Loxo@Lilly Announces Details of Presentations at 2023 European Hematology Association (EHA) Annual Meeting

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INDIANAPOLIS, May 11, 2023 /PRNewswire/ -- Loxo@Lilly, the oncology unit of Eli Lilly and Company (NYSE: LLY), today announced that data from its oncology portfolio will be presented at the 2023 European Hematology Association (EHA) Annual Meeting, to be held June 8 – 11, 2023, in Frankfurt, Germany, and virtually. The company-sponsored abstracts include new analyses of clinical data in approved and investigational uses based on the BRUIN Phase 1/2 trial evaluating Jaypirca™ (pirtobrutinib) in patients with B-cell malignancies previously treated with a covalent Bruton's tyrosine kinase (BTK) inhibitor, including mantle cell lymphoma (MCL) and chronic lymphocytic leukemia (CLL).

A list of presentations, along with their viewing details, are shared below.

Medicine	Abstract Title	Presentation Details
Jaypirca (pirtobrutinib)	Genomic Evolution and Resistance to Pirtobrutinib in Covalent BTK-Inhibitor (cBTKi) Pre-treated Chronic Lymphocytic Leukemia (CLL) Patients: Results from the Phase 1/2 BRUIN Study	**Abstract Number:** S146 **Session Type**: Oral **Session Date / Time:** June 9 at 14:45 – 16:00 CEST
Jaypirca (pirtobrutinib)	Comparison of Bleeding-Related Events in Patients who Received Pirtobrutinib with and without Antithrombotic Agents	**Abstract Number:** P1088 **Session Type**: Poster **Session Date / Time:** June 9 at 18:00 – 19:00 CEST
Jaypirca (pirtobrutinib)	Matching-Adjusted Indirect Comparison (MAIC) of Pirtobrutinib vs Venetoclax Continuous Monotherapy in Patients with Relapsed/Refractory CLL Previously Treated with a Covalent BTK Inhibitor	**Abstract Number:** P623 **Session Type**: Poster **Session Date / Time:** June 9 at 18:00 – 19:00 CEST
Jaypirca (pirtobrutinib)	Patient-Reported Outcomes (PRO) Among Patients with Mantle Cell Lymphoma Receiving Pirtobrutinib After Prior Covalent BTKi: Interim PRO Analysis from the BRUIN Phase 1/2 Study	**Abstract Number:** P1112 **Session Type**: Poster **Session Date / Time:** June 9 at 18:00 – 19:00 CEST
LOXO-338	A First-in-Human Phase 1 Study of Oral LOXO-338, a Selective BCL2 Inhibitor, in Patients with Advanced Hematologic Malignancies	**Abstract Number:** P636 **Session Type**: Poster **Session Date / Time:** June 9 at 18:00 – 19:00 CEST

About Jaypirca™ (pirtobrutinib)
Jaypirca (pirtobrutinib, formerly known as LOXO-305) (pronounced jay-pihr-kaa) is a highly selective (300 times more selective for BTK versus 98% of other kinases tested in preclinical studies), non-covalent (reversible) inhibitor of the enzyme BTK.[1] BTK is a validated molecular target found across numerous B-cell leukemias and lymphomas including mantle cell lymphoma.[2,3] Jaypirca is a U.S. FDA-approved oral prescription medicine, 100 mg or 50 mg tablets taken as a once-daily 200 mg dose with or without food until disease progression or unacceptable toxicity.

INDICATION FOR JAYPIRCA
Jaypirca is a kinase inhibitor indicated for the treatment of adult patients with relapsed or refractory (R/R) mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor.

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

IMPORTANT SAFETY INFORMATION FOR JAYPIRCA ™(pirtobrutinib)

Infections: Fatal and serious infections (including bacterial, viral, or fungal) and opportunistic infections have occurred in patients treated with Jaypirca. In the clinical trial, Grade ≥3 infections occurred in 17% of 583 patients with hematologic malignancies, most commonly pneumonia (9%); fatal infections occurred in 4.1% of patients. Sepsis (4.5%) and febrile neutropenia (2.9%) occurred. Opportunistic infections after Jaypirca treatment included, but are not limited to, *Pneumocystis jirovecii* pneumonia and fungal infection. Consider prophylaxis, including vaccinations and antimicrobial prophylaxis, in patients at increased risk for infection, including opportunistic infections. Monitor patients for signs and symptoms, evaluate promptly, and treat appropriately. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

