Jazz Pharmaceuticals Announces First Patient Enrolled in IMforte Phase 3 Trial Evaluating Zepzelca® (lurbinectedin) in Combination with a PD-L1 Inhibitor in Small Cell Lung Cancer

November 30, 2021

Registrational trial will assess the potential for a novel combination therapy in extensive-stage small cell lung cancer to deliver better long-term outcomes

DUBLIN, Nov. 30, 2021 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the first patient was enrolled in a Phase 3 clinical trial evaluating Zepzelca® (lurbinectedin) in combination with the PD-L1 inhibitor Tecentriq® (atezolizumab) as a first-line maintenance treatment for patients with extensive-stage small cell lung cancer (ES-SCLC). The trial, IMforte, conducted in collaboration with F. Hoffmann-La Roche Ltd, will measure the progression-free survival and overall survival benefits of *Zepzelca* and *Tecentriq* administered in combination compared to *Tecentriq* alone.

"Small cell lung cancer can progress faster than most forms of lung cancer, although new treatment options can prolong life and improve long-term care options," said Luis Paz-Ares, M.D., Ph.D., professor of medicine at Hospital Universitario 12 de Octubre in Madrid, Spain. "Jazz's collaborative research with Roche will provide much-needed insights into a potentially new small cell lung cancer therapeutic option in the first-line setting. With approximately a quarter million patients diagnosed globally with small cell lung cancer each year – including thousands in the U.S. alone – a new first-line maintenance combination treatment would be a welcome advancement for patients with extensive disease."

"We've already witnessed strong clinical demand for *Zepzelca* as a therapy for metastatic small cell lung cancer patients in the second-line setting," said Rob Iannone, M.D., M.S.C.E., executive vice president, research and development and chief medical officer at Jazz Pharmaceuticals. "This collaboration with Roche marks an opportunity to further study *Zepzelca's* safety and efficacy in combination with the PD-L1 inhibitor, *Tecentriq*, in a pivotal Phase 3 clinical trial, as part of a first-line, standard-of-care, immunotherapy treatment option for patients with extensive-stage small cell lung cancer, a devastating disease for which novel treatments and strategies are needed."

About the IMforte Phase 3 Trial

As part of the IMforte Phase 3, randomized, multicenter maintenance trial, Jazz and Roche will evaluate the efficacy, safety and pharmacokinetics of *Zepzelca* plus *Tecentriq* in adults with ES-SCLC following induction therapy with carboplatin, etoposide and atezolizumab. The primary objective is to determine the ability of this new combination to improve outcomes for patients with ES-SCLC, compared with standard-of-care first-line maintenance as measured by progression-free survival and overall survival. The trial is sponsored by Roche and co-funded by Jazz Pharmaceuticals.

If successful, the trial could potentially support an FDA supplemental new drug application for *Zepzelca* combined with *Tecentriq* in first-line maintenance ES-SCLC.

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 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.[1]

Zepzelca is a prescription medicine used to treat adults with small cell lung cancer 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. *Zepzelca* is not approved as part of a combination therapy or as a first-line maintenance treatment for patients with extensive-stage small cell lung cancer.

Important Safety Information for Patients

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 final 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 your final 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 final 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, or products that contain grapefruit juice 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)

Your healthcare provider may temporarily stop treatment, lower your dose, or permanently stop ZEPZELCA if you develop low blood cell counts or liver problems 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.

More information about Zepzelca, including Full Prescribing Information and Patient Information, is available here.

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

About Small Cell Lung Cancer
In the U.S., approximately 13 percent of lung cancers are small cell.[2] There are approximately 30,000 to 35,000 patients in the U.S. and 260,000 patients worldwide who are newly diagnosed with small cell lung cancer (SCLC) 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.[2]

About Jazz Pharmaceuticals plc
Jazz Pharmaceuticals plc (NASDAQ: JAZZ) is a global biopharmaceutical 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 and novel product candidates, from early- to late-stage development, in neuroscience and oncology. Within these therapeutic areas, we are identifying new options for patients by actively exploring small molecules and biologics, and through innovative delivery technologies and cannabinoid science. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in nearly 75 countries. For more information, please visit www.jazzpharmaceuticals.com and follow @JazzPharma on Twitter.

Caution Concerning Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to Jazz Pharmaceuticals' belief in the potential of Zepzelca to provide a potentially new SCLC therapeutic option in the first-line setting 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, effectively launching and commercializing new products; obtaining and maintaining adequate coverage and reimbursement for the company's products; delays or problems in the supply or manufacture of the company's products; and other risks and uncertainties affecting the company, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals' Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including Jazz Pharmaceuticals' Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 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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