Jazz Pharmaceuticals Announces Zepzelca® (lurbinectedin) and Atezolizumab (Tecentriq®) Combination Significantly Improves Survival as First-Line Maintenance Therapy for Extensive-Stage Small Cell Lung Cancer

June 02, 2025

First-line maintenance combination therapy reduced the risk of disease progression or death by 46%, with a median overall survival of 13.2 months vs 10.6 months for atezolizumab alone from the point of randomization

First Phase 3 study to demonstrate statistically significant and clinically meaningful improvements in both progression-free and overall survival in ES-SCLC first-line maintenance

Results presented at the ASCO 2025 Annual Meeting and simultaneously published in The Lancet

Jazz to host investor webcast on Tuesday, June 10 to review Zepzelca data

For U.S. media and investors only

DUBLIN, June 2, 2025 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced positive results from the Phase 3 IMforte study of Zepzelca® (lurbinectedin) in combination with atezolizumab (Tecentriq®) as a first-line maintenance treatment for people with extensive-stage small cell lung cancer (ES-SCLC), following induction therapy with carboplatin, etoposide and atezolizumab. The study met both primary endpoints, demonstrating statistically significant improvements in progression-free survival (PFS) and overall survival (OS) compared to atezolizumab alone.

IMforte is the first global Phase 3 trial to demonstrate clinically meaningful PFS and OS benefits in the first-line maintenance setting for ES-SCLC and supports maintenance therapy with *Zepzelca* plus atezolizumab as a new standard of care for patients. The data were presented today in an oral session at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago and published simultaneously in *The Lancet*. Data from the trial served as the basis for the supplemental New Drug Application (sNDA) submission to the U.S. Food and Drug Administration (FDA).

Following induction therapy with carboplatin, etoposide and atezolizumab, patients who did not have disease progression were randomized to receive *Zepzelca* plus atezolizumab or atezolizumab alone. From the point of randomization, the median PFS was 5.4 months for the *Zepzelca* plus atezolizumab combination versus 2.1 months for atezolizumab alone (stratified HR = 0.54, 95% CI: 0.43–0.67; p < 0.0001), and median OS was 13.2 months versus 10.6 months (stratified hazard ratio [HR] = 0.73; 95% CI: 0.57–0.95; p = 0.0174). The combination reduced the risk of disease progression or death by 46% and the risk of death by 27% compared to atezolizumab alone. The *Zepzelca* plus atezolizumab combination had no new or unexpected safety signals.

"Small cell lung cancer is an aggressive and devastating disease; at the time of diagnosis, the large majority of patients have already progressed to extensive-stage disease and only one out of five survive longer than two years,[1]" said Luis Paz-Ares, M.D., Ph.D., Head of Medical Oncology at the Hospital Universitario 12 de Octubre in Madrid, Spain, and IMforte trial principal investigator. "The IMforte results are very encouraging showing a potentially practice-changing option that could improve survival for patients with a very high unmet need."

"In the U.S., approximately 30,000 new cases of small cell lung cancer are diagnosed each year, and the IMforte results demonstrate a combination treatment approach that can meaningfully extend the survival benefit for people with extensive-stage small cell lung cancer who complete induction therapy without progression,[2,3]" said Stephen V. Liu, M.D., Associate Professor of Medicine, Lombardi Comprehensive Cancer Center, Georgetown University, and IMforte trial investigator. "Unfortunately, a significant number of patients are not able to receive any therapy at the time of progression. This combination gives oncologists a new evidence-based option to help patients before progression occurs and improve outcomes in a setting where options have been limited."

"The IMforte trial results underscore the potential of *Zepzelca* with atezolizumab to deliver clinically meaningful benefit as a first-line maintenance option for patients with extensive-stage small cell lung cancer and is a significant advance for these patients," 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. "These results represent important progress in expanding *Zepzelca's* potential utility earlier in the treatment journey. We look forward to engaging with the FDA to bring this indication to market as quickly as possible."

Phase 3 IMforte Trial Results
These primary results are from the global Phase 3 IMforte trial, which evaluated *Zepzelca* plus atezolizumab as a first-line maintenance therapy in patients with ES-SCLC. 483 patients were randomized after completion of 4 cycles of induction therapy with atezolizumab plus carboplatin and etoposide. From the point of randomization, the median OS for the *Zepzelca* plus atezolizumab regimen was 13.2 months versus 10.6 months for atezolizumab alone (stratified hazard ratio [HR] = 0.73; 95% CI: 0.57–0.95; p = 0.0174). From the point of randomization, the median PFS by independent assessment was 5.4 months versus 2.1 months, respectively (stratified HR = 0.54, 95% CI: 0.43–0.67; p < 0.0001). Treatment duration for patients in the *Zepzelca* plus atezolizumab arm was twice as long as the atezolizumab arm, with a median maintenance treatment duration of 4.2 months versus 2.1 months, respectively.

