Jazz Pharmaceuticals Provides Update on Zepzelca® (lurbinectedin) Phase 3 LAGOON Trial in Second-Line Small Cell Lung Cancer

June 12, 2026

For U.S. media and investors only

DUBLIN, June 12, 2026 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced top-line results from the Phase 3 LAGOON trial, conducted by PharmaMar, evaluating Zepzelca® (lurbinectedin) in patients with relapsed (second-line) metastatic small cell lung cancer (SCLC). The trial did not meet its primary endpoint of overall survival (OS) evaluating *Zepzelca* as monotherapy or in combination with irinotecan compared to investigators' choice of topotecan or irinotecan. No new safety signals were identified with *Zepzelca* monotherapy or in combination with irinotecan, and the overall safety profiles of the investigational arms were consistent with the known safety profile of each agent.

"Relapsed SCLC is an aggressive cancer with a poor prognosis and patients continue to need treatment options, including in later lines of therapy. We thank the investigators, trial sites and patients who were involved in the LAGOON trial, along with our partner, PharmaMar," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development, and chief medical officer of Jazz Pharmaceuticals. "*Zepzelca* is an important treatment in SCLC and, based on the strength of the IMforte trial results, we believe its most beneficial use is in the first-line maintenance setting in combination with immunotherapy given the rapid progression of metastatic SCLC after first-line chemotherapy induction."

The full U.S. approval of *Zepzelca* in 2025 is based on the Phase 3 IMforte trial, which evaluated *Zepzelca* in combination with atezolizumab as first-line maintenance treatment for patients with extensive-stage SCLC. In the IMforte trial, the *Zepzelca* and atezolizumab combination demonstrated a statistically significant improvement in the primary endpoints of OS and progression-free survival (PFS), as assessed by an independent review facility, compared to treatment with atezolizumab alone. The *Zepzelca* and atezolizumab combination reduced the risk of disease progression or death by 46% and the risk of death by 27%, compared to atezolizumab maintenance therapy alone. The LAGOON results are distinct from the IMforte trial and do not impact *Zepzelca's* approval in the first-line maintenance setting.

The company has shared the LAGOON results with the FDA and will discuss next steps with the agency regarding its post-marketing requirements for the *Zepzelca* second-line indication.

The study results do not impact the company's 2026 guidance.

Key Results from the Phase 3 LAGOON Trial
The LAGOON trial included a broader patient population than the Phase 2 pivotal trial that supported the second-line accelerated approval, including patients with a history of CNS involvement. Efficacy of *Zepzelca* in the subset of patients without a history of CNS involvement was more comparable to the control arm, which performed better than historical precedent.

Trial Population	*Zepzelca* monotherapy Median OS	*Zepzelca* + irinotecan Median OS	Control Median OS	HR (95% CI) *Zepzelca* vs Control	HR (95% CI) *Zepzelca*+irinotecan vs Control
Overall	8.7 (n=240)	10.9 (n=242)	10.7 (n=242)	1.190 (0.959, 1.476)	0.902 (0.729, 1.115)
Without CNS metastases	9.6 (n=182)	11.1 (n=189)	10.7 (n=186)	1.106 (0.875, 1.398)	0.922 (0.729, 1.166)
With CNS metastases	7.1 (n=58)	10.5 (n= 53)	10.3 (n=56)	1.791 (1.162, 2.760)	1.107 (0.724, 1.692)

The overall safety profile for *Zepzelca* was favorable relative to the control arm. Treatment-related adverse events (TRAE) were 78.5% with *Zepzelca*, 95% with *Zepzelca* + irinotecan, and 93.8% with the control arm. TRAEs Grade ≥ 3 were 35% with *Zepzelca*, 62.6% with Zepzelca + irinotecan, and 64.4% with the control arm.

About the LAGOON Trial
LAGOON (NCT05153239) is a Phase 3, randomized (1:1:1), multicenter, open-label clinical trial with three arms: one arm to receive lurbinectedin 3.2 mg/m^2 as monotherapy (the approved dose in the U.S.), the second arm to receive lurbinectedin 2.0 mg/m^2 in combination with irinotecan 75 mg/m^2, and the third arm to receive topotecan or irinotecan based on the investigators' choice. The trial was conducted in patients with SCLC, whose disease has progressed following prior platinum-containing chemotherapy with or without anti-PD-1 or anti-PD-L1 agents. The LAGOON trial enrolled 724 patients from more than 200 sites globally, including in the U.S., Canada and Europe. The trial is sponsored by Jazz's partner, PharmaMar.