Hemorrhage: Fatal and serious hemorrhage has occurred with Jaypirca. Major hemorrhage (Grade ≥3 bleeding or any central nervous system bleeding) occurred in 2.4% of 583 patients with hematologic malignancies treated with Jaypirca, including gastrointestinal hemorrhage; fatal hemorrhage occurred in 0.2% of patients. Bleeding of any grade, excluding bruising and petechiae, occurred in 14% of patients. Major hemorrhage occurred in patients taking Jaypirca with (0.7%) and without (1.7%) antithrombotic agents. Consider risks/benefits of co-administering antithrombotic agents with Jaypirca. Monitor patients for signs of bleeding. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca. Consider benefit/risk of withholding Jaypirca 3-7 days pre- and post-surgery depending on type of surgery and bleeding risk.

Cytopenias: Grade 3 or 4 cytopenias, including neutropenia (24%), anemia (11%), and thrombocytopenia (11%), have developed in patients with hematologic malignancies treated with Jaypirca. In a clinical trial, Grade 4 neutropenia (13%) and Grade 4 thrombocytopenia (5%) developed. Monitor complete blood counts regularly during treatment. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

Atrial Fibrillation and Atrial Flutter: Atrial fibrillation or flutter were reported in 2.7% of patients, with Grade 3 or 4 atrial fibrillation or flutter reported in 1% of 583 patients with hematologic malignancies treated with Jaypirca. Patients with cardiac risk factors such as hypertension or previous arrhythmias may be at increased risk. Monitor for signs and symptoms of arrhythmias (e.g., palpitations, dizziness, syncope, dyspnea) and manage appropriately. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

Second Primary Malignancies: Second primary malignancies, including non-skin carcinomas, developed in 6% of 583 patients with hematologic malignancies treated with Jaypirca monotherapy. The most frequent malignancy was non-melanoma skin cancer (3.8%). Other second primary malignancies included solid tumors (including genitourinary and breast cancers) and melanoma. Advise patients to use sun protection and monitor for development of second primary malignancies.

Embryo-Fetal Toxicity: Based on animal findings, Jaypirca can cause fetal harm in pregnant women. Administration of pirtobrutinib to pregnant rats during organogenesis caused embryo-fetal toxicity, including embryo-fetal mortality and malformations at maternal exposures (AUC) approximately 3-times the recommended 200 mg/day dose. Advise pregnant women of potential risk to a fetus and females of reproductive potential to use effective contraception during treatment and for one week after last dose.

Adverse Reactions (ARs) in Patients with Mantle Cell Lymphoma Who Received Jaypirca
Serious ARs occurred in 38% of patients. Serious ARs occurring in ≥2% of patients were pneumonia (14%), COVID-19 (4.7%), musculoskeletal pain (3.9%), hemorrhage (2.3%), pleural effusion (2.3%), and sepsis (2.3%). **Fatal ARs** within 28 days of last dose of Jaypirca occurred in 7% of patients, most commonly due to infections (4.7%), including COVID-19 (3.1%).

Dose Modifications and Discontinuations: ARs led to dosage reductions in 4.7%, treatment interruption in 32%, and permanent discontinuation of Jaypirca in 9% of patients. ARs resulting in dosage modification in >5% of patients included pneumonia and neutropenia. ARs resulting in permanent discontinuation of Jaypirca in >1% of patients included pneumonia.

ARs (all Grades %; Grade 3-4 %) in ≥10% of Patients: fatigue (29; 1.6), musculoskeletal pain (27; 3.9), diarrhea (19; -), edema (18; 0.8), dyspnea (17; 2.3), pneumonia (16; 14), bruising (16; -), peripheral neuropathy (14; 0.8), cough (14; -), rash (14; -), fever (13; -), constipation (13; -), arthritis/arthralgia (12; 0.8), hemorrhage (11; 3.1), abdominal pain (11; 0.8), nausea (11; -), upper respiratory tract infections (10; 0.8), dizziness (10; -).

Select Laboratory Abnormalities (all Grades %; Grade 3 or 4 %) that Worsened from Baseline in ≥10% of Patients: hemoglobin decreased (42; 9), platelet count decreased (39; 14), neutrophil count decreased (36; 16), lymphocyte count decreased (32; 15), creatinine increased (30; 1.6), calcium decreased (19; 1.6), AST increased (17; 1.6), potassium decreased (13; 1.6), sodium decreased (13; -), lipase increased (12; 4.4), alkaline phosphatase increased (11; -), ALT increased (11; 1.6), potassium increased (11; 0.8). Grade 4 laboratory abnormalities in >5% of patients included neutrophils decreased (10), platelets decreased (7), lymphocytes decreased (6).

