Lilly to present data from two positive Phase 3 studies of Jaypirca (pirtobrutinib) in chronic lymphocytic leukemia at the 2025 American Society of Hematology (ASH) Annual Meeting

November 24, 2025

Results from the BRUIN CLL-314 study comparing Jaypirca (pirtobrutinib) to Imbruvica (ibrutinib) – the first-ever head-to-head Phase 3 study versus a covalent BTK inhibitor to include treatment-naïve CLL/SLL patients – will be presented as an oral presentation

Results from the Phase 3 BRUIN CLL-313 study of pirtobrutinib in patients with treatment-naïve CLL/SLL will be featured as a late-breaking oral presentation

Both BRUIN CLL-314 and BRUIN CLL-313 were selected to be part of the official ASH press program

INDIANAPOLIS, Nov. 24, 2025 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced that data from studies of Jaypirca (pirtobrutinib), the first and only approved non-covalent (reversible) Bruton tyrosine kinase (BTK) inhibitor, will be presented at the 67th American Society of Hematology (ASH) Annual Meeting and Exposition, taking place Dec. 6-9 in Orlando, Florida.

Key data presentations for Jaypirca include:

- In an oral presentation, Lilly will share results from the BRUIN CLL-314 study, comparing pirtobrutinib to Imbruvica (ibrutinib), a covalent BTK inhibitor, in patients with chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL). Lilly previously announced that pirtobrutinib met the primary endpoint of response rate non-inferiority, favoring pirtobrutinib with a nominal P-value for superiority < 0.05. BRUIN CLL-314 is the first-ever head-to-head Phase 3 study versus a covalent BTK inhibitor to include treatment-naïve patients. These results were also selected to be highlighted in the ASH Annual Meeting press program session on Dec. 7.
- In a late-breaking oral presentation, Lilly will share results from the Phase 3 BRUIN CLL-313 study of pirtobrutinib versus chemoimmunotherapy in patients with treatment-naïve CLL/SLL without del(17p). Lilly previously announced the study met its primary endpoint, demonstrating a highly statistically significant and clinically meaningful improvement in progression-free survival with pirtobrutinib compared to chemoimmunotherapy. These results were also selected to be highlighted in the ASH Annual Meeting press program session on Dec. 8.
- In other oral and poster presentations, Lilly will share additional data from the Phase 1/2 BRUIN study in patients with relapsed or refractory CLL, mantle cell lymphoma (MCL) and Waldenström macroglobulinemia (WM). These long-term data include efficacy and safety results with approximately five years of follow-up.
- In an oral presentation, results will be shared from an investigator-initiated Phase 2 study of time-limited treatment with a combination of pirtobrutinib, venetoclax, and obinutuzumab in treatment-naïve CLL.

"Building on our previous announcements of positive topline results for the Phase 3 BRUIN CLL-313 and CLL-314 studies, we are excited to share the full results at ASH," said Jacob Van Naarden, executive vice president and president of Lilly Oncology. "Collectively, data from across the pirtobrutinib development program and investigator-led studies reinforce the medicine's unique clinical profile and its potential role across treatment settings and B-cell malignancies."

A full list of abstract titles and viewing details are listed below:

Abstract Title	**Author**	**Presentation Type/#**	**Session Title**	**Session Date/Time (EST)**
Pirtobrutinib in relapsed/refractory (R/R) Waldenström macroglobulinemia (WM): Up to 5 years of follow-up from the Phase 1/2 BRUIN study	Chan Cheah	Oral Abstract #226	623. Mantle Cell, Follicular, Waldenstrom's, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological: FL and WM	Saturday, Dec. 6 2:45-3 p.m. EST
Real-world treatment patterns, patient characteristics, and outcomes of cBTKi-based therapies amongst a contemporary cohort of patients with R/R MCL in the United States	Kami Maddocks	Poster Abstract #2725	906. Outcomes Research: Lymphoid Malignancies Excluding Plasma Cell Disorders:	Saturday, Dec. 6 5:30-7:30 p.m. EST

