



## Lilly Announces Details of Presentations at 2021 American Association for Cancer Research (AACR)

March 10, 2021

**Presentation of Phase 1/2 LIBRETTO-001 trial data will highlight safety and efficacy data of Retevmo® (selpercatinib) in the treatment of RET fusion-positive cancers outside of lung and thyroid cancer**

**Preclinical characterization data will be presented for oral SERD, BCL2 inhibitor, next-generation KRAS-G12C, and RET inhibitors**

INDIANAPOLIS, March 10, 2021 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced that data from programs across its oncology portfolio and pipeline will be presented at the 2021 American Association for Cancer Research (AACR) Annual Meeting, to be held virtually April 10-15, 2021. During the meeting, Lilly Oncology will present data from a study exploring safety and efficacy of its selective RET-kinase inhibitor Retevmo® (selpercatinib, 40 mg & 80 mg capsules) in patients with rearranged during transfection (*RET*) fusion-positive cancers outside of lung and thyroid cancer. Additionally, Loxo Oncology at Lilly, a research and development group of Eli Lilly and Company, will present preclinical characterization data for an oral selective estrogen receptor degrader (SERD), BCL2 inhibitor, next-generation KRAS-G12C inhibitor, and next-generation RET inhibitor.

### Portfolio Highlights

Last May, Lilly's first-in-class oral precision medicine, Retevmo received Accelerated Approval from the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with metastatic *RET* fusion-positive non-small cell lung cancer (NSCLC) in adult and pediatric patients 12 years of age and older with advanced or metastatic *RET*-mutant medullary thyroid cancer (MTC) who require systemic therapy, and in adult and pediatric patients 12 years of age and older with advanced or metastatic *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). Retevmo was approved under the FDA's Accelerated Approval regulations based on the LIBRETTO-001 Phase 1/2 trial's endpoints of overall response rate (ORR) and duration of response (DoR). Given that *RET* alterations are implicated in the pathogenesis of cancer types other than lung and thyroid cancer, Lilly continues to investigate the potential benefits of treatment with Retevmo in patients with other *RET*-altered cancers. At AACR, Lilly will feature data evaluating the safety and efficacy of Retevmo in patients with *RET* fusion-positive cancers other than lung and thyroid cancer. Lilly will present findings from a post-hoc safety analysis of the Phase 1/2 LIBRETTO-001 trial, the largest clinical trial in patients with *RET*-altered cancers.

Lilly will also present post-hoc efficacy data on Merck's Phase 3 KEYNOTE-189 trial, which evaluated ALIMTA® (pemetrexed for injection) in combination with KEYTRUDA® (pembrolizumab) and cisplatin or carboplatin compared with ALIMTA in combination with placebo and cisplatin or carboplatin, in untreated patients with metastatic nonsquamous NSCLC, regardless of PD-L1 expression.

Additionally, Lilly will present data on the Phase 3 ORIENT-3 trial, which evaluated sintilimab injection compared with docetaxel in patients with previously treated advanced/metastatic squamous NSCLC (sqNSCLC).

### Pipeline Highlights

During AACR, Loxo Oncology at Lilly will present preclinical characterization data for an oral selective estrogen receptor degrader (SERD), BCL2 inhibitor, next-generation KRAS-G12C inhibitor, and next-generation *RET* inhibitor. LY3484356, an oral SERD, is currently being studied in a Phase 1/2 clinical trial. Phase 1 clinical studies of the BCL2 inhibitor and the KRAS-G12C inhibitor are expected to begin in 2021. Loxo Oncology at Lilly plans to file an Investigational New Drug Application (IND) for the next-generation RET inhibitor in 2021.

All posters will be available on-demand on the AACR website at [www.aacr.org](http://www.aacr.org) from April 10 – June 21. Loxo Oncology at Lilly posters can also be viewed at [www.loxooncology.com](http://www.loxooncology.com).

A list of the oral and poster presentations, along with viewing details, is highlighted below.

