Jazz Pharmaceuticals Showcases Transformative Data at ASCO 2025, Highlighting Advances in Small Cell Lung Cancer, HER2+ Gastroesophageal Cancer and Diffuse Glioma

April 23, 2025

Statistically significant and clinically meaningful progression-free survival (PFS) and overall survival (OS) data for Zepzelca® (lurbinectedin) and atezolizumab (Tecentriq®) combination underscore potential of first-line maintenance therapy for extensive-stage small cell lung cancer, a much-needed advancement for patients

Long-term outcomes and survival data for Ziihera® (zanidatamab-hrii) highlight its potential to reshape the treatment paradigm for newly diagnosed HER2+ gastroesophageal cancer patients

Efficacy and safety of dordaviprone (ONC201) in prospective clinical trials of adult and pediatric recurrent H3 K27M-mutant diffuse glioma patients

Jazz to host investor webcast on Tuesday, June 10 to review Zepzelca data

For U.S. media and investors only

DUBLIN, April 23, 2025 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the company, along with its partners, will present seven abstracts at the American Society of Clinical Oncology (ASCO) Annual Meeting from May 30-June 3, 2025, in Chicago and online. The presentations will feature data from clinical trials evaluating Zepzelca® (lurbinectedin), Ziihera® (zanidatamab-hrii), Vyxeos® (daunorubicin and cytarabine) and investigational dordaviprone (ONC201).

Key presentations include:

- An oral abstract of the Phase 3 IMforte trial, which showed statistically significant and clinically meaningful survival benefit (progression-free survival (PFS) and overall survival (OS) for the combination of *Zepzelca* and atezolizumab (Tecentriq®) for extensive-stage small cell lung cancer (ES-SCLC) patients receiving treatment in the first-line maintenance setting
- A rapid oral abstract of four-year follow-up data, including new OS and translational biomarker data, from an ongoing Phase 2 trial of *Ziihera* in combination with chemotherapy for the first-line treatment of HER2-positive advanced or metastatic gastroesophageal adenocarcinoma (mGEA)
- An oral abstract of efficacy and safety data from a Phase 2 trial of dordaviprone (ONC201), from the recently completed Chimerix acquisition, in prospective clinical trials of adult and pediatric recurrent H3 K27M-mutant diffuse glioma patients

"Along with our partner Roche, we look forward to presenting the potentially practice-changing Phase 3 IMforte trial data of *Zepzelca* in combination with atezolizumab in the first-line maintenance setting for extensive-stage small cell lung cancer. Data from the trial served as the basis for our recent supplemental New Drug Application submission to FDA, marking an important milestone in our efforts to bring *Zepzelca* to more patients earlier in their treatment journey," 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 also eager to share updated long-term outcomes and the first report of median overall survival findings from the Phase 2 trial of *Ziihera* in combination with standard of care chemotherapy in HER2-positive metastatic gastroesophageal adenocarcinoma, ahead of expected Phase 3 findings later this year, which further reinforce *Ziihera's* potential as a differentiated HER2-targeted therapy. Additionally, we are encouraged by new efficacy and safety findings for dordaviprone in adult and pediatric patients with recurrent H3 K27M-mutant diffuse glioma from studies ONC013 and ONC014. We believe strongly in the potential of dordaviprone, a medicine that addresses a significant unmet need with no other FDA-approved therapies for this patient population. These updates build on our commitment to advancing targeted treatment options that address pressing patient needs and may help shape future treatment approaches."

The full ASCO abstracts will be available on May 22, 2025, after 5 p.m. ET. The abstract titles are available at: https://www.asco.org/abstracts.

The Company will host an investor webcast on June 10 at 4:30 p.m. ET / 9:30 p.m. IST to review Zepzelca data being presented at this year's ASCO Annual Meeting. The webcast will include commentary from a leading small cell lung cancer expert and Company senior management. The webcast may be accessed from the Investors section of the Jazz Pharmaceuticals website at www.jazzpharmaceuticals.com. Additional details will be provided prior to the webcast.

The full list of Jazz or partner-supported presentations at the 2025 ASCO Annual Meeting are:

Zepzelca

Presentation Title	Author	Presentation Details
Lurbinectedin (lurbi) + atezolizumab (atezo) as first-line (1L) maintenance treatment (tx) in patients (pts) with extensive-stage small cell lung cancer (ES-SCLC): Primary results of the Phase 3 IMforte trial	Luis Paz-Ares, Hossein Borghaei, Stephen V. Liu, Solange Peters, Roy S. Herbst, Katarzyna Stencel, Margarita Majem, Grzegorz Czyżewicz, Reyes Bernabé Caro, Ki Hyeong Lee, Melissa L. Johnson, Nuri Karadurmuş, Christian Grohé,	**Type:** Oral Abstract **Session:** Lung Cancer—Non–Small Cell Local-Regional/Small Cell/Other Thoracic Cancers

