (n=2), cardiac arrest, malnutrition, and sudden death (n=1 each).

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%).

Common adverse reactions (all grades) occurring in ≥15% of patients who received Retevmo or chemotherapy with or without pembrolizumab in LIBRETTO-431 were hypertension (48% vs 7%), diarrhea (44% vs 24%), edema (41% vs 28%), dry mouth (39% vs 6%), rash (33% vs 30%), fatigue (32% vs 50%), abdominal pain (25% vs 19%), musculoskeletal pain (25% vs 28%), constipation (22% vs 40%), electrocardiogram QT prolonged (20% vs 1.0%), COVID19 infection (19% vs 18%), stomatitis (18% vs 16%), decreased appetite (17% vs 34%), nausea (13% vs 44%), vomiting (13% vs 23%), and pyrexia (13% vs 23%).

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%).

Laboratory abnormalities (all grades ≥20%; Grade 3-4) worsening from baseline in patients who received Retevmo or chemotherapy with or without pembrolizumab in LIBRETTO-431 were increased ALT (81%; 21% vs 63%; 4.1%), increased AST (77%; 10% vs 46%; 0%), decreased calcium (53%; 1.9% vs 24%; 1.0%), decreased platelets (53%; 3.2% vs 39%; 5%), decreased lymphocytes (53%; 8% vs 64%; 15%), decreased neutrophils (53%; 2.0% vs 58%; 11%), increased bilirubin (52%; 1.3% vs 9%; 0%), increased alkaline phosphatase (35%; 1.3% vs 22%; 0%), decreased sodium (31%; 3.2% vs 41%; 2.1%), decreased albumin (25%; 0% vs 5%; 0%), increased blood creatinine (23%; 0% vs 21%; 0%), decreased hemoglobin (21%; 0% vs 91%; 5%), decreased potassium (17%; 1.3% vs 15%; 1.0%), and decreased magnesium (16%; 0.6% vs 8%; 0%).

Concomitant use of **acid-reducing agents** decreases selpercatinib plasma concentrations which may reduce Retevmo anti-tumor 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) and BCRP inhibitor. Concomitant use of Retevmo with **P-gp or BCRP substrates** increases their plasma concentrations, which may increase the risk of adverse reactions related to these substrates. Avoid coadministration of Retevmo with P-gp or BCRP substrates where minimal concentration changes may lead to increased adverse reactions. If coadministration cannot be avoided, follow recommendations for P-gp and BCRP substrates provided in their approved product labeling.

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.

Retevmo (selpercatinib) is available as 40 mg and 80 mg capsules, and 40 mg, 80 mg, 120 mg, and 160 mg tablets.

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Please see full Prescribing Information, including Instructions for Use, for Retevmo.

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

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 as a potential treatment for *rearranged during transfection* (*RET)* fusion-positive stage IB-IIIA NSCLC following completion of definitive radiotherapy or surgery with curative intent, and other adjuvant therapy if indicated, 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. 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.

Endnotes & References

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Refer to: Kyle Owens; owens_kyle@lilly.com; (332) 259-3932 (Media)
Michael Czapar; czapar_michael_c@lilly.com; (317) 617-0983 (Investors)

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