### Retevmo (selpercatinib)

**Presentation Title:** Efficacy and Safety of Selpercatinib in RET Fusion-Positive Cancers Other than Lung or Thyroid Cancers

**Abstract Number:** CT011

**Session Title:** Targeted Therapy and Ovarian Cancer Trials

**Session Type:** Clinical Trials Plenary Session

**Session Date and Time:** Sunday, April 11, 2021 2:00 PM – 3:45 PM ET

**Presentation Title:** Safety of selpercatinib for RET-altered advanced solid tumors: a post hoc analysis of LIBRETTO-001

**Abstract Number:** CT160

**Session Category:** Phase II Clinical Trials

**Session Title:** Phase II Clinical Trials

**Session Type:** E-Poster Session

### Alimta (pemetrexed)

**Presentation Title:** Pemetrexed and Platinum plus Pembrolizumab in Patients with Metastatic Non-Squamous Non-Small Cell Lung Cancer By Tumor Burden at Baseline: A Post-hoc Efficacy Analysis of KEYNOTE-189

**Abstract Number:** 442

**Session Category:** Clinical Research (Excluding Trials)

**Session Title:** Combination Immunotherapies

**Session Type:** E-Poster Session

### Sintilimab

**Presentation Title:** ORIENT-3: A randomized, open-label, phase 3 study of sintilimab versus docetaxel in previously treated advanced/metastatic squamous non-small-cell lung cancer (sqNSCLC)

**Abstract Number:** CT041

**Session Title:** Disease-Oriented Innovative Clinical Research and Trials

**Session Type:** Clinical Trials Minisymposium

**Session Date and Time:** Monday, April 12, 2021 1:30 PM – 3:15 PM ET

### Pipeline

**Presentation Title:** Preclinical characterization of LY3484356, a novel, potent and orally bioavailable selective estrogen receptor degrader (SERD)

**Abstract Number:** 1236

**Session Category:** Experimental and Molecular Therapeutics

**Session Title:** Novel Antitumor Agents

**Poster Title:** Preclinical characterization of LOXO-338, a novel, oral and selective BCL2 inhibitor

**Abstract Number:** 1258

**Session Category:** Experimental and Molecular Therapeutics

**Session Title:** Novel Antitumor Agents

**Presentation Title:** Preclinical characterization of LY3537982, a novel, highly selective and potent KRAS-G12C inhibitor

**Abstract Number:** 1259

**Session Category:** Experimental and Molecular Therapeutics

**Session Title:** Novel Antitumor Agents

**Poster Title:** Preclinical characterization of potent and selective next-generation RET inhibitors

**Abstract Number:** 1464

**Session Category:** Experimental and Molecular Therapeutics

**Session Title:** Tyrosine Kinase and Phosphatase Inhibitors

### About Retevmo® (selpercatinib)

Retevmo (selpercatinib, formerly known as LOXO-292) (pronounced reh-TEHV-moh) is a selective and potent RET kinase inhibitor. 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 an 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.<sup>1</sup> Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials.

### About ALIMTA® (pemetrexed for injection)

ALIMTA is indicated in combination with pembrolizumab and platinum chemotherapy for the initial treatment of patients with metastatic nonsquamous non-small cell lung cancer, with no EGFR or ALK genomic tumor aberrations. **Limitation of Use:** ALIMTA is not indicated for the treatment of patients with squamous cell non-small cell lung cancer. For all FDA-approved indications for ALIMTA, please see full [Prescribing Information](#).

### About Sintilimab

Sintilimab injection is an innovative drug with global quality standards jointly developed by Innovent and Lilly in China. Sintilimab has been granted marketing approval by the NMPA for the treatment of relapsed or refractory classic Hodgkin's lymphoma after at least two lines of systemic chemotherapy and was included in the 2019 Guidelines of Chinese Society of Clinical Oncology for Lymphoid Malignancies.

In April 2020, the NMPA accepted the supplemental new drug application for sintilimab in combination with ALIMTA (pemetrexed for injection) and platinum as first-line therapy in advanced or recurrent non-squamous non-small cell lung cancer (NSCLC). In May 2020, sintilimab combined with gemcitabine and platinum chemotherapy met the predefined primary endpoint in the Phase 3 ORIENT-12 study as first-line therapy in patients with locally advanced or metastatic squamous NSCLC. Sintilimab monotherapy met the primary endpoint in the ORIENT-2 study as second-line therapy in patients with advanced or metastatic esophageal squamous cell carcinoma as well. In August 2020, the NMPA accepted the sNDA for sintilimab in combination with gemcitabine and platinum chemotherapy as first-line therapy in patients with locally advanced or metastatic squamous NSCLC.

