Updated Data from the Phase 1/2 Study of Olomorasib in KRAS G12C-Mutant Advanced Solid Tumors Presented at the 2024 ASCO® Annual Meeting

June 1, 2024

Data demonstrated promising monotherapy activity with olomorasib across a range of KRAS G12C-mutant solid tumors, including non-small cell lung cancer, and a tolerability profile in combination with pembrolizumab that is well-suited to first-line lung cancer development

INDIANAPOLIS, June 1, 2024 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced updated data from the Phase 1/2 clinical trial evaluating olomorasib as a monotherapy in patients with *KRAS* G12C-mutant advanced solid tumors and in combination with Merck's anti-PD-1 therapy KEYTRUDA® (pembrolizumab) in patients with *KRAS* G12C-mutant advanced non-small cell lung cancer (NSCLC). Olomorasib is an investigational, oral, potent, and highly selective second-generation inhibitor of the KRAS G12C protein. These data will be shared in oral presentations at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting.

"Despite recent advances, there remains a significant unmet need for patients with *KRAS* G12C-mutant cancers," said Timothy Burns, M.D., Ph.D., Associate Professor of Medicine, University of Pittsburgh Medical Center Hillman Cancer Center. "These data show efficacy with olomorasib across tumor types and, importantly, tolerability that suggests it can be combined with immunotherapy, the backbone of first-line treatment for *KRAS*-mutant NSCLC. In NSCLC, it is also exciting to see promising activity in patients previously treated with a KRAS G12C inhibitor as well as central nervous system (CNS) activity, consistent with the improved potency of this second generation KRAS G12C inhibitor. Collectively, these data point to a promising emerging profile for olomorasib, particularly in NSCLC where new options are needed to improve outcomes for patients."

"As a second generation KRAS G12C inhibitor, olomorasib was specifically designed to offer a differentiated profile that could potentially overcome limitations of currently available treatment options," said David Hyman, M.D., chief medical officer, Lilly. "With these updated data, we are pleased to see our thesis for olomorasib continuing to translate clinically. Through our SUNRAY-01 study, we look forward to further investigating the potential of olomorasib in combination with pembrolizumab-containing regimens in first-line NSCLC, where there remains great need to further impact the disease trajectory for patients with *KRAS* G12C-mutant lung cancers."

Data from the LOXO-RAS-20001 Phase 1/2 Study
Results presented at ASCO utilized a cutoff date of March 18, 2024. Efficacy results are based on investigator response assessments, and objective response rates (ORR) include responses that are confirmed, as well as those pending confirmation and ongoing.

Olomorasib as Monotherapy in KRAS G12C-Mutant Advanced Solid Tumors

An oral presentation (abstract #3007) detailed updated data for olomorasib monotherapy in patients with *KRAS* G12C-mutant advanced solid tumors. This dataset consisted of 184 patients, including 42 with NSCLC naïve to a KRAS G12C inhibitor (six with active brain metastases), 41 with NSCLC who had received a prior KRAS G12C inhibitor, 32 with colorectal cancer (CRC), 24 with pancreatic cancer, and 45 with other solid tumors. Patients had received a median of three prior lines of therapy (range 0-11).

Efficacy for olomorasib monotherapy was consistent across a range of solid tumors with an ORR of 35% (37/105) in patients with non-CRC solid tumors. Median progression free survival (PFS) in all patients with KRAS G12C inhibitor-naive non-CRC solid tumors was 7.1 months (95% CI: 5.5-8.9) and 7.9 months (95% CI: 4.1-NE) in patients with KRAS G12C inhibitor-naive NSCLC. In patients with NSCLC previously treated with a KRAS G12C inhibitor, the ORR was 41% (16/39), with 63% having received a KRAS G12C inhibitor as their immediate prior therapy, and median PFS was 8.1 months (95% CI: 5.6-15.6). Preliminary CNS activity was seen, with CNS responses observed in patients with NSCLC and measurable brain metastases.

