Lilly Receives FDA Priority Review for the Selpercatinib New Drug Application

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INDIANAPOLIS, Jan. 29, 2020 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today that the U.S. Food and Drug Administration (FDA) has granted priority review for the New Drug Application (NDA) for selpercatinib (LOXO-292), for the treatment of patients with advanced *RET* fusion-positive non-small cell lung cancer (NSCLC), *RET*-mutant medullary thyroid cancer (MTC) and *RET* fusion-positive thyroid cancer. The NDA is based on data from the LIBRETTO-001 Phase 1/2 trial in *RET*-altered lung and thyroid cancers. The FDA has filed the NDA and set a Prescription Drug User Fee Act (PDUFA) date in the third quarter of this year.

"We are pleased the FDA granted priority review status for the NDA for selpercatinib. This represents an important step toward providing a new precision therapy for people living with certain *RET*-driven cancers," said Anne White, president of Lilly Oncology. "Combined with the recent opening of our two Phase 3 selpercatinib clinical trials, we are thrilled with the positive momentum of this program and hope to deliver a practice-changing treatment to patients with *RET*-driven cancers as soon as possible."

In previous regulatory actions, based on early data from the Phase 1/2 LIBRETTO-001 trial, the FDA granted selpercatinib Breakthrough Therapy Designation for treatment in people with:

- Metastatic *RET*-fusion-positive NSCLC who require systemic therapy and have progressed following platinum-based chemotherapy and an anti-PD-1 or anti-PD-L1 therapy;
- *RET*-mutant MTC who require systemic therapy, have progressed following prior treatment and have no acceptable alternative treatment option; and
- Advanced *RET*-fusion-positive thyroid cancer who require systemic therapy, have progressed following prior treatment and have no acceptable alternative treatment options.

In 2019, selpercatinib received orphan drug designation for the treatment of *RET* fusion-positive NSCLC and for the treatment of *RET* fusion-positive and *RET*-mutant thyroid cancers including poorly differentiated thyroid cancer, undifferentiated or anaplastic thyroid cancer, MTC and locally advanced or metastatic follicular or papillary thyroid cancer.

In December of 2019, Lilly opened two selpercatinib Phase 3 trials: LIBRETTO-431 for patients with treatment-naïve *RET* fusion-positive NSCLC, and LIBRETTO-531 for patients with treatment-naïve *RET*-mutant MTC. Each trial will enroll 400 patients.

About *RET*-Driven 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 NSCLC, 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 LIBRETTO-001
The LIBRETTO-001 Phase 1/2 trial was the largest clinical trial of patients with *RET*-driven cancers treated with a *RET* inhibitor. The trial included 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 (DoR), progression free survival (PFS) and safety. Results from the NSCLC population were presented at the 2019 IASLC World Congress on Lung Cancer (WCLC), while results from the thyroid populations were presented at the European Society for Medical Oncology (ESMO) 2019 Congress.

About LIBRETTO-431
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 efficacy endpoints are PFS, overall survival (OS), ORR, DoR, and intracranial ORR. For patients randomized to the control arm, crossover is allowed at progression.

About LIBRETTO-531
LIBRETTO-531 is a randomized Phase 3 clinical trial of patients with treatment-naïve *RET*-mutant MTC. The trial will enroll 400 patients with advanced or metastatic *RET*-mutant MTC who have received no prior systemic therapy for metastatic disease. Enrolled trial participants will be randomized 2:1 to receive either selpercatinib or physician's choice of cabozantinib or vandetanib as initial treatment of their advanced or metastatic *RET*-mutant MTC. *RET* mutations may be identified using local testing. This trial's efficacy endpoints are PFS, treatment failure-free survival (TFFS), OS, ORR, and DoR. For patients randomized to the control arm, crossover is allowed at progression.

About Selpercatinib (LOXO-292)
Selpercatinib (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.

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 *RET* fusion-positive and *RET*-mutant thyroid cancers 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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