Jazz Pharmaceuticals Announces Statistically Significant Overall Survival and Progression-Free Survival Results for Zepzelca® (lurbinectedin) and Atezolizumab Combination in First-Line Maintenance Therapy for Extensive-Stage Small Cell Lung Cancer

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Jazz plans to submit supplemental New Drug Application in first half of 2025 for this combination therapy as a first-line maintenance treatment for ES-SCLC

DUBLIN, Oct. 15, 2024 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced positive top-line results from the Phase 3 clinical trial evaluating Zepzelca® (lurbinectedin) in combination with the PD-L1 inhibitor atezolizumab (Tecentriq®) compared to atezolizumab alone when administered as a maintenance treatment for adults with extensive-stage small cell lung cancer (ES-SCLC) following induction therapy with carboplatin, etoposide and atezolizumab. The combination of *Zepzelca* and atezolizumab demonstrated a statistically significant improvement in the primary endpoints of overall survival (OS) and progression-free survival (PFS), as assessed by an independent review facility (IRF), compared to treatment with atezolizumab alone.

"Each year, approximately 30,000 new cases of small cell lung cancer (SCLC) are reported in the U.S. A majority of these patients are diagnosed with extensive stage disease, which is aggressive and often difficult to treat, with poor prognosis,[i,ii,iii]" 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. "These trial results demonstrate the efficacy of lurbinectedin, the most widely used agent in second-line SCLC in the United States, in combination with standard-of-care atezolizumab for patients in first-line maintenance treatment, a much-needed advancement for patients with extensive disease."

"The results of the Phase 3 IMforte trial are highly encouraging and showed a statistically significant benefit for the *Zepzelca* and atezolizumab combination for extensive-stage small cell lung cancer patients receiving this treatment in the first-line maintenance setting. These results demonstrate the potential of this regimen to delay disease progression and extend survival for patients with this aggressive disease," 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. "We are pleased with these clinically meaningful results and plan to submit an sNDA in the first half of 2025 to support this combination in the first-line maintenance setting. We thank the investigators and patients who are involved in this trial, along with our partners at Roche."

The combination was generally well-tolerated. The preliminary safety data in the ongoing trial was consistent with the known safety profiles of *Zepzelca* and atezolizumab with no new safety signals observed in the combination arm.

Jazz and Roche plan to submit these data for presentation at a future medical meeting.

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 IRF-assessed PFS.

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: https://clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT05091567).

About Small Cell Lung Cancer
In the U.S., approximately 13 percent of lung cancers are small cell.[ii] Approximately 30,000 new cases of small cell lung cancer (SCLC) are reported in the U.S. each year.[ii,iii] 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.[iv] 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.[v,vi] 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.[ii]

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 eventual cell death.[iv]

The FDA approved *Zepzelca* under accelerated approval in June 2020 for the treatment of adult patients with metastatic 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 small cell lung cancer (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.

Important Safety Information for ZEPZELCA

Before receiving ZEPZELCA, tell your healthcare provider about all of your medical conditions, including if you:

- have liver or kidney problems.
- are pregnant or plan to become pregnant. ZEPZELCA can harm your unborn baby.

Females who are able to become pregnant:

- Your healthcare provider should do a pregnancy test before you start treatment with ZEPZELCA.
- You should use effective birth control (contraception) during treatment with and for 6 months after your last dose of ZEPZELCA.
- Tell your healthcare provider right away if you become pregnant or think that you are pregnant during treatment with ZEPZELCA.

Males with female partners who are able to become pregnant should use effective birth control during treatment with and for 4 months after their last dose of ZEPZELCA.

- are breastfeeding or plan to breastfeed. It is not known if ZEPZELCA passes into your breastmilk. Do not breastfeed during treatment with ZEPZELCA and for 2 weeks after your last dose of ZEPZELCA. Talk to your healthcare provider about the best way to feed your baby during treatment with ZEPZELCA.
  Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Certain other medicines may affect how ZEPZELCA works.