About Small Cell Lung Cancer
In the U.S., approximately 13 percent of lung cancers are small cell.[1] Approximately 30,000 new cases of small cell lung cancer (SCLC) are reported in the U.S. each year.[2] The risk for developing SCLC is much higher among current or former tobacco smokers; however, SCLC can also be caused by exposure to secondhand smoke, asbestos, some inhaled chemicals, radiation and air pollution. People with a family history of lung cancer may also be at a higher risk.[3] SCLC is an aggressive form of lung cancer and it tends to spread quickly to other parts of the body including the brain, liver and bone.[4,5] A large percentage of SCLC patients on treatment briefly achieve a response, although the cancer often returns and is usually more aggressive and resistant to regimens that were previously effective.[6]

About Zepzelca® (lurbinectedin)
Zepzelca is an alkylating drug that binds guanine residues within DNA. This triggers a cascade of events that can affect the activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in disruption of the cell cycle and potentially cell death.[7]

In October 2025, the FDA approved *Zepzelca* in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, as maintenance treatment for

adults with extensive-stage small cell lung cancer (ES-SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab or atezolizumab and hyaluronidase-tqjs, carboplatin and etoposide.

In June 2020, the FDA approved *Zepzelca* for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy. This indication is approved under accelerated approval based on ORR and DOR.

Important Safety Information for ZEPZELCA

Myelosuppression
ZEPZELCA can cause severe and fatal myelosuppression including febrile neutropenia and sepsis, thrombocytopenia and anemia.

Administer ZEPZELCA only to patients with baseline neutrophil count of at least 1,500 cells/mm^3 and platelet count of at least 100,000/mm^3. To reduce the risk of febrile neutropenia during treatment with ZEPZELCA in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs, administer granulocyte colony-stimulating factor (G-CSF). Monitor blood counts including neutrophils, red blood cells and platelets prior to each ZEPZELCA administration. For neutrophil count less than 500 cells/mm^3 or any value less than lower limit of normal, the use of G-CSF is recommended. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

- *ZEPZELCA with Intravenous Atezolizumab*
  - In the IMforte study, primary prophylaxis of G-CSF was administered to 84% of patients. Based on laboratory values, decreased neutrophils occurred in 36%, including 18% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased neutrophil cells was 31 days and a median duration of 10 days. Febrile neutropenia occurred in 1.7%. Sepsis occurred in 1%. There were 7 fatal infections: pneumonia (n=3), sepsis (n=3), and febrile neutropenia (n=1).
  - Based on laboratory values, decreased platelets occurred in 54%, including 15% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased platelet cells was 31 days and a median duration of 12 days.
  - Based on laboratory values, decreased hemoglobin occurred in 51%, including 13% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. The median time to onset of Grade 3 and 4 decreased hemoglobin was 64 days and a median duration of 8 days.
- *ZEPZELCA as a Single Agent*
  - In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA as a single agent, Grade 3 or 4 neutropenia occurred in 41% of patients, with a median time to onset of 15 days and a median duration of 7 days. Febrile neutropenia occurred in 7% of patients. Sepsis occurred in 2% of patients and was fatal in 1% (all cases occurred in patients with solid tumors other than SCLC). Grade 3 or 4 thrombocytopenia occurred in 10%, with a median time to onset of 10 days and a median duration of 7 days. Grade 3 or 4 anemia occurred in 17% of patients.

Hepatotoxicity
ZEPZELCA can cause hepatotoxicity which may be severe.