	Vaikunth Cuchelkar, Vilma Graupner, Monika Kaul, Ya-Chen Lin, Debasis Chakrabarti, Kamalnayan Bhatt, Martin Reck	**Date:** Monday, June 2, 3:00-6:00 p.m. CDT **Number:** 8006
Safety and Efficacy of Lurbinectedin Plus Atezolizumab as Second-Line Treatment for Advanced Small-Cell Lung Cancer: Results of the 2SMALL Phase 1/2 Study [Investigator Sponsored Trial]	Santiago Ponce Aix, Alejandro Navarro, Maria Eugenia Olmedo Garcia, Laura Mezquita, Margarita Majem, David Vicente, Reyes Bernabé, Alba Moratiel Pellitero, Manuel Cobo, Javier de Castro Carpeño, Silverio Ros, Marta Lopez Brea, Rosario Garcia Campelo, Javier Baena, Helena Bote, Mercedes Herrera, Pedro Rocha, Jon Zugazagoitia, Enriqueta Felip, Luis G. Paz-Ares	**Type:** Rapid Oral Abstract **Session:** Lung Cancer—Non–Small Cell Local-Regional/Small Cell/Other Thoracic Cancers **Date:** Sunday, June 1, 4:30-6:00 p.m. CDT **Number:** 8013

Ziihera

Presentation Title	Author	Presentation Details
Long-term outcomes and overall survival for zanidatamab + chemotherapy in HER2-positive advanced or metastatic gastroesophageal adenocarcinoma: 4-year follow-up of a phase 2 trial	Elena Elimova, Jaffer Ajani, Howard Burris, Crystal S. Denlinger, Syma Iqbal, Yoon-Koo Kang, Jwa Hoon Kim, Keun-Wook Lee, Bruce Lin, Rutika Mehta, Do-Youn Oh, Sun Young Rha, Chengzhi Xie, Diana Shpektor, Phillip M. Garfin, Geoffrey Ku	**Type:** Rapid Oral Abstract **Session:** Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary **Date:** Monday, June 2, 11:30 a.m.-1:00 p.m. CDT **Number:** 4013
Concordance analysis between tumor tissue HER2 status by immunohistochemistry (IHC) and in situ hybridization (ISH) and a translational analysis of plasma ctDNA in patients (pts) with biliary tract cancer (BTC): An exploratory analysis from phase 2 HERIZON-BTC-01 Trial	James J. Harding, Jin Won Kim, Do-Youn Oh, Heung-Moon Chang, Emerson Y. Chen, Dong Uk Kim, Eric Chen, Joon Oh Park, Mohamedtaki A. Tejani, Jean-Phillippe Metges, John A. Bridgewater, Teresa Macarulla, Xiaotian Wu, Yi Zhao, Diana Shpektor, Phillip M. Garfin, Shubham Pant	**Type:** Poster **Session:** Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary **Date:** Saturday, May 31, 9:00 a.m.-12:00 p.m. CDT **Number:** 4102
Survival outcomes for zanidatamab-hrii compared to chemotherapy in previously treated HER2-positive (IHC3+) biliary tract cancer (BTC): HERIZON-BTC-01 vs a real-world (RW) external control arm (ECA)	Richard Kim, Xiaozhou Fan, Javier Sabater, Wayne Su, Kathleen Hurwitz, Kayla Hendrickson, Kara Bennett, Catherine Wiener, Phillip M. Garfin, Joan Zape, Mark A. Ozog, John A. Bridgewater, Juan W. Valle, Farshid Dayyani	**Type:** Poster **Session:** Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary **Date:** Saturday, May 31, 9:00 a.m.-12:00 p.m. CDT **Number:** 4101

Vyxeos

Presentation Title	Author	Presentation Details

V-RULES: real-world effectiveness and safety of CPX-351 in patients with secondary acute myeloid leukemia (AML)	Thomas W. LeBlanc, Catherine Lai, Amir Ali, Onyee Chan, Doria Cole, Jesus D. Gonzalez-Lugo, Kristin L. Koenig, Mimi Lo, Matthew J. Newman, Saemi Park, Giuseppe Piccoli, Charlotte B. Wagner, Amanda Lopez, George Yaghmour, Eunice S. Wang	**Type:** Poster **Session:** Hematologic Malignancies—Leukemia, Myelodysplastic Syndromes, and Allotransplant **Date:** Sunday, June 1, 9:00 a.m. -12:00 p.m. CDT **Number:** 6520

Dordaviprone

Presentation Title	Author	Presentation Details
Efficacy and safety of dordaviprone (ONC201) in prospective clinical trials of adult and pediatric recurrent H3 K27M-mutant diffuse glioma patients	Ashley Sumrall, Joshua E. Allen, Stephen Bagley, Thomas Brundage, Nicholas Butowski, Jessica Clymer, Aya Haggiagi, Carl Koschmann, Sylvia Kurz, Tobey J. MacDonald, Nazanin K. Majd, Sabine Mueller, Samuel C Ramage, Rohinton S Tarapore, Reena Thomas, Yoshie Umemura, Wafik Zaky, Yazmin Odia	**Type:** Oral Abstract **Session:** Pediatric Oncology II **Date:** Monday, June 2, 8:00-10:00 a.m. CDT **Number:** 10017

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 potentially cell death.[1]

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

Myelosuppression

ZEPZELCA can cause myelosuppression. In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, Grade 3 or 4 neutropenia occurred in 41% of patients, with a median time to onset of 15 days and a median duration of 7 days. Febrile neutropenia occurred in 7% of patients.

