Jazz Pharmaceuticals to Showcase Growing Impact in Solid Tumor Oncology Research at ESMO 2023

October 16, 2023

Zanidatamab data demonstrate clinical potential of novel bispecific antibody in HER2-targeted biliary tract and gastric cancers

Additional presentations, including a lurbinectedin oral presentation in small cell lung cancer (SCLC), underscore the strength of Jazz's solid tumor portfolio and the company's commitment to address difficult-to-treat tumors

DUBLIN, Oct. 16, 2023 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the company, along with partners, will present six abstracts including data from trials of bispecific antibody zanidatamab and Zepzelca® (lurbinectedin), as well as the study design for a Phase 1 trial of the pan-RAF inhibitor JZP815, at the European Society for Medical Oncology (ESMO) Congress 2023, taking place in Madrid, Spain, from October 20-24, 2023.

"The compelling data being presented at ESMO by Jazz and partners, in particular for zanidatamab in biliary tract and gastric cancers, demonstrate the clinical potential of our solid tumor oncology development programs to raise the standard of care for some of the most difficult-to-treat cancers," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "Through our expanding research in solid tumors – including targeted therapies and immuno-oncology – Jazz is advancing novel investigational therapies that target specific proteins like HER2 and important signaling pathways such as the RAS-RAF-MAPK pathway."

Notable presentations include:

- A poster presentation featuring progression-free survival (PFS) and duration of response (DoR) results from a Phase 1b/2 study of zanidatamab plus chemotherapy in combination with tislelizumab for the first-line treatment of HER2-positive gastric/gastroesophageal junction adenocarcinoma (G/GEJC). The study, sponsored by BeiGene, Ltd., showed zanidatamab plus chemotherapy and tislelizumab produced antitumor activity with a confirmed objective response rate (ORR) of 75.8% and median PFS of 16.7 months; and safety was consistent with previous findings.[1]
- A poster presentation featuring quality-of-life data from a Phase 2b study of zanidatamab for the second-line treatment of HER2-amplified biliary tract cancers (BTC), finding that patients with HER2-positive BTC who responded to zanidatamab reported improved health-related quality of life (HRQoL) compared with baseline. Overall, zanidatamab led to a meaningful clinical benefit, which may reduce disease burden and potentially result in improved patient HRQoL compared with baseline.[2]
- A mini oral presentation highlighting results of the Phase 1/2 LUPER study evaluating the efficacy of lurbinectedin in combination with pembrolizumab for the second-line treatment of small cell lung cancer (SCLC), which includes the following data: preliminary ORR of 46.4%, median DoR of 11.4 months, median PFS of 5.3 months and median OS of 11.1 months; the combination resulted in a manageable safety profile.[3]

The full ESMO abstracts are available at: https://cslide.ctimeetingtech.com/esmo2023/attendee/confcal_2/presentation

The full list of Jazz or partner-supported presentations at the 2023 ESMO Annual Meeting includes:

Zanidatamab Presentations

Presentation Title	Author	Presentation Details
Zanidatamab (zani) plus chemotherapy (chemo) and tislelizumab (TIS) as first-line (1L) therapy for patients (pts) with advanced HER2-positive (+) Gastric/gastroesophageal junction adenocarcinoma (GC/GEJC): updated results from a phase 1b/2 study	Keun-Wook Lee, et al.	**Type:** Poster Session **Date:** Monday, October 23; 12:00-1:00 PM CEST **Abstract Number**:1518P
Quality of life (QoL) outcomes in patients (pts) with zanidatamab (zani)-treated HER2-positive (HER2+) biliary tract cancer (BTC) in the Phase 2b HERIZON-BTC-01 study	Harpreet Wasan, et al.	**Type:** Poster Session **Date:** Monday, October 23; 12:00-1:00 PM CEST **Abstract Number**: 101P

Zepzelca Presentations

Presentation Title	Author	Presentation Details
Lurbinectedin (LUR) in combination with pembrolizumab (PBL) in relapsed small cell lung cancer (SCLC): the phase 1/2	Antonio Calles, et al.	**Type**: Mini Oral **Session:** Mini Oral Session 1 - Non-Metastatic NSCLC and Other