			Poster I	
Real-world characteristics, treatment patterns and outcomes of patients with mantle cell lymphoma (MCL) after receiving covalent Bruton tyrosine kinase inhibitors (cBTKi) in China	Yuqin Song	Poster Abstract #2704	906. Outcomes Research: Lymphoid Malignancies Excluding Plasma Cell Disorders: Poster I	Saturday, Dec. 6 5:30-7:30 p.m. EST
Pirtobrutinib in post-cBTKi CLL/SLL: Final update from the Phase 1/2 BRUIN study with more than 5 years follow-up	William Wierda	Poster Abstract #2115	642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Poster I	Saturday, Dec. 6 5:30-7:30 p.m. EST
Pirtobrutinib in relapsed/refractory (R/R) mantle cell lymphoma (MCL): final update from the Phase 1/2 BRUIN study	Michael Wang	Oral Abstract #665	623. Mantle Cell, Follicular, Waldenstrom's, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological - Novel Treatments for and Insights into Mantle Cell Lymphoma	Sunday, Dec. 7 5:30-5:45 p.m. EST
Pirtobrutinib vs ibrutinib in treatment-naïve and relapsed/refractory CLL/SLL: Results from the first randomized Phase 3 study comparing a non-covalent and covalent BTK inhibitor	Jennifer Woyach	Oral Abstract #683	642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Frontline Treatment Strategies for CLL	Sunday, Dec. 7 5:30-5:45 p.m. EST
Efficacy of pirtobrutinib monotherapy in treatment-naïve chronic lymphocytic leukemia: A Bayesian network meta-analysis of randomized controlled trials	Toby Eyre	Poster Abstract #5684	642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Poster III	Monday, Dec. 8 6-8 p.m. EST
Pirtobrutinib outcomes in second-line (2L) chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) after first-line (1L) cBTKi therapy: A pooled analysis from the BRUIN LOXO-BTK-18001 and BRUIN CLL-321 studies	Toby Eyre	Poster Abstract #5670	642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Poster III	Monday, Dec. 8 6-8 p.m. EST
Pirtobrutinib vs bendamustine plus rituximab (BR) in patients with CLL/SLL: First results from a randomized Phase 3 study examining a non-covalent BTK inhibitor in untreated patients	Wojciech Jurczak	Oral Abstract #LBA-3	Late-Breaking Abstracts Session	Tuesday, Dec. 9 8-8:15 a.m. EST
Investigator-Initiated				
Pirtobrutinib, venetoclax, and obinutuzumab for patients with Richter transformation: A Phase 2 trial	Nitin Jain	Oral Abstract #89	642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Treatment of CLL in Relapse and in Richter Transformation	Saturday, Dec. 6 10:30-10:45 a.m. EST
High VGPR/CR rates with pirtobrutinib plus venetoclax in previously treated Waldenström macroglobulinemia: Results from a multicenter Phase 2 study	Jorge Castillo	Oral Abstract #225	623. Mantle Cell, Follicular, Waldenstrom's, and Other Indolent B Cell Lymphomas: Clinical and Epidemiological:	Saturday, Dec. 6 2:30-2:45 p.m. EST

			FL and WM	
Time-limited pirtobrutinib, venetoclax, and obinutuzumab combination in first-line chronic lymphocytic leukemia	Nitin Jain	Oral Abstract #680	642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Frontline Treatment Strategies for CLL	Sunday, Dec. 7 4:45-5 p.m. EST
Pirtobrutinib, a non-covalent BTK inhibitor, enhances T-cell anti-tumor immunity in chronic lymphocytic leukemia (CLL)	Sonia Rodriguez-Rodriguez	Poster Abstract #3878	641. Chronic Lymphocytic Leukemia: Basic and Translational: Poster II	Sunday, Dec. 7 6-8 p.m. EST
Pirtobrutinib versus usual care for patients with Richter transformation of chronic lymphocytic leukemia: Inverse probability of treatment weighting-based analysis of BRUIN trial and mayo observational cohort	Yucai Wang	Poster Abstract #5673	642. Chronic Lymphocytic Leukemia: Clinical and Epidemiological: Poster III	Monday, Dec. 8 6-8 p.m. EST

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 (MCL) and chronic lymphocytic leukemia (CLL).[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.