Sintilimab is a type of immunoglobulin G4 monoclonal antibody, which binds to PD-1 molecules on the surface of T-cells, blocks the PD-1/ PD-Ligand 1 (PD-L1) pathway and reactivates T-cells to kill cancer cells. Innovent is currently conducting more than 20 clinical studies with sintilimab to evaluate its safety and efficacy in a wide variety of cancer indications, including more than 10 registrational or pivotal clinical trials.

Sintilimab injection is not an approved product in the United States. ALIMTA (pemetrexed for injection) is not approved for use in combination with sintilimab in the United States.

### IMPORTANT SAFETY INFORMATION FOR RETEVMO® (selpercatinib)

**Hepatotoxicity:** Serious hepatic adverse reactions occurred in 2.6% of patients treated with Retevmo. Increased aspartate aminotransferase (AST) occurred in 51% of patients, including Grade 3 or 4 events in 8% and increased alanine aminotransferase (ALT) occurred in 45% of patients, including Grade 3 or 4 events in 9%. The median time to first onset for increased AST was 4.1 weeks (range: 5 days to 2 years) and increased ALT was 4.1 weeks (range: 6 days to 1.5 years). 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.

**Hypertension** occurred in 35% of patients, including Grade 3 hypertension in 17% and Grade 4 in one (0.1%) patient. Overall, 4.6% 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 6% of patients and an increase in the QTcF interval of at least 60 ms over baseline was measured in 15% 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 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  $\geq 3$  hemorrhagic events occurred in 2.3% of patients treated with Retevmo including 3 (0.4%) patients with fatal hemorrhagic events, including one case each of cerebral hemorrhage, tracheostomy site hemorrhage, and hemoptysis. Permanently discontinue Retevmo in patients with severe or life-threatening hemorrhage.

**Hypersensitivity** occurred in 4.3% of patients receiving Retevmo, including Grade 3 hypersensitivity in 1.6%. The median time to onset was 1.7 weeks (range 6 days to 1.5 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 1% 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.

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 seliperatinib 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 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 at least 1 week after the final dose. There are no data on the presence of seliperatinib 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 final dose.

**Severe adverse reactions (Grade 3-4) occurring in  $\geq 15\%$  of patients who received Retevmo in LIBRETTO-001**, were hypertension (18%), prolonged QT interval (4%), diarrhea (3.4%), dyspnea (2.3%), fatigue (2%), abdominal pain (1.9%), hemorrhage (1.9%), headache (1.4%), rash (0.7%), constipation (0.6%), nausea (0.6%), vomiting (0.3%), and edema (0.3%).

**Serious adverse reactions occurred in 33%** of patients who received Retevmo. The most frequently reported serious adverse reaction (in  $\geq 2\%$  of patients) was pneumonia.

**Fatal adverse reactions occurred in 3% of patients**; fatal adverse reactions which occurred in >1 patient included sepsis (n=3), cardiac arrest (n=3) and respiratory failure (n=3).

**Common adverse reactions (all grades) occurring in  $\geq 15\%$  of patients who received Retevmo in LIBRETTO-001**, were dry mouth (39%), diarrhea (37%), hypertension (35%), fatigue (35%), edema (35%), rash (27%), constipation (25%), nausea (23%), abdominal pain (23%), headache (23%), cough (18%), prolonged QT interval (17%), dyspnea (16%), vomiting (15%), and hemorrhage (15%).

**Laboratory abnormalities (all grades; Grade 3-4)  $\geq 20\%$  worsening from baseline in patients who received Retevmo in LIBRETTO-001**, were AST increased (51%; 8%), ALT increased (45%; 9%), increased glucose (44%; 2.2%), decreased leukocytes (43%; 1.6%), decreased albumin (42%; 0.7%), decreased calcium (41%; 3.8%), increased creatinine (37%; 1.0%), increased alkaline phosphatase (36%; 2.3%), decreased platelets (33%; 2.7%), increased total cholesterol (31%; 0.1%), decreased sodium (27%; 7%), decreased magnesium (24%; 0.6%), increased potassium (24%; 1.2%), increased bilirubin (23%; 2.0%), and decreased glucose (22%; 0.7%).