The *Zepzelca* plus atezolizumab combination as maintenance therapy was generally well tolerated with no new safety signals identified. In the *Zepzelca* plus atezolizumab and atezolizumab arms, respectively, treatment-related adverse events (TRAEs) occurred in 83.5% versus 40.0% of patients, with Grade 3-4 TRAEs in 25.6% versus 5.8% and Grade 5 TRAEs in 0.8% (two patients with sepsis and febrile neutropenia) versus 0.4% (one patient with sepsis). AEs led to treatment discontinuation in 6.2% of patients in the *Zepzelca* plus atezolizumab arm and 3.3% of patients in the atezolizumab arm.

The Company will host an investor webcast on June 10 at 4:30 p.m. ET / 9:30 p.m. IST to review *Zepzelca* data. The webcast will include commentary from a leading small cell lung cancer expert and Company senior management. The webcast may be accessed from the Investors section of the Jazz Pharmaceuticals website at www.jazzpharmaceuticals.com.

About the IMforte Phase 3 Trial

IMforte (NCT05091567) is an ongoing Phase 3, randomized, multicenter maintenance trial evaluating the efficacy, safety and pharmacokinetics of *Zepzelca* plus atezolizumab, compared with standard-of-care first-line maintenance with atezolizumab alone, in adults (≥18 years) with ES-SCLC, following induction therapy with carboplatin, etoposide and atezolizumab. The primary endpoints for this study are OS and independent review facility (IRF)-assessed PFS in the maintenance phase.

The trial consists of two phases: an induction phase and a maintenance phase. Participants were required to have an ongoing response or stable disease per the Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 after the induction phase of four cycles of carboplatin, etoposide, and atezolizumab to be considered for eligibility screening for the maintenance phase. Eligible participants were randomized in a 1:1 ratio to receive either lurbinectedin plus atezolizumab or atezolizumab in the maintenance phase.

The trial is sponsored by Roche and co-funded by Jazz Pharmaceuticals. Additional information about the trial, including eligibility criteria and a list of clinical trial sites, can be found at: ClinicalTrials.gov (Identifier: NCT05091567).

About Small Cell Lung Cancer

In the U.S., approximately 13 percent of lung cancers are small cell.[2] Approximately 30,000 new cases of small cell lung cancer (SCLC) are reported in the U.S. each year.[2,3] 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, too.[4] SCLC is the most aggressive form of lung cancer and it tends to spread quickly to other parts of the body including the brain, liver and bone.[5,6] 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.[5]

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.[4]

The FDA approved *Zepzelca* under accelerated approval in June 2020 for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy. The approval is based on overall response rate (ORR) and duration of response demonstrated in an open-label, monotherapy clinical study. In December 2021, Jazz and PharmaMar announced the initiation of LAGOON, a confirmatory Phase 3 clinical trial of *Zepzelca* for the treatment of patients with relapsed small cell lung cancer. If positive, LAGOON could confirm the benefit of *Zepzelca* in the treatment of SCLC when patients progress following 1L treatment with a platinum-based regimen and support full approval in the U.S.

Zepzelca is a prescription medicine used to treat adults with SCLC that has spread to other parts of the body (metastatic) and who have received treatment with chemotherapy that contains platinum, and it did not work or is no longer working. *Zepzelca* is approved based on response rate and how long the response lasted. Additional studies will further evaluate the benefit of *Zepzelca* for this use.

Important Safety Information

Myelosuppression

ZEPZELCA can cause myelosuppression. In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, 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.

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.

Monitor blood counts including neutrophil count and platelet count prior to each 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.

Hepatotoxicity

ZEPZELCA can cause hepatotoxicity. In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, 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.

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

Extravasation Resulting in Tissue Necrosis

Extravasation of ZEPZELCA resulting in skin and soft tissue injury, including necrosis requiring debridement, can occur. 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.

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.

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 6 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.

MOST COMMON ADVERSE REACTIONS

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
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%).

Please see accompanying full Prescribing Information.

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

Tecentriq (atezolizumab) is a registered trademark of Genentech, a member of the Roche Group.

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 potentially life-changing medicines for people with serious diseases — often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines, including leading therapies for sleep disorders and epilepsy, and a growing portfolio of cancer treatments. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics in oncology and neuroscience. 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.

Jazz Pharmaceuticals plc Caution Concerning Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to Zepzelca's potential as a first-line maintenance therapy for extensive-stage small cell lung cancer, the potential for Zepzelca in combination with atezolizumab to become a new standard of care for patients with ES-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, 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 plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2024, as supplement by Jazz Pharmaceuticals' Quarterly Report on Form 10-Q for the quarter ended March 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.

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