Loxo Oncology at Lilly Announces Publication of Pirtobrutinib (LOXO-305) Phase 1/2 Data in The Lancet

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INDIANAPOLIS, March 5, 2021 /PRNewswire/ -- Loxo Oncology at Lilly, a research and development group of Eli Lilly and Company (NYSE: LLY), today announced that *The Lancet* has published data from the pirtobrutinib (previously referred to as LOXO-305) global Phase 1/2 BRUIN clinical trial in relapsed or refractory chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), mantle cell lymphoma (MCL), and other non-Hodgkin's lymphomas. Pirtobrutinib is an investigational, highly selective, non-covalent Bruton's tyrosine kinase (BTK) inhibitor.

The data in the publication include key findings previously presented at the 2020 American Society of Hematology (ASH) Annual Meeting. The publication includes safety and efficacy data for 323 relapsed or refractory patients (including 170 with CLL/SLL, 61 with MCL, 26 with Waldenström's macroglobulinemia and 66 with other B-cell lymphomas) that were enrolled to the BRUIN Phase 1/2 trial as of September 27, 2020.

"Patients with B-cell malignancies who have been previously treated with the most commonly used regimens represent an area of growing and urgent unmet need", said Anthony Mato, M.D., director of the CLL Program at Memorial Sloan Kettering Cancer Center and lead author of *The Lancet* paper. "These data establish that the third generation BTK inhibitor pirtobrutinib possesses a compelling efficacy and safety profile with the potential to address this exact unmet need."

"While covalent BTK inhibitors and venetoclax have transformed the treatment of CLL, we now see many patients needing new therapeutic alternatives," said Brian Koffman, MDCM (retired), chief medical officer of the CLL Society. "In the coming years, we envision that this need will grow, and we are pleased to see data that pirtobrutinib may be a new option for these patients."

"We are extremely pleased to see the pirtobrutinib data from the ongoing Phase 1/2 BRUIN study published in *The Lancet* and shared with the broader clinical community", said David Hyman, M.D., chief medical officer of Loxo Oncology at Lilly. "The data to date from this study have continued to strengthen our conviction that pirtobrutinib has the potential to meaningfully improve the inadequate treatment options available to CLL and MCL patients who have been previously treated with the main treatment classes of today's standard of care. We are focused on quickly advancing the pirtobrutinib development program, including through a series of Phase 3 studies that will be initiated over the course of 2021."

In addition to the Phase 1/2 BRUIN clinical trial, Loxo Oncology at Lilly plans to initiate four global, randomized Phase 3 studies for pirtobrutinib in 2021, three in CLL and one in MCL.

About Pirtobrutinib (LOXO-305)
Pirtobrutinib is an investigational, oral, highly selective, non-covalent Bruton's tyrosine kinase (BTK) inhibitor. BTK plays a key role in the B-cell antigen receptor signaling pathway, which is required for the development, activation and survival of normal white blood cells, known as B-cells, and malignant B-cells. BTK is a validated molecular target found across numerous B-cell leukemias and lymphomas including chronic lymphocytic leukemia, mantle cell lymphoma, Waldenström macroglobulinemia, and marginal zone lymphoma. Currently available BTK inhibitors irreversibly inhibit BTK and the long-term efficacy of these therapies can be limited by acquired resistance, most commonly through BTK C481 mutations. In rapidly growing tumors with inherently high rates of BTK turnover, resistance to covalent BTK therapies may be the result of incomplete target inhibition. Pirtobrutinib was designed to reversibly bind BTK, deliver consistently high target coverage regardless of BTK turnover rate, preserve activity in the presence of the C481 acquired resistance mutations, and avoid off-target kinases that have complicated the development of both covalent and investigational non-covalent BTK inhibitors. Interested patients and physicians can contact the Loxo Oncology at Lilly Physician and Patient BTK Clinical Trial Hotline at 1-855-LOXO-305 or email clinicaltrials@loxooncology.com.

About the BRUIN Phase 1/2 Trial
This first-in-human, global, multi-center Phase 1/2 trial evaluates pirtobrutinib as a single agent in patients with previously treated chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), or non-Hodgkin's lymphomas (NHL). The trial includes a Phase 1 dose escalation phase and a Phase 2 dose expansion phase. The Phase 1 dose escalation enrolls patients with CLL/SLL or NHL who have received at least two prior lines of therapy and have progressed or are intolerant to standard of care. The dose escalation phase followed a "3+3" design with pirtobrutinib dosed orally in 28-day cycles. As dose cohorts were cleared, additional patients could enroll in cleared cohorts and intra-patient dose escalation was permitted. The primary objective of the Phase 1 portion of the trial is to determine the maximum tolerated dose and recommended Phase 2 dose. Key secondary objectives include measures of safety, pharmacokinetics, and anti-tumor activity (i.e. Overall Response Rate (ORR) and Duration of Response, as determined by appropriate histology-specific response criteria). In the Phase 2, patients are enrolled across various cohorts, depending on disease type and prior therapy. The primary endpoint for Phase 2 is ORR. Secondary endpoints include duration of response (DOR), overall survival (OS), safety, and pharmacokinetics (PK).

About Loxo Oncology at Lilly
Loxo Oncology at Lilly was created in December 2019, combining the Lilly Research Laboratories oncology organization and Loxo Oncology, which was acquired by Lilly in early 2019. Loxo Oncology at Lilly brings together the focus and spirit of a biotech with the scale and resources of large pharma, with the goal of rapidly delivering impactful new medicines for people with cancer. Our approach centers on creating new oncology medicines that unequivocally work early in clinical development and will matter to patients.

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

Disclosure: Dr. Mato has provided consulting and advisory services to Loxo Oncology at Lilly and Eli Lilly and Company.

Lilly 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 pirtobrutinib (LOXO-305) for the potential treatment of previously treated chronic lymphocytic leukemia, small lymphocytic lymphoma, mantle cell lymphoma and other non-Hodgkin lymphomas and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of research, development, and commercialization. Among other things, there can be no guarantee that studies will be initiated or completed as planned, that future study results will be consistent with the results to date, or that pirtobrutinib (LOXO-305) 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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View original content to download multimedia:http://www.prnewswire.com/news-releases/loxo-oncology-at-lilly-announces-publication-of-pirtobrutinib-loxo-305-phase-12-data-in-the-lancet-301241157.html

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