LUPER study [PharmaMar-supported IST]		Thoracic Malignancies **Date**: Sat, October 21; 2:50-2:55 PM CEST **Abstract Number:** 1989MO
Lurbinectedin (LRB) pharmacokinetics (PK) and safety when co-administered with itraconazole (ITZ) in patients with advanced solid tumor	Irene Moreno, et al.	**Type:** Poster Session **Date:** Monday, October 23; 12:00-1:00 PM CEST **Abstract Number**: 679P
Supportive measures to control myelosuppression and costs for patients with SCLC with lurbinectedin, CAV or topotecan with or without trilaciclib: a review on the basis of clinical trials	Manuel Dómine, et al.	**Type:** Poster Session **Date:** Saturday, October 21; 12:00-1:00 PM CEST **Abstract Number**: 2024P

JZP815 Presentations

Presentation Title	Author	Presentation Details
Phase 1, open-label, first-in-human (FIH) study of JZP815 in advanced or metastatic solid tumors harboring mitogen-activated protein kinase (MAPK) alterations	Abdul-Rafeh Naqash, et al.	**Type**: Poster Session **Date**: Monday, October 23; 12:00-1:00 PM CEST **Abstract Number:** 720TiP

About Zanidatamab
Zanidatamab is an investigational bispecific antibody that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. This unique design results in multiple mechanisms of action including dual HER2 signal blockade, increased binding and removal of HER2 protein from the cell surface, and potent effector function leading to encouraging antitumor activity in patients. Zanidatamab is being developed in multiple clinical trials as a targeted treatment option for patients with solid tumors that express HER2. Zanidatamab is being developed by Jazz and BeiGene, Ltd. (BeiGene) under license agreements from Zymeworks, which first developed the molecule.

The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation for zanidatamab in patients with previously treated HER2 gene-amplified biliary tract cancers (BTC), and two Fast Track designations for zanidatamab: one as a single agent for refractory BTC and one in combination with standard of care chemotherapy for first-line gastroesophageal adenocarcinoma (GEA). Additionally, zanidatamab has received Orphan Drug designations from FDA for the treatment of BTC and GEA, as well as Orphan Drug designation from the European Medicines Agency for the treatment of gastric cancer. Zanidatamab was also granted Breakthrough Therapy designation from the Center for Drug Evaluation (CDE) in China.

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.[4]

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. Additional studies will further evaluate the benefit of *Zepzelca* for this use.

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 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 JZP815
JZP815 is an investigational pan-RAF kinase inhibitor that was discovered and developed using state-of-the-art screening methodologies and medicinal chemistry. JZP815 targets specific components of the mitogen-activated protein kinase (MAPK) pathway that, when activated by oncogenic mutations, can be a frequent driver of human cancer. JZP815 potently inhibits both monomer- and dimer-driven RAF signaling (e.g., RAS-induced), prevents paradoxical pathway activation induced by BRAF selective inhibition, and is active against class 1, class 2, and class 3 BRAF mutants, as well as BRAF fusions and CRAF mutants. JZP815 is not currently approved for use anywhere in the world. JZP815 is part of Jazz's growing early-stage R&D pipeline focused on solid tumors and targeted therapy.

About Jazz Pharmaceuticals
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. 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 raising the standard of care for some of the most difficult-to-treat cancer 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, 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, 2022, as supplemented by our Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, 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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[1] Lee K, et al. Zanidatamab (zani) plus chemotherapy (chemo) and tislelizumab (TIS) as first-line (1L) therapy for patients (pts) with advanced HER2-positive (+) Gastric/gastroesophageal junction adenocarcinoma (GC/GEJC): updated results from a phase 1b/2 study. European Society for Medical Oncology. 2023.
[2] Wasan H, et al. Quality of life (QoL) outcomes in patients (pts) with zanidatamab (zani)-treated HER2-positive (HER2+) biliary tract cancer (BTC) in the Phase 2b HERIZON-BTC-01 study. European Society for Medical Oncology. 2023.
[3] Calles A, et al. Lurbinectedin (LUR) in combination with pembrolizumab (PBL) in relapsed small cell lung cancer (SCLC): the phase 1/2 LUPER study. European Society for Medical Oncology. 2023.
[4] ZEPZELCA (lurbinectedin) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

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