Monitor liver function tests prior to initiating ZEPZELCA and periodically during treatment as clinically indicated. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

- *ZEPZELCA with Intravenous Atezolizumab*
  - In the IMforte study, based on laboratory values, increased alanine aminotransferase (ALT) occurred in 25%, including 3% Grade 3 or Grade 4 in patients who received ZEPZELCA in combination with atezolizumab. Increased aspartate aminotransferase (AST) occurred in 24% including 3% Grade 3 or Grade 4. The median time to onset of Grade ≥3 elevation in transaminases was 52 days (range: 6 to 337).
- *ZEPZELCA as a Single Agent*
  - In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA as a single agent, Grade 3 elevations of ALT and AST were observed in 6% and 3% of patients, respectively, and Grade 4 elevations of ALT and AST were observed in 0.4% and 0.5% of patients, respectively. The median time to onset of Grade ≥3 elevation in transaminases was 8 days (range: 3 to 49), with a median duration of 7 days.

Extravasation Resulting in Tissue Necrosis
Extravasation of ZEPZELCA can cause skin and soft tissue injury, including necrosis requiring debridement. Consider use of a central venous catheter to reduce the risk of extravasation, particularly in patients with limited venous access. Monitor patients for signs and symptoms of extravasation during the ZEPZELCA infusion. If extravasation occurs, immediately discontinue the infusion, remove the infusion catheter, and monitor for signs and symptoms of tissue necrosis. The time to onset of necrosis after extravasation may vary.

ZEPZELCA with Intravenous Atezolizumab

- In the IMforte study, extravasation resulting in skin necrosis occurred in one patient who received ZEPZELCA in combination with atezolizumab.

Administer supportive care and consult with an appropriate medical specialist as needed for signs and symptoms of extravasation. Administer subsequent infusions at a site that was not affected by extravasation.

Rhabdomyolysis
Rhabdomyolysis has been reported in patients treated with ZEPZELCA.

Monitor creatine phosphokinase (CPK) prior to initiating ZEPZELCA and periodically during treatment as clinically indicated. Withhold or reduce the dose based on severity.

ZEPZELCA with Intravenous Atezolizumab

- In the IMforte study, among 235 patients who had a creatine phosphokinase laboratory evaluation, increased creatine phosphokinase occurred in 9% who received ZEPZELCA in combination with atezolizumab.

Embryo-Fetal Toxicity
ZEPZELCA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise female patients of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 7 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the last dose.

Lactation
There are no data on the presence of ZEPZELCA in human milk, however, because of the potential for serious adverse reactions from ZEPZELCA in breastfed children, advise women not to breastfeed during treatment with ZEPZELCA and for 2 weeks after the last dose.

ADVERSE REACTIONS

- *ZEPZELCA with Intravenous Atezolizumab*
  - Serious adverse reactions occurred in 31% of patients receiving ZEPZELCA in combination with atezolizumab. Serious adverse reactions occurring in >2% were pneumonia (2.5%), respiratory tract infections (2.1%), dyspnea (2.1%), and decreased platelet count (2.1%). Fatal adverse reactions occurred in 5% of patients receiving ZEPZELCA with atezolizumab including pneumonia (3 patients), sepsis (3 patients), cardio-respiratory arrest (2 patients), myocardial infarction (2 patients), and febrile neutropenia (1 patient).
  - The most common adverse reactions (≥30%), including laboratory abnormalities, in patients who received ZEPZELCA with atezolizumab were decreased lymphocytes (55%), decreased platelets (54%), decreased hemoglobin (51%), decreased neutrophils (36%), nausea (36%), and fatigue/asthenia (32%).
- *ZEPZELCA as a Single Agent*
  - Serious adverse reactions occurred in 34% of patients who received ZEPZELCA. Serious adverse reactions in ≥3% of patients included pneumonia, febrile neutropenia, neutropenia, respiratory tract infection, anemia, dyspnea, and thrombocytopenia.
  - The most common adverse reactions, including laboratory abnormalities, (≥20%) are leukopenia (79%), lymphopenia (79%), fatigue (77%), anemia (74%), neutropenia (71%), increased creatinine (69%), increased alanine aminotransferase (66%), increased glucose (52%), thrombocytopenia (37%), nausea (37%), decreased appetite (33%), musculoskeletal pain (33%), decreased albumin (32%), constipation (31%), dyspnea (31%), decreased sodium (31%), increased aspartate aminotransferase (26%), vomiting (22%), decreased magnesium (22%), cough (20%), and diarrhea (20%).