All grade ARs with higher frequencies in the total BRUIN population of patients with hematologic malignancies (n=583) were decreased neutrophil count (41%), bruising (20%), diarrhea (20%).

Drug Interactions
Strong CYP3A Inhibitors: Concomitant use with Jaypirca increased pirtobrutinib systemic exposure, which may increase risk of Jaypirca adverse reactions. Avoid use of strong CYP3A inhibitors during Jaypirca treatment. If concomitant use is unavoidable, reduce Jaypirca dosage according to the approved labeling.

Strong or Moderate CYP3A Inducers: Concomitant use with Jaypirca decreased pirtobrutinib systemic exposure, which may reduce Jaypirca efficacy. Avoid concomitant use of Jaypirca with strong or moderate CYP3A inducers. If concomitant use with moderate CYP3A inducers is unavoidable, increase the Jaypirca dosage according to the approved labeling.

Sensitive CYP2C8, CYP2C19, CYP3A, P-gP, BCRP Substrates: Concomitant use with Jaypirca increased their plasma concentrations, which may increase risk of adverse reactions related to these substrates for drugs that are sensitive to minimal concentration changes. Follow recommendations for these sensitive substrates in their approved labeling.

Use in Special Populations
Pregnancy and Lactation: Inform pregnant women of potential for Jaypirca to cause fetal harm. Verify pregnancy status in females of reproductive potential prior to starting Jaypirca and advise use of effective contraception during treatment and for one week after last dose. Presence of pirtobrutinib in human milk and effects on the breastfed child or on milk production is unknown. Advise women not to breastfeed while taking Jaypirca and for one week after last dose.

Geriatric Use: In the pooled safety population of patients with hematologic malignancies, 392 (67%) were ≥65 years of age. Patients aged ≥65 years experienced higher rates of Grade ≥3 ARs and serious ARs compared to patients <65 years of age.

Renal Impairment: Severe renal impairment (eGFR 15-29 mL/min) increases pirtobrutinib exposure. Reduce Jaypirca dosage in patients with severe renal impairment according to the approved labeling. No dosage adjustment is recommended in patients with mild or moderate renal impairment.

PT HCP ISI MCL APP

Please see Prescribing Information and Patient Information for Jaypirca.

About Lilly
Lilly unites caring with discovery to create medicines that make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 51 million people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges, redefining diabetes care, treating obesity and curtailing its most devastating long-term effects, advancing the fight against Alzheimer's disease, providing solutions to some of the most debilitating immune system disorders, and transforming the most difficult-to-treat cancers into manageable

diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/newsroom or follow us on Facebook, Instagram, Twitter and LinkedIn. P-LLY

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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 Lilly's oncology portfolio and pipeline, including Jaypirca™ as a treatment for people with mantle cell lymphoma (MCL) previously treated with a BTK inhibitor and as a potential treatment for patients with chronic lymphocytic leukemia (CLL) and LOXO-338 as a potential treatment for people with advanced hematologic malignancies and other conditions and the timeline for future readouts, presentations, and other milestones relating to Jaypirca and LOXO-338 and their clinical trials, and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned that future study results will be consistent with study results to date, that LOXO-338 will receive regulatory approvals or Jaypirca will receive additional regulatory approvals, that LOXO-338 or Jaypirca will be commercially successful, or that Lilly will execute its strategy as expected. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's 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. Mato AR, Shah NN, Jurczak W, et al. Pirtobrutinib in relapsed or refractory B-cell malignancies (BRUIN): a phase 1/2 study. *Lancet*. 2021;397(10277):892-901. doi:10.1016/S0140-6736(21)00224-5
2. Hanel W, Epperla N. Emerging therapies in mantle cell lymphoma. *J Hematol Oncol*. 2020;13(1):79. Published 2020 Jun 17. doi:10.1186/s13045-020-00914-1
3. Gu D, Tang H, Wu J, Li J, Miao Y. Targeting Bruton tyrosine kinase using non-covalent inhibitors in B cell malignancies. *J Hematol Oncol*. 2021;14(1):40. Published 2021 Mar 6. doi:10.1186/s13045-021-01049-7

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