Concomitant use of **acid-reducing agents** decreases seliperatinib 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 seliperatinib 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 seliperatinib 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.

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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## **IMPORTANT SAFETY INFORMATION FOR ALIMTA® (pemetrexed for injection)**

### **CONTRAINDICATION**

- ALIMTA is contraindicated in patients who have a history of severe hypersensitivity reaction to pemetrexed.

### **WARNINGS AND PRECAUTIONS**

#### **Myelosuppression and Increased Risk of Myelosuppression Without Vitamin Supplementation**

- ALIMTA can cause severe myelosuppression resulting in a requirement for transfusions and which may lead to neutropenic infection. The risk of myelosuppression is increased in patients who do not receive vitamin supplementation.
- Prior to treatment with ALIMTA, patients must be instructed to initiate supplementation with oral folic acid. Intramuscular injections of vitamin B12 are also required prior to ALIMTA treatment. Folic acid and vitamin B12 supplementation should be continued during treatment and for 21 days after the last dose of ALIMTA as they may reduce the severity of treatment-related hematologic and gastrointestinal toxicities. Obtain a complete blood count at the beginning of each cycle. Do not administer ALIMTA until the ANC is at least 1500 cells/mm<sup>3</sup> and platelet count is at least 100,000 cells/mm<sup>3</sup>. Permanently reduce ALIMTA in patients with an ANC of less than 500 cells/mm<sup>3</sup> or platelet count of less than 50,000 cells/mm<sup>3</sup> in previous cycles.
- In Studies JMDB and JMCH, among patients who received vitamin supplementation, incidence of Grade 3-4 neutropenia was 15% and 23%, the incidence of Grade 3-4 anemia was 6% and 4%, and incidence of Grade 3-4 thrombocytopenia was 4% and 5%, respectively. In Study JMCH, 18% of patients in the ALIMTA arm required red blood cell transfusions compared to 7% of patients in the cisplatin arm. In Studies JMEN, PARAMOUNT, and JMEI, where all patients received vitamin supplementation, incidence of Grade 3-4 neutropenia ranged from 3% to 5%, and incidence of Grade 3-4 anemia ranged from 3% to 5%.

#### **Renal Failure**

- ALIMTA can cause severe, and sometimes fatal, renal toxicity. Determine creatinine clearance before each dose and periodically monitor renal function during treatment with ALIMTA.
- The incidences of renal failure in clinical studies in which patients received ALIMTA with cisplatin were 2.1% in Study JMDB and 2.2% in Study JMCH. The incidence of renal failure in clinical studies in which patients received ALIMTA as a single agent ranged from 0.4% to 0.6% (Studies JMEN, PARAMOUNT, and JMEI).
- Withhold ALIMTA in patients with a creatinine clearance of less than 45 mL/min.

#### **Bullous and Exfoliative Skin Toxicity**

- Serious and sometimes fatal, bullous, blistering, and exfoliative skin toxicity, including cases suggestive of Stevens-Johnson Syndrome/toxic epidermal necrolysis, can occur with ALIMTA. Permanently discontinue ALIMTA for severe and life-threatening bullous, blistering, or exfoliating skin toxicity.

#### **Interstitial Pneumonitis**

- Serious interstitial pneumonitis, including fatal cases, can occur with ALIMTA treatment. Withhold ALIMTA for acute onset of new or progressive unexplained pulmonary symptoms such as dyspnea, cough, or fever pending diagnostic evaluation. If pneumonitis is confirmed, permanently discontinue ALIMTA.

## Radiation Recall

- Radiation recall can occur with ALIMTA in patients who have received radiation weeks to years previously. Monitor patients for inflammation or blistering in areas of previous radiation treatment. Permanently discontinue ALIMTA for signs of radiation recall.

