



Jazz Pharmaceuticals Announces U.S. FDA Accelerated Approval of Zepzelca™ (lurbinectedin) for the Treatment of Metastatic Small Cell Lung Cancer

June 15, 2020

Approval represents an important advance for adult patients whose metastatic SCLC has progressed on or after platinum-based chemotherapy

Zepzelca is approved under accelerated approval based on overall response rate and duration of response demonstrated in an open-label, monotherapy clinical trial

Zepzelca is expected to be commercially available in the U.S. in early July

Investor webcast on Wednesday, June 17 at 6:15 p.m. EDT

DUBLIN, June 15, 2020 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced along with its partner PharmaMar (MSE: PHM) that the U.S. Food and Drug Administration (FDA) approved Zepzelca™ (lurbinectedin) for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.¹ Zepzelca was approved under accelerated approval based on overall response rate (ORR) and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.¹

The FDA approval of Zepzelca is based on monotherapy clinical data from an open-label, multi-center, single-arm study in 105 adult platinum-sensitive and platinum-resistant patients with SCLC who had disease progression after treatment with platinum-based chemotherapy.² The data, which appeared in *The Lancet Oncology* May 2020 issue, showed that in patients with relapsed SCLC, Zepzelca demonstrated an ORR of 35 percent and a median duration of response of 5.3 months as measured by investigator assessment (30 percent and 5.1 months respectively, as measured by an independent review committee (IRC)).¹

"Small cell lung cancer is a disease with limited treatment options, and the approval of Zepzelca represents an important advance for patients whose metastatic SCLC has progressed on or after platinum-based therapy," said Bruce Cozadd, chairman and CEO of Jazz Pharmaceuticals. "While patients may initially respond to traditional chemotherapy, they often experience an aggressive recurrence that is historically resistant to treatment. Jazz congratulates PharmaMar on the successful development of Zepzelca and we are proud to partner with them to bring this new therapy to the U.S. market, expanding our presence in oncology."

Zepzelca will be commercially available in the U.S. in early July. As previously announced in December 2019, PharmaMar and Jazz entered into an exclusive license agreement, which became effective in January 2020, granting Jazz U.S. commercialization rights to Zepzelca.

"Seeing first-hand the aggressive nature of SCLC and knowing that the large majority of those diagnosed will experience relapse, I am excited to see an effective new treatment demonstrating durable responses," said Dr. Jeff Petty, oncology specialist, Wake Forest Baptist Health. "For doctors, patients and their families, Zepzelca is an important and much-needed addition to the treatment landscape for relapsing SCLC."

"We are pleased to bring a new treatment choice to relapsed SCLC patients," said José María Fernández Sousa-Faro, PhD, president of PharmaMar. "The U.S. FDA accelerated approval of Zepzelca underscores its potential to fill an unmet need in this often-overlooked SCLC community."

Zepzelca is administered by an intravenous (IV) infusion delivering a 3.2 mg/m² dose over the course of one hour, repeated every 21 days until disease progression or unacceptable toxicity.¹ Zepzelca can be administered in an outpatient clinic and its dosing schedule of a single infusion every 21 days may result in less time a patient receives treatment in the clinic or hospital compared to other options.

The most common adverse reactions (≥20%), including laboratory abnormalities, are leukopenia, lymphopenia, fatigue, anemia, neutropenia, increased creatinine, increased alanine aminotransferase, increased glucose, thrombocytopenia, nausea, decreased appetite, musculoskeletal pain, decreased albumin, constipation, dyspnea, decreased sodium, increased aspartate aminotransferase, vomiting, cough, decreased magnesium and diarrhea.¹

"In addition to the physical toll it takes on patients, a relapse of SCLC also takes a mental and emotional toll on the entire family," said Andrea Stern Ferris, president and CEO, LUNGEvity. "The availability of Zepzelca presents new hope for patients and their loved ones, and we're eager to see its impact on the SCLC community."