Patients were on treatment for a median of 4.7 months and treatment-related adverse events (TRAEs) were predominantly grade 1 with only diarrhea seen in greater than 15% of patients. The most common TRAEs of any grade were diarrhea (23%), nausea (11%), and fatigue (10%). The safety profile for patients who discontinued a prior KRAS G12C inhibitor due to toxicity was similar to all patients treated with olomorasib monotherapy including patients who discontinued their previous first KRAS G12C inhibitor due to toxicity. TRAEs led to discontinuation of olomorasib in 1% of patients.

Olomorasib in Combination with Pembrolizumab in KRAS G12C-Mutant Advanced NSCLC

An oral presentation (abstract #8510) detailed updated data for olomorasib in combination with pembrolizumab in patients with *KRAS* G12C-mutant advanced NSCLC, studying the two doses (50mg and 100mg BID) under ongoing investigation in first-line NSCLC. This dataset consisted of 64 patients, including patients with first-line metastatic disease and those previously treated (prior KRAS G12C inhibitor, chemotherapy, and/or immunotherapy). Patients received a median of two prior lines of therapy (range: 0-8).

In patients with first-line metastatic NSCLC, across a range of PD-L1 levels, the ORR for olomorasib in combination with pembrolizumab was 77% (13/17) and median PFS was not reached with follow-up ongoing. The most common TRAEs of any grade were diarrhea (23%), increased ALT (20%), pruritus (19%), increased AST (16%), and fatigue (16%). TRAEs led to discontinuation of olomorasib only in 3% of patients (2/64), pembrolizumab only in 11% of patients (7/64) and both drugs in 5% of patients (3/64).

The SUNRAY-01 trial (NCT06119581), a global, registrational study investigating olomorasib in combination with pembrolizumab or pembrolizumab plus chemotherapy in first-line NSCLC, is currently enrolling.

About the LOXO-RAS-20001 Study
LOXO-RAS-20001 is an open-label, multicenter, Phase 1/2 study evaluating the safety, tolerability and preliminary efficacy of olomorasib in patients with *KRAS* G12C-mutant advanced solid tumors (NCT04956640). The study includes a Phase 1a dose escalation phase of olomorasib monotherapy in *KRAS* G12C-mutant solid tumors and a Phase 1b dose expansion and optimization phase which are evaluating olomorasib as a monotherapy and in combination with other treatments.

About Olomorasib
Olomorasib (LY3537982) is an investigational, oral, potent, and highly selective second-generation inhibitor of the KRAS G12C protein. *KRAS* is the most common oncogene across all tumor types, and *KRAS* G12C mutations occur in 13% of patients with non-small cell lung cancer (NSCLC) and 1-3% of patients with other solid tumors.[1,2] Olomorasib was specifically designed to target *KRAS* G12C mutations and has pharmacokinetic properties which allow for high predicted target occupancy and high potency when used as monotherapy or in combination.[3]

Olomorasib is currently being studied in the LOXO-RAS-20001 Phase 1/2 trial (NCT04956640) in patients with *KRAS* G12C-mutant NSCLC and other advanced solid tumors and in the pivotal, registrational SUNRAY-01 global study (NCT06119581) investigating olomorasib in combination with pembrolizumab with or without chemotherapy for first-line treatment of *KRAS* G12C-mutant advanced NSCLC. For additional information about olomorasib clinical trials, please refer to clinicaltrials.gov.

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 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 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 olomorasib as a potential treatment for people with certain *KRAS* G12C-mutant advanced solid tumors 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, that olomorasib will prove to be a safe and effective treatment for people with certain *KRAS* G12C-mutant advanced solid tumors, that olomorasib receive regulatory approval, or that Lilly will execute its strategy as expected. 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.

[1] Canon J. et al. Nature 2019, 575, 217-223

[2] Salem M. et al. Ann Oncol 2021, 32 (3 Suppl): S218

[3] Peng S-B, Si C, Zhang Y, et al. Abstract 1259: Preclinical characterization of Ly3537982, a novel, highly selective and potent KRAS-G12C inhibitor. *Cancer Research*. 2021;81(13_Supplement):1259-1259. doi:10.1158/1538-7445.am2021-1259

Refer to: Megan Talon; megan.talon@lilly.com; 463-209-1470 (Media)
Joe Fletcher; jfletcher@lilly.com; 317-296-2884 (Investors)

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