## Increased Risk of Toxicity With Ibuprofen in Patients With Renal Impairment

- Exposure to ALIMTA is increased in patients with mild to moderate renal impairment who take concomitant ibuprofen, increasing the risks of adverse reactions of ALIMTA. In patients with creatinine clearances between 45 mL/min and 79 mL/min, avoid administration of ibuprofen for 2 days before, the day of, and 2 days following administration of ALIMTA. If concomitant ibuprofen use cannot be avoided, monitor patients more frequently for ALIMTA adverse reactions, including myelosuppression, renal, and gastrointestinal toxicity.

## Embryo-Fetal Toxicity

- Based on findings from animal studies and its mechanism of action, ALIMTA can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, intravenous administration of pemetrexed to pregnant mice during the period of organogenesis was teratogenic, resulting in developmental delays and increased malformations at doses lower than the recommended human dose of 500 mg/m<sup>2</sup>. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with ALIMTA and for 6 months after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with ALIMTA and for 3 months after the final dose.

## DRUG INTERACTIONS

- Ibuprofen increases exposure (AUC) of pemetrexed. In patients with creatinine clearance between 45 mL/min and 79 mL/min:
- Avoid administration of ibuprofen for 2 days before, the day of, and 2 days following administration of ALIMTA.
- Monitor patients more frequently for myelosuppression, renal, and gastrointestinal toxicity, if concomitant administration of ibuprofen cannot be avoided.

## ADVERSE REACTIONS

- Severe adverse reactions (Grade 3-4) occurring in ≥20% of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC) receiving ALIMTA in combination with pembrolizumab and platinum chemotherapy (carboplatin or cisplatin) versus ALIMTA with platinum chemotherapy + placebo for initial treatment (KEYNOTE-189), respectively, were fatigue (12% vs 6%); diarrhea (5% vs 3%); dyspnea (3.7% vs 5%); vomiting (3.7% vs 3%); nausea (3.5% vs 3.5%); rash (2% vs 2.5%); decreased appetite (1.5% vs 0.5%); constipation (1% vs 0.5%); and pyrexia (0.2% vs 0%).
- Common adverse reactions (all grades) occurring in ≥20% of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC) receiving ALIMTA in combination with pembrolizumab and platinum chemotherapy (carboplatin or cisplatin) versus ALIMTA with platinum chemotherapy + placebo for initial treatment (KEYNOTE-189), respectively, were nausea (56% vs 52%); fatigue (56% vs 58%); constipation (35% vs 32%); diarrhea (31% vs 21%); decreased appetite (28% vs 30%); rash (25% vs 17%); vomiting (24% vs 23%); cough (21% vs 28%); dyspnea (21% vs 26%); and pyrexia (20% vs 15%).

## USE IN SPECIFIC PATIENT POPULATIONS

- **Lactation:** There is no information regarding the presence of pemetrexed or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for serious adverse reactions in breastfed infants from ALIMTA, advise women not to breastfeed during treatment with ALIMTA and for one week after the last dose.
- **Males of Reproductive Potential:** ALIMTA may impair fertility in males of reproductive potential. It is not known whether these effects on fertility are reversible.
- **Pediatric Use:** The safety and effectiveness of ALIMTA in pediatric patients have not been established. Adverse reactions observed in pediatric patients studied were similar to those observed in adults.
- **Patients with Renal Impairment:** ALIMTA is primarily excreted by the kidneys. Decreased renal function results in reduced clearance and greater exposure (AUC) to ALIMTA compared with patients with normal renal function. No dose is recommended for patients with creatinine clearance less than 45 mL/min.
- **Geriatric:** The incidences of Grade 3-4 anemia, fatigue, thrombocytopenia, hypertension, and neutropenia were higher in patients 65 years of age and older as compared to younger patients: in at least one of five randomized clinical trials.

sections in the full [Prescribing Information](#) and [Patient Prescribing Information](#).

#### 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](http://lilly.com) and [lilly.com/newsroom](http://lilly.com/newsroom). 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 various therapies under development by Lilly and Loxo Oncology at Lilly, presentation of related data, and Lilly and Loxo Oncology's strategy and pipeline, 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, and commercialization. Among other things, there can be no guarantee that studies will be initiated or completed as planned, that future study results will be consistent with the results to date, or that any of these therapies will receive initial regulatory approvals or approvals for additional indications, as applicable, 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.

<sup>i</sup> RETEVMO [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021.

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