Lilly Opens First Ever Randomized Phase 3 Clinical Trial in Treatment-Naïve RET Fusion-Positive Non-Small Cell Lung Cancer

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- LIBRETTO-431 Phase 3 trial to examine selpercatinib (LOXO-292) against standard of care

- Trial aims to enroll 400 patients with advanced or metastatic treatment-naïve RET fusion-positive NSCLC

INDIANAPOLIS, Dec. 11, 2019 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced the opening of the LIBRETTO-431 clinical trial [NCT04194944] for selpercatinib, also known as LOXO-292, for treatment-naïve *RET* fusion-positive non-small cell lung cancer (NSCLC) patients. Enrolled trial participants will be randomized to receive either selpercatinib or platinum-based (carboplatin or cisplatin) and pemetrexed therapy with or without pembrolizumab as initial treatment of their advanced or metastatic *RET* fusion-positive NSCLC.

"Given the remarkable results of the LIBRETTO-001 trial, I am excited to open this important Phase 3 trial of selpercatinib, a highly selective and potent molecule that has previously demonstrated sustained responses with a well-tolerated safety profile," said Professor Ben Solomon, principal investigator at the Peter MacCallum Cancer Centre in Melbourne Australia. "This trial endeavors to generate outcome data that place patients with *RET* fusions alongside those with EGFR mutations and ALK fusions, as driver-positive populations that should be treated with targeted therapies in the first-line setting, rather than chemoimmunotherapy."

"This is an important milestone in the journey to further demonstrate the benefit of selpercatinib and the potential for people living with advanced or metastatic *RET* fusion-positive non-small cell lung cancer in the first-line setting against the current standard of care," said Anne White, president of Lilly Oncology. "Launching a trial of this size underscores the importance of now including *RET* fusions in the paradigm of genomic testing in lung cancer."

Trial Background

LIBRETTO-431 is a randomized Phase 3 clinical trial of patients with treatment-naïve *RET* fusion-positive NSCLC. The trial will enroll 400 patients with advanced or metastatic *RET* fusion-positive NSCLC who have received no prior systemic therapy for metastatic disease. Enrolled trial participants will be randomized 1:1 to receive either selpercatinib or platinum-based (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 progression-free survival (PFS) and secondary endpoints include overall survival (OS), overall response rate (ORR), duration of response (DoR), and intracranial ORR. For patients randomized to the control arm, crossover is allowed at progression.

About Selpercatinib (LOXO-292)

Selpercatinib, also known as LOXO-292, is a highly selective and potent, oral investigational new medicine in clinical development for the treatment of patients with cancers that harbor abnormalities in the rearranged during transfection (RET) kinase. *RET* fusions and mutations occur across multiple tumor types with varying frequency. Selpercatinib was designed to inhibit native RET signaling as well as anticipated acquired resistance mechanisms.

Selpercatinib has received breakthrough designations in *RET* fusion-positive NSCLC, *RET*-mutant medullary thyroid cancer (MTC) and *RET* fusion-positive thyroid cancers.

About *RET*-Altered Cancers

Genomic alterations in 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 2 percent of non-small cell lung cancer, 10-20 percent of papillary and other thyroid cancers and a subset of other cancers. Activating *RET* point mutations account for approximately 60 percent of MTC. *RET* fusion cancers and *RET*-mutant MTC are primarily dependent on this single activated kinase for their proliferation and survival. This dependency, often referred to as "oncogene addiction," renders such tumors highly susceptible to small molecule inhibitors targeting RET.

About Lilly Oncology

For more than 50 years, Lilly has been dedicated to delivering life-changing medicines and support to people living with cancer and those who care for them. Lilly is determined to build on this heritage and continue making life better for all those affected by cancer around the world. To learn more about Lilly's commitment to people with cancer, please visit www.LillyOncology.com.

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 and lilly.com/newsroom. P-LLY

Lilly Forward-Looking Statement

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Lilly's oral selpercatinib monotherapy (LOXO-292) for the potential treatment of *RET* fusion-positive non-small cell lung cancer and reflects Lilly's current

belief. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date or that selpercatinib will receive regulatory approvals 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.

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