What should I avoid while using ZEPZELCA?
Avoid eating or drinking grapefruit, Seville oranges, or products that contain grapefruit juice and Seville oranges during treatment with ZEPZELCA.
ZEPZELCA can cause serious side effects, including:

- **Low blood cell counts.** Low blood counts including low neutrophil counts (neutropenia) and low platelet counts (thrombocytopenia) are common with ZEPZELCA, and can also be severe. Some people with low white blood cell counts may get fever, or an infection throughout the body (sepsis), that can cause death. Your healthcare provider should do blood tests before you receive each treatment with ZEPZELCA to check your blood cell counts.
  Tell your healthcare provider right away if you develop:
  - fever or any other signs of infection
  - unusual bruising or bleeding
  - tiredness
  - pale colored skin
- **Liver problems.** Increased liver function tests are common with ZEPZELCA and can also be severe. Your healthcare provider should do blood tests to check your liver function before you start and during treatment with ZEPZELCA.
  Tell your healthcare provider right away if you develop symptoms of liver problems including:
  - loss of appetite
  - nausea or vomiting
  - pain on the right side of your stomach area (abdomen)
- **Leakage of ZEPZELCA out of your vein during the infusion.** If ZEPZELCA leaks into the tissues around your infusion site, it can cause damage and death of tissue cells around the infusion site. You may need to have surgery to remove any dead tissue. Tell your healthcare provider right away if you see any ZEPZELCA leaking out of your vein or around the catheter during your infusion, or if you notice any redness, swelling, itching or discomfort at the infusion site at any time.
- **Severe muscle problems (rhabdomyolysis).** Tell your healthcare provider if you have severe muscle pain or weakness.

Your healthcare provider may temporarily stop treatment, lower your dose, or permanently stop ZEPZELCA if you develop serious side effects during treatment with ZEPZELCA.

The most common side effects of ZEPZELCA include:

- tiredness
- low white and red blood cell counts
- increased kidney function blood test (creatinine)
- increased liver function blood tests
- increased blood sugar (glucose)
- nausea
- decreased appetite

- muscle and joint (musculoskeletal) pain
- low level of albumin in the blood
- constipation
- trouble breathing
- low levels of sodium and magnesium in the blood
- vomiting
- cough
- diarrhea

These are not all of the possible side effects of ZEPZELCA.

Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to Jazz Pharmaceuticals at 1-800-520-5568.

Please see full Prescribing Information including Patient Information, and discuss with your doctor.

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.

What is atezolizumab?
Atezolizumab is a prescription medicine used to treat:

Adults with a type of lung cancer called small cell lung cancer (SCLC). Atezolizumab may be used with the chemotherapy medicines carboplatin and etoposide as your first treatment when your lung cancer:

- is a type called "extensive-stage small cell lung cancer," which means that it has spread or grown.

It is not known if atezolizumab is safe and effective when used in children for the treatment of SCLC.

Important Safety Information

What is the most important information about atezolizumab?
Atezolizumab can cause your immune system to attack normal organs and tissues in any area of your body and can affect the way they work. These problems can sometimes become severe or life-threatening and can lead to death. You can have more than one of these problems at the same time. These problems may happen anytime during your treatment or even after your treatment has ended.

