Lilly Opens Phase 3 Clinical Trial in RET-Mutant Medullary Thyroid Cancer

December 30, 2019

- LIBRETTO-531 is first ever Phase 3 trial in RET-mutant medullary thyroid cancer
- Randomized trial will examine selpercatinib against standard of care in 400 patients with advanced or metastatic treatment-naïve RET-mutant medullary thyroid cancer

INDIANAPOLIS, Dec. 30, 2019 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced the opening of the LIBRETTO-531 clinical trial [NCT04211337] for selpercatinib, also known as LOXO-292, for treatment-naïve *RET*-mutant medullary thyroid cancer (MTC) patients. This is the second Phase 3 trial to open for selpercatinib, 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. Enrolled trial participants will be randomized to receive either selpercatinib or physician's choice of cabozantinib or vandetanib as initial treatment of their advanced or metastatic *RET*-mutant MTC.

"Approximately 60 percent of people with medullary thyroid cancer have an activating *RET* point mutation, yet the current therapeutic options are not ideal for many patients," said Lori Wirth, MD, medical director of the Center for Head and Neck Cancer, Massachusetts General Hospital Cancer Center. "This Phase 3 trial of selpercatinib in patients with advanced or metastatic *RET*-mutant MTC seeks to confirm a new standard of care that we hope will provide a more effective treatment option for this patient population."

"While medullary thyroid cancer is rare, the occurrence of *RET* mutations in MTC is high," said Gary Bloom, executive director for ThyCa: Thyroid Cancer Survivors' Association, Inc. "For that reason, we are very excited about the opening of this Phase 3 trial because it shows promise for patients with advanced and metastatic *RET*-mutant MTC. Due to new treatment options, it is imperative that MTC patients discuss with their medical doctors if and when they should undergo genomic testing of their tumors. This will ensure that people with *RET* tissue mutations have access to potential treatments and clinical trials such as this one for selpercatinib."

Trial Background
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 progression-free survival (PFS), treatment failure-free survival (TFFS), overall survival (OS), overall response rate (ORR), and duration of response (DoR). 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*-altered 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.

Refer to: Becky Polston; becky.polston@lilly.com; 317-796-1028 (Lilly) – media
Kevin Hern; hern_kevin_r@lilly.com; 317-277-1838 (Lilly) – investors

View original content to download multimedia:http://www.prnewswire.com/news-releases/lilly-opens-phase-3-clinical-trial-in-ret-mutant-medullary-thyroid-cancer-300979626.html

SOURCE Eli Lilly and Company