Lilly Announces Positive Results for Selpercatinib (LOXO-292), Demonstrating a 68 Percent Objective Response Rate and Sustained Durability in Heavily Pretreated RET Fusion-Positive Non-Small Cell Lung Cancer

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- LIBRETTO-001 is the largest trial ever reported in RET-altered cancer patients
- 68 percent objective response rate (ORR) in the registration dataset (n=105) of RET fusion-positive NSCLC patients who had previously received chemotherapy
- 85 percent ORR in treatment-naïve RET fusion-positive NSCLC patients
- First and only RET inhibitor to demonstrate a robust CNS ORR (91%)
- Sustained durability, measured by both Duration of Response and Progression-Free Survival
- Well-tolerated safety profile; low rate of discontinuation (1.7%) for treatment-related adverse events
- New Drug Application to be submitted by year-end

INDIANAPOLIS, Sept. 9, 2019 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today presented data from the LIBRETTO-001 clinical trial intended to support the registration of oral selpercatinib[1] monotherapy, also known as LOXO-292, for the treatment of *RET* fusion-positive non-small cell lung cancer (NSCLC). In the registration dataset consisting of the first 105 enrolled *RET* fusion-positive NSCLC patients with prior platinum-based chemotherapy, selpercatinib treatment resulted in a 68 percent objective response rate (ORR) (95% CI: 58-76%). This population was heavily pretreated (median of three prior systemic regimens; 55 percent previously treated with an anti-PD-1/PD-L1 antibody and 48 percent previously treated with at least one multikinase inhibitor) and ORR was similar regardless of prior therapy. Up to 50 percent of *RET* fusion-positive NSCLCs can metastasize to the brain, and in the subset of patients with brain metastases in the registrational dataset, selpercatinib treatment demonstrated a CNS (Central Nervous System) ORR of 91 percent (95% CI: 59-100%).

As of the data cut-off date of June 17, 2019, median duration of response (DOR) was 20.3 months (95% CI: 13.8-24.0) and median progression-free survival (PFS) was 18.4 months (95% CI: 12.9-24.9). Since the majority of patients remain in response or progression-free as of the data cut-off date, these medians will continue to mature over time. In a safety analysis of all 531 patients enrolled to LIBRETTO-001, selpercatinib was well-tolerated, with only 9 patients (1.7%) discontinuing therapy due to treatment-related toxicity. The most commonly observed adverse events, regardless of attribution, were dry mouth, diarrhea, hypertension, increased liver enzymes, fatigue, constipation, and headache. These results were presented in the Presidential Symposium Session at the 2019 World Conference on Lung Cancer (WCLC) in Barcelona, Spain, hosted by the International Association for the Study of Lung Cancer (IASLC). Selpercatinib has received breakthrough therapy designation from the U.S. Food and Drug Administration.

"In this large cohort, selpercatinib's response rate, durability, robust CNS activity, and safety show promise. Furthermore, this continues to confirm that *RET* fusions are clinically targetable alterations, placing them in the company of activating EGFR/ALK/ROS1 alterations. We are encouraged by these data as there is currently an unmet need to provide genomically-tailored therapy to patients with *RET* fusion-positive NSCLCs," said Alexander Drilon, M.D., lead investigator, Memorial Sloan Kettering Cancer Center in New York City.

Additional Data in Treatment-Naïve *RET* Fusion-Positive NSCLC Patients
Investigators also presented the results of selpercatinib in treatment-naïve *RET* fusion-positive NSCLC patients. In this analysis of 34 patients, selpercatinib treatment resulted in an 85 percent ORR (95% CI: 69-95%). Median DOR and PFS were not reached in this treatment-naïve population, as the majority of patients remain in response or progression-free.

"We're seeing the importance of precision medicines, designed for specific patients, grow in oncology," said Anne White, president of Lilly Oncology. "The data from LIBRETTO-001 show that selpercatinib, also known as LOXO-292, represents an important new advance for patients with *RET* fusion-positive non-small cell lung cancer, emblematic of the kinds of new oncology medicines we hope to continue to bring forward at Lilly Oncology. We're very excited to partner with Loxo Oncology to continue to accelerate this important medicine. In two and half years, Loxo Oncology advanced this molecule from first human dose to submission ready data, demonstrating the power of precision oncology to rapidly translate scientific discovery into treatments for patients."

"When we first started the selpercatinib discovery program, we hoped to build a RET inhibitor that would deliver for patients with *RET*-altered cancers in the way that medicines such as osimertinib and alectinib have delivered for EGFR-mutated and ALK-fusion patients, respectively. We believe that the selpercatinib data presented at World Lung validate these efforts," said Josh Bilenker, M.D., interim senior vice president of oncology research and early phase development at Lilly, and CEO of Loxo Oncology, a wholly owned subsidiary of Lilly. "We look forward to submitting the NDA later this year, and should selpercatinib receive regulatory approval, patients with *RET* fusion-positive NSCLC will finally have their first genomically-guided medicine."

Trial Background
The LIBRETTO-001 Phase 1/2 trial is the largest clinical trial of patients with *RET*-altered cancers treated with a RET inhibitor. The trial includes a dose escalation phase (Phase 1) and a dose expansion phase (Phase 2). The Phase 2 portion of the trial had a primary endpoint of objective response rate (ORR) and secondary endpoints of duration of response, progression free survival and safety. The primary analysis set for NSCLC

regulatory submissions, as defined with the U.S. Food and Drug Administration, consists of the first 105 enrolled patients with *RET* fusion-positive non-small cell lung cancer who have experienced prior platinum-based chemotherapy. All data presented at WCLC were as of a data cut-off date of June 17, 2019, and all efficacy measures utilized investigator assessments.

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 designation for the treatment of patients with:

- Metastatic *RET* fusion-positive non-small cell lung cancer who require systemic therapy and have progressed following platinum-based chemotherapy and an anti-PD-1 or anti-PD-L1 therapy;
- *RET*-mutant medullary thyroid cancer (MTC) who require systemic therapy, have progressed following prior treatment and have no acceptable alternative treatment options; and for
- Advanced *RET*-fusion-positive thyroid cancer who require systemic therapy, have progressed following prior treatment and have no acceptable alternative treatment options.

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-positive 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.

[1] PINN, pending USAN approval

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View original content to download multimedia:http://www.prnewswire.com/news-releases/lilly-announces-positive-results-for-selpercatinib-loxo-292-demonstrating-a-68-percent-objective-response-rate-and-sustained-durability-in-heavily-pretreated-ret-fusion-positive-non-small-cell-lung-cancer-300913590.html

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