Call or see your healthcare provider right away if you develop any new or worse signs or symptoms, including**:**

Lung problems

- cough
- shortness of breath
- chest pain

Intestinal problems

- diarrhea (loose stools) or more frequent bowel movements than usual
- stools that are black, tarry, sticky, or have blood or mucus
- severe stomach-area (abdomen) pain or tenderness

Liver problems

- yellowing of your skin or the whites of your eyes
- severe nausea or vomiting
- pain on the right side of your stomach area (abdomen)
- dark urine (tea colored)
- bleeding or bruising more easily than normal

Hormone gland problems

- headaches that will not go away or unusual headaches
- eye sensitivity to light
- eye problems
- rapid heartbeat
- increased sweating
- extreme tiredness
- weight gain or weight loss
- feeling more hungry or thirsty than usual

- urinating more often than usual
- hair loss
- feeling cold
- constipation
- your voice gets deeper
- dizziness or fainting
- changes in mood or behavior, such as decreased sex drive, irritability, or forgetfulness

Kidney problems

- decrease in your amount of urine
- blood in your urine
- swelling of your ankles
- loss of appetite

Skin problems

- rash
- itching
- skin blistering or peeling
- painful sores or ulcers in mouth or nose, throat, or genital area
- fever or flu-like symptoms
- swollen lymph nodes

Problems can also happen in other organs.
These are not all of the signs and symptoms of immune system problems that can happen with atezolizumab. Call or see your healthcare provider right away for any new or worse signs or symptoms, including:

- Chest pain, irregular heartbeat, shortness of breath, or swelling of ankles
- Confusion, sleepiness, memory problems, changes in mood or behavior, stiff neck, balance problems, tingling or numbness of the arms or legs
- Double vision, blurry vision, sensitivity to light, eye pain, changes in eyesight
- Persistent or severe muscle pain or weakness, muscle cramps
- Low red blood cells, bruising

Infusion reactions that can sometimes be severe or life-threatening. Signs and symptoms of infusion reactions may include:

- chills or shaking
- itching or rash
- flushing
- shortness of breath or wheezing
- dizziness
- feeling like passing out
- fever
- back or neck pain

Complications, including graft-versus-host disease (GVHD), in people who have received a bone marrow (stem cell) transplant that uses donor stem cells (allogeneic). These complications can be serious and can lead to death. These complications may happen if you underwent transplantation either before or after being treated with atezolizumab. Your healthcare provider will monitor you for these complications.

Getting medical treatment right away may help keep these problems from becoming more serious. Your healthcare provider will check you for these problems during your treatment with atezolizumab. Your healthcare provider may treat you with corticosteroid or hormone replacement medicines. Your healthcare provider may also need to delay or completely stop treatment with atezolizumab if you have severe side effects.

Before you receive atezolizumab, tell your healthcare provider about all of your medical conditions, including if you:

- have immune system problems such as Crohn's disease, ulcerative colitis, or lupus
- have received an organ transplant
- have received or plan to receive a stem cell transplant that uses donor stem cells (allogeneic)
- have received radiation treatment to your chest area
- have a condition that affects your nervous system, such as myasthenia gravis or Guillain-Barré syndrome
- are pregnant or plan to become pregnant. Atezolizumab can harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with atezolizumab. **Females who are able to become pregnant:**
    - Your healthcare provider should do a pregnancy test before you start treatment with atezolizumab.

    - You should use an effective method of birth control during your treatment and for at least 5 months after the last dose of atezolizumab.
- are breastfeeding or plan to breastfeed. It is not known if atezolizumab passes into your breast milk. Do not breastfeed during treatment and for at least 5 months after the last dose of atezolizumab.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

The most common side effects of atezolizumab when used in lung cancer with other anti-cancer medicines include:

- feeling tired or weak
- nausea
- hair loss
- constipation
- diarrhea
- decreased appetite

Atezolizumab may cause fertility problems in females, which may affect the ability to have children. Talk to your healthcare provider if you have concerns about fertility.

These are not all the possible side effects of atezolizumab. Ask your healthcare provider or pharmacist for more information about the benefits and side effects of atezolizumab.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-835-2555.

Please see http://www.Tecentriq.com for full Prescribing Information and additional Important Safety Information.

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 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.

Caution Concerning Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to the potential to delay disease progression and extend survival, plans to submit an sNDA in first half of 2025 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 pharmaceutical product development, 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, 2023, as supplemented by our Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, 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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