INDICATIONS FOR JAYPIRCA (pirtobrutinib)
Jaypirca is a kinase inhibitor indicated for the treatment of

- Adult patients with relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhibitor.
- Adult patients with chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) who have received at least two prior lines of therapy, including a BTK inhibitor and a BCL-2 inhibitor.

These indications are approved under accelerated approval based on response rate. Continued approval for these indications 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, fungal) and opportunistic infections occurred in Jaypirca-treated patients. In a clinical trial, Grade ≥3 infections occurred in 24% of patients with hematologic malignancies, most commonly pneumonia (14%); fatal infections occurred (4.4%). Sepsis (6%) and febrile neutropenia (4%) occurred. In patients with CLL/SLL, Grade ≥3 infections occurred (32%), with fatal infections occurring in 8%. Opportunistic infections included *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 3% of patients, including gastrointestinal hemorrhage; fatal hemorrhage occurred (0.3%). Bleeding of any grade, excluding bruising and petechiae, occurred (17%). Major hemorrhage occurred in patients taking Jaypirca with (0.7%) and without (2.3%) 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: Jaypirca can cause cytopenias, including neutropenia, thrombocytopenia, and anemia. In a clinical trial, Grade 3 or 4 cytopenias, including decreased neutrophils (26%), decreased platelets (12%), and decreased hemoglobin (12%), developed in Jaypirca-treated patients. Grade 4 decreased neutrophils (14%) and Grade 4 decreased platelets (6%) developed. Monitor complete blood counts regularly during treatment. Based on severity, reduce dose, temporarily withhold, or permanently discontinue Jaypirca.

Cardiac Arrhythmias: Cardiac arrhythmias occurred in patients who received Jaypirca. In a clinical trial of patients with hematologic malignancies, atrial fibrillation or flutter were reported in 3.2% of Jaypirca-treated patients, with Grade 3 or 4 atrial fibrillation or flutter in 1.5%. Other serious cardiac arrhythmias such as supraventricular tachycardia and cardiac arrest occurred (0.5%). 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 9% of Jaypirca-treated patients. The most frequent malignancy was non-melanoma skin cancer (4.6%). 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.

Hepatotoxicity, Including Drug-Induced Liver Injury (DILI): Hepatotoxicity, including severe, life-threatening, and potentially fatal cases of DILI, has occurred in patients treated with BTK inhibitors, including Jaypirca. Evaluate bilirubin and transaminases at baseline and throughout Jaypirca

treatment. For patients who develop abnormal liver tests after Jaypirca, monitor more frequently for liver test abnormalities and clinical signs and symptoms of hepatic toxicity. If DILI is suspected, withhold Jaypirca. Upon confirmation of DILI, discontinue Jaypirca.

Embryo-Fetal Toxicity: Jaypirca can cause fetal harm in pregnant women. Administration of pirtobrutinib to pregnant rats 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 fetal risk and females of reproductive potential to use effective contraception during treatment and for one week after last dose.

Adverse Reactions (ARs) in Patients Who Received Jaypirca

The most common (≥20%) ARs in the BRUIN pooled safety population of patients with hematologic malignancies (n=593) were decreased neutrophil count (46%), decreased hemoglobin (39%), fatigue (32%), decreased lymphocyte count (31%), musculoskeletal pain (30%), decreased platelet count (29%), diarrhea (24%), COVID-19 (22%), bruising (21%), cough (20%).

Mantle Cell Lymphoma

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 Jaypirca dose occurred in 7% of patients, most commonly due to infections (4.7%), including COVID-19 (3.1% of all patients).

Dose Modifications and Discontinuations: ARs led to dose 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 in >1% of patients included pneumonia.