About the Phase 2 Monotherapy Trial

The Phase 2 trial of Zepzelca was an open-label, single-arm study, which enrolled a total of 105 SCLC patients at 26 hospitals in six European countries and the U.S.² In the trial, platinum-sensitive and platinum-resistant patients were treated with Zepzelca 3.2 mg/m², administered as a 60-minute IV infusion repeated every 21 days until disease progression or unacceptable toxicity. The primary endpoint, ORR, was 35 percent and the median duration of response was 5.3 months as measured by investigator assessment (30 percent and 5.1 months respectively, as measured by an IRC).¹ Zepzelca was discontinued in 1.9 percent of patients and was delayed in 30.5 percent of patients due to an adverse reaction. Dose reductions for an adverse reaction occurred in 25 percent of patients.¹

Investor Webcast on Wednesday, June 17, 2020 at 6:15 p.m. EDT

The company will host a webcast on Wednesday, June 17, 2020 at 6:15 p.m. EDT/11:15 p.m. IST to provide investors with an update on Zepzelca.

The investor webcast will include an overview of SCLC, *Zepzelca* and launch plans from the company's senior management.

A live webcast of the presentation may be accessed from the Investors section of the Jazz Pharmaceuticals website at www.jazzpharmaceuticals.com. Please connect to the website prior to the start of the presentation to ensure adequate time for any software downloads that may be necessary to listen to the webcast. An archive of the webcast will be available for at least one week following the presentation on the Investors section of the company's website at www.jazzpharmaceuticals.com.

More information about *Zepzelca*, including Full Prescribing Information and Patient Information, is [available here](#).
< <http://pp.jazzpharma.com/pi/zepzelca.en.USPI.pdf> >

About *Zepzelca*™ (lurbinectedin)

Zepzelca, also known as PM1183, 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 for injection 4 mg is a prescription medicine used to treat adults with a kind of lung cancer called small cell lung cancer (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

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.

About PharmaMar

Headquartered in Madrid, PharmaMar is a biopharmaceutical company, focused on oncology and committed to research and development which takes its inspiration from the sea to discover molecules with antitumor activity. It is a company that seeks innovative products to provide healthcare professionals with new tools to treat cancer. Its commitment to patients and to research has made it one of the world leaders in the discovery of antitumor drugs of marine origin.

PharmaMar has a pipeline of drug candidates and a robust R&D oncology program. It develops and commercializes Yondelis® in Europe and has other clinical-stage programs under development for several types of solid cancers: lurbinectedin (PM1183), PM184 and PM14. With subsidiaries in Germany, Italy, France, Switzerland, Belgium, Austria and the United States. PharmaMar wholly owns other companies: GENOMICA, a molecular diagnostics company; Sylentis, dedicated to researching therapeutic applications of gene silencing (RNAi). To learn more about PharmaMar, please visit us at www.pharmamar.com.

About Jazz Pharmaceuticals plc

Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharmaceutical company dedicated to developing life-changing medicines for people with serious diseases — often with limited or no options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in key therapeutic areas. Our focus is in neuroscience, including sleep medicine and movement disorders, and in oncology, including hematologic and solid tumors. We actively explore new options for patients including novel compounds, small molecule advancements, biologics and innovative delivery technologies. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in more than 90 countries. For more information, please visit www.jazzpharmaceuticals.com and follow @JazzPharma on Twitter.

Jazz Pharmaceuticals "Safe Harbor" Statement under the Private Securities Litigation Reform Act of 1995

This press release contains forward-looking statements, including, but not limited to, statements related to Jazz Pharmaceuticals' expectations regarding the timing of commercial availability of *Zepzelca* in the U.S., its potential to fill an unmet need and have an impact on the SCLC community; 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: effectively commercializing *Zepzelca*, including risks related to the impact of COVID-19 pandemic on the successful launch of *Zepzelca*; and other risks and uncertainties affecting Jazz Pharmaceuticals, 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 the company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2020 and future filings and reports by the company. Other risks and uncertainties of which Jazz Pharmaceuticals is not currently aware may also affect the company's 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.

References:

1. ZEPZELCA (lurbinectedin) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.
2. Trigo J, Subbiah V, Besse B, et al. Lurbinectedin as second-line treatment for patients with small-cell lung cancer: a single-arm, open-label, phase 2 basket trial. *Lancet Oncol*. 2020 May;21(5):645–654.

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