DRUG INTERACTIONS
Effect of CYP3A Inhibitors and Inducers

Avoid coadministration with a strong or a moderate CYP3A inhibitor (including grapefruit and Seville oranges) as this increases lurbinectedin systemic exposure which may increase the incidence and severity of adverse reactions to ZEPZELCA. If coadministration cannot be avoided, reduce the ZEPZELCA dose as appropriate.

Avoid coadministration with a strong CYP3A inducer as it may decrease systemic exposure to lurbinectedin, which may decrease the efficacy of ZEPZELCA.

GERIATRIC USE

- *ZEPZELCA with Intravenous Atezolizumab*
  - Of the 242 patients with ES-SCLC treated with ZEPZELCA and atezolizumab in IMforte, 124 (51%) patients were 65 years of age and older, while 29 (12%) patients were 75 years of age and older. No overall differences in effectiveness were observed between older and younger patients. There was no overall difference in the incidence of serious adverse reactions in patients ≥65 years of age and patients <65 years of age (33% vs. 29%, respectively). There was a higher incidence of Grade 3 or 4 adverse reactions in patients ≥65 years of age compared to younger patients (45% vs. 31%, respectively).
- *ZEPZELCA as a Single Agent*
  - Of the 105 patients with SCLC administered ZEPZELCA in clinical studies, 37 (35%) patients were 65 years of age and older, while 9 (9%) patients were 75 years of age and older. No overall difference in effectiveness was observed between patients aged 65 and older and younger patients.
  - There was a higher incidence of serious adverse reactions in patients ≥65 years of age than in patients <65 years

of age (49% vs. 26%, respectively). The serious adverse reactions most frequently reported in patients ≥65 years of age were related to myelosuppression and consisted of febrile neutropenia (11%), neutropenia (11%), thrombocytopenia (8%), and anemia (8%). There was a higher incidence of Grade 3 or 4 adverse reactions in patients ≥65 years of age compared to younger patients (76% vs. 50%, respectively).

HEPATIC IMPAIRMENT
Avoid administration of ZEPZELCA in patients with severe hepatic impairment. If administration cannot be avoided, reduce the dose. Monitor for increased adverse reactions in patients with severe hepatic impairment.

Reduce the dose of ZEPZELCA in patients with moderate hepatic impairment. Monitor for increased adverse reactions in patients with moderate hepatic impairment.

No dose adjustment of ZEPZELCA is recommended for patients with mild hepatic impairment.

The full Prescribing Information for ZEPZELCA is available at: https://pp.jazzpharma.com/pi/zepzelca.en.USPI.pdf

Zepzelca is a trademark of Pharma Mar S.A. used by Jazz Pharmaceuticals under license.

About Jazz Pharmaceuticals
Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharma company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with rare disease — often with limited or no therapeutic options. We have a diverse portfolio of medicines, including leading therapies addressing epilepsies, cancers and sleep disorders. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics. Jazz is headquartered in Dublin, Ireland with research and development laboratories, manufacturing facilities and employees in multiple countries committed to serving patients worldwide. Please visit www.jazzpharmaceuticals.com for more information.

Cautionary Note Concerning Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to the possibility of unfavorable results from ongoing or additional clinical trials, including the LAGOON trial and those involving Zepzelca monotherapy and in combination with irinotecan; uncertainties relating to regulatory applications and approval timelines, including those related pending or potential applications for Zepzelca in the second-line indication for treatment of relapsed SCLC, and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with the successful completion of regulatory activities and uncertain regulatory approval, risks related to failure or delays in successfully initiating or completing clinical trials and assessing patients and other risks and uncertainties affecting Jazz Pharmaceuticals and its development programs, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals' Securities and Exchange Commission filings and reports, including Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2025, and future filings and reports by Jazz Pharmaceuticals. Other risks and uncertainties of which Jazz Pharmaceuticals is not currently aware may also affect Jazz Pharmaceuticals' forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. The forward-looking statements herein are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by Jazz Pharmaceuticals on its website or otherwise. Jazz Pharmaceuticals undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

Contacts:
Media:
CorporateAffairsMediaInfo@jazzpharma.com
Ireland +353 1 637 2141
U.S. +1 215 867 4948

Investor:
InvestorInfo@jazzpharma.com
Ireland +353 1 634 3211
U.S. +1 650 496 2717

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