Most common ARs (≥15%), excluding laboratory terms (all Grades %; Grade 3-4 %): fatigue (29; 1.6), musculoskeletal pain (27; 3.9), diarrhea (19; -), edema (18; 0.8), dyspnea (17; 2.3), pneumonia (16; 14), bruising (16; -).

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).

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Serious ARs occurred in 56% of patients. Serious ARs occurring in ≥5% of patients were pneumonia (18%), COVID-19 (9%), sepsis (7%), and febrile neutropenia (7%). **Fatal ARs** within 28 days of last Jaypirca dose occurred in 11% of patients, most commonly due to infections (10%), including sepsis (5%) and COVID-19 (2.7%).

Dose Modifications and Discontinuations: ARs led to dose reductions in 3.6%, treatment interruption in 42%, and permanent discontinuation of Jaypirca in 9% of patients. ARs resulting in dose reductions in >1% included neutropenia; treatment interruptions in >5% of patients included pneumonia, neutropenia, febrile neutropenia, and COVID-19; permanent discontinuation in >1% of patients included second primary malignancy, COVID-19, and sepsis.

Most common ARs (≥20%), excluding laboratory terms (all Grades %; Grade 3-4 %): fatigue (36; 2.7), bruising (36; -), cough (33; -), musculoskeletal pain (32; 0.9), COVID-19 (28; 7), pneumonia (27; 16), diarrhea (26; -), abdominal pain (25; 2.7), dyspnea (22; 2.7), hemorrhage (22; 2.7), edema (21; -), nausea (21; -), pyrexia (20; 2.7), headache (20; 0.9).

Select Laboratory Abnormalities (all Grades %; Grade 3 or 4 %) that Worsened from Baseline in ≥20% of Patients: neutrophil count decreased (63; 45), hemoglobin decreased (48; 19), calcium decreased (40; 2.8), platelet count decreased (30; 15), sodium decreased (30; -), lymphocyte count decreased (23; 8), ALT increased (23; 2.8), AST increased (23; 1.9), creatinine increased (23; -), lipase increased (21; 7), alkaline phosphatase increased (21; -). Grade 4 laboratory abnormalities in >5% of patients included neutrophils decreased (23).

Drug Interactions

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

Sensitive CYP2C8, CYP2C19, CYP3A, P-gp, or 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: Due to 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 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, 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 increases pirtobrutinib exposure. Reduce Jaypirca dosage in patients with severe renal impairment according to approved labeling.

PT HCP ISI MCL_CLL AA JUN2024

Please see Prescribing Information and Patient Information for Jaypirca.

About Lilly
Lilly is a medicine company turning science into healing to make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help tens of millions of 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/news, or follow us on Facebook, Instagram, and LinkedIn. P-LLY

Trademarks and Trade Names
All trademarks or trade names referred to in this press release are the property of the company, or, to the extent trademarks or trade names belonging to other companies are referenced in this press release, the property of their respective owners. Solely for convenience, the trademarks and trade names in this press release are referred to without the ® and ™ symbols, but such references should not be construed as any indicator that the company or, to the extent applicable, their respective owners will not assert, to the fullest extent under applicable law, the company's or their rights thereto. We do not intend the use or display of other companies' trademarks and trade names to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

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 Jaypirca as a potential treatment for adults with chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL), mantle cell lymphoma (MCL) and Waldenström macroglobulinemia (WM), 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, or that Jaypirca will receive additional regulatory approvals. 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.

Endnotes & References

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

Refer to: Kyle Owens; Owens_Kyle@lilly.com; (332) 259-3932 (Media)
Michael Czapar; czapar_michael_c@lilly.com; 317-617-0983 (Investors)

View original content to download multimedia:https://www.prnewswire.com/news-releases/lilly-to-present-data-from-two-positive-phase-3-studies-of-jaypirca-pirtobrutinib-in-chronic-lymphocytic-leukemia-at-the-2025-american-society-of-hematology-ash-annual-meeting-302623695.html

SOURCE Eli Lilly and Company