Jazz Pharmaceuticals Announces First Patient Enrolled in EMERGE-201 Phase 2 Basket Trial Evaluating Zepzelca® (lurbinectedin) Monotherapy in Patients with Select Advanced or Metastatic Solid Tumors

March 24, 2022

Open-label basket trial will assess the safety and efficacy of Zepzelca in patients with advanced urothelial carcinoma, large cell neuroendocrine carcinoma of the lung, or homologous recombination deficient tumors

DUBLIN, March 24, 2022 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced the first patient was enrolled in EMERGE-201, a Phase 2 clinical trial evaluating the safety and efficacy of Zepzelca® (lurbinectedin) as a monotherapy in three cohorts of patients with advanced urothelial carcinoma, large cell neuroendocrine carcinoma of the lung, or homologous recombination deficient (HRD) tumors who have progressed on a platinum-containing regimen. EMERGE-201 will primarily assess patient objective response rates (ORR), according to the Response Evaluation Criteria in Solid Tumors (RECIST).

"Even with the rapid advancements in medical technology and care delivery across many tumor types over the last decade, there still remain many patients who continue to face unmet needs and experience a high burden of morbidity and mortality," said Arielle Heeke, M.D., breast medical oncologist at the Levine Cancer Institute and a primary investigator in the EMERGE-201 trial. "With the EMERGE-201 trial now underway, we look forward to seeing the potential clinical impact of *Zepzelca* on advanced solid tumor cancers, including HRD cancers, that have limited approved treatment options other than traditional chemotherapy. The trial will evaluate if this treatment can elicit tumor response based upon the underlying biology of these cancers and *Zepzelca*'s novel method of action."

"This trial initiation is an exciting milestone for *Zepzelca*'s clinical development program, as we seek to evaluate its clinical utility beyond treating small cell lung cancer," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "Given *Zepzelca* triggers a cascade of events that can affect the activity of DNA binding proteins – including transcription factors and DNA repair pathways – we look forward to analyzing *Zepzelca's* activity in additional difficult-to-treat cancers where driver oncogenes are actively transcribed and DNA repair mechanisms are inefficient, such as urothelial carcinoma, large cell neuroendocrine carcinoma of the lung and HRD-positive tumors."

EMERGE-201 Trial Details

EMERGE-201 is a Phase 2, multicenter, open-label trial designed to assess the safety and efficacy of *Zepzelca* as a monotherapy in three cohorts of patients with solid tumors, who will receive 3.2 mg/m^2 doses of *Zepzelca* intravenously on day one of an every-three-week dosing cycle, until confirmed disease progression. The three cohorts are: patients with advanced urothelial carcinoma, large cell neuroendocrine carcinoma of the lung, or HRD tumors who have progressed on a platinum-containing regimen.

The primary objective is to determine *Zepzelca's* ability to improve patient outcomes, as measured by ORR. Key secondary endpoints include investigator-assessed progression free survival, time-to-response, duration of response, and disease control rate as assessed by RECIST, as well as overall survival in participants treated with *Zepzelca*. The trial is sponsored and is being conducted by Jazz Pharmaceuticals.

Approximately 20 sites in the U.S. will participate in this trial. Additional information about the trial, including eligibility criteria, can be found here.

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.

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 successful, LAGOON will serve as the confirmatory trial for *Zepzelca* to secure full approval in the U.S.

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.

Females who 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 Pharma Mar, S.A. used by Jazz Pharmaceuticals under license.

About Urothelial Carcinoma

Urothelial carcinoma (UC) is the fourth most common tumor in the United States and is highly aggressive compared to other tumor types.[1] UC tumors often times spread locally, causing them to become more advanced and difficult to treat. Progressive disease after frontline chemotherapy is characterized by a short survival.[2]

About Large Cell Neuroendocrine Carcinoma

Large cell neuroendocrine carcinoma (LCNEC) is a rare type of cancer that can occur in the lungs and colon. There is no standard of care for LCNEC in lung cancer due to limited data on its pathology and clinical trials, making it a condition with great unmet needs in treatment and management.[3]

About Homologous Recombination Deficient-Positive Tumors

Homologous recombination deficiency (HRD) occurs across a variety of solid tumors including endometrial, biliary tract, urothelial, breast, pancreatic, gastric and esophageal. HRD hinders the body's essential mechanism that repairs damaged DNA in cells.[4] HRD tumors are seen in almost a fourth (17.4%) of tumors across 21 cancer types.

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 therapeutic option for certain solid tumor types 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' Annual Report on Form 10-K for the year ended December 31, 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.

Media Contact:
Kristin Bhavnani
Head of Global Corporate Communications
Jazz Pharmaceuticals plc
CorporateAffairsMediaInfo@jazzpharma.com
Ireland +353 1 637 2141
U.S. +1 215 867 4948

Investors:
Andrea N. Flynn, Ph.D.
Vice President, Head, Investor Relations
Jazz Pharmaceuticals plc
investorinfo@jazzpharma.com
Ireland +353 1 634 3211
U.S. +1 650 496 2717

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