Sepsis occurred in 2% of patients and was fatal in 1% (all cases occurred in patients with solid tumors other than SCLC). Grade 3 or 4 thrombocytopenia occurred in 10%, with a median time to onset of 10 days and a median duration of 7 days. Grade 3 or 4 anemia occurred in 17% of patients.

Administer ZEPZELCA only to patients with baseline neutrophil count of at least 1,500 cells/mm^3 and platelet count of at least 100,000/mm^3.

Monitor blood counts including neutrophil count and platelet count prior to each administration. For neutrophil count less than 500 cells/mm^3 or any value less than lower limit of normal, the use of G-CSF is recommended. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

Hepatotoxicity

ZEPZELCA can cause hepatotoxicity. In clinical studies of 554 patients with advanced solid tumors receiving ZEPZELCA, Grade 3 elevations of ALT and AST were observed in 6% and 3% of patients, respectively, and Grade 4 elevations of ALT and AST were observed in 0.4% and 0.5% of patients, respectively. The median time to onset of Grade ≥3 elevation in transaminases was 8 days (range: 3 to 49), with a median duration of 7 days. Monitor liver function tests prior to initiating ZEPZELCA, periodically during treatment, and as clinically indicated. Withhold, reduce the dose, or permanently discontinue ZEPZELCA based on severity.

Extravasation Resulting in Tissue Necrosis

Extravasation of ZEPZELCA resulting in skin and soft tissue injury, including necrosis requiring debridement, can occur. Consider use of a central venous catheter to reduce the risk of extravasation, particularly in patients with limited venous access. Monitor patients for signs and symptoms of extravasation during the ZEPZELCA infusion.

If extravasation occurs, immediately discontinue the infusion, remove the infusion catheter, and monitor for signs and symptoms of tissue necrosis. The time to onset of necrosis after extravasation may vary.

Administer supportive care and consult with an appropriate medical specialist as needed for signs and symptoms of extravasation. Administer subsequent infusions at a site that was not affected by extravasation.

Rhabdomyolysis

Rhabdomyolysis has been reported in patients treated with ZEPZELCA.
Monitor creatine phosphokinase (CPK) prior to initiating ZEPZELCA and periodically during treatment as clinically indicated. Withhold or reduce the dose based on severity.

Embryo-Fetal Toxicity

ZEPZELCA can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise female patients of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZEPZELCA and for 4 months after the last dose.
Lactation
There are no data on the presence of ZEPZELCA in human milk, however, because of the potential for serious adverse reactions from ZEPZELCA in breastfed children, advise women not to breastfeed during treatment with ZEPZELCA and for 2 weeks after the last dose.

MOST COMMON ADVERSE REACTIONS

The most common adverse reactions, including laboratory abnormalities, (≥20%) are leukopenia (79%), lymphopenia (79%), fatigue (77%), anemia (74%), neutropenia (71%), increased creatinine (69%), increased alanine aminotransferase (66%), increased glucose (52%), thrombocytopenia (37%), nausea (37%), decreased appetite (33%), musculoskeletal pain (33%), decreased albumin (32%), constipation (31%), dyspnea (31%), decreased sodium (31%), increased aspartate aminotransferase (26%), vomiting (22%), decreased magnesium (22%), cough (20%), and diarrhea (20%).

DRUG INTERACTIONS

Effect of CYP3A Inhibitors and Inducers
Avoid coadministration with a strong or a moderate CYP3A inhibitor (including grapefruit and Seville oranges) as this increases lurbinectedin systemic exposure which may increase the incidence and severity of adverse reactions to ZEPZELCA. If coadministration cannot be avoided, reduce the ZEPZELCA dose as appropriate.
Avoid coadministration with a strong CYP3A inducer as it may decrease systemic exposure to lurbinectedin, which may decrease the efficacy of ZEPZELCA.

GERIATRIC USE
Of the 105 patients with SCLC administered ZEPZELCA in clinical studies, 37 (35%) patients were 65 years of age and older, while 9 (9%) patients were 75 years of age and older. No overall difference in effectiveness was observed between patients aged 65 and older and younger patients. There was a higher incidence of serious adverse reactions in patients ≥65 years of age than in patients <65 years of age (49% vs 26%, respectively). The serious adverse reactions most frequently reported in patients ≥65 years of age were related to myelosuppression and consisted of febrile neutropenia (11%), neutropenia (11%), thrombocytopenia (8%), and anemia (8%).

Please see accompanying full Prescribing Information.

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.

About Ziihera® (zanidatamab-hrii)
Ziihera (zanidatamab-hrii) is a bispecific HER2-directed antibody that binds to two extracellular sites on HER2. Binding of zanidatamab-hrii with HER2 results in internalization leading to a reduction in HER2 expression of the receptor on the tumor cell surface. Zanidatamab-hrii induces complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP). These mechanisms result in tumor growth inhibition and cell death in vitro and in vivo.[2] In the United States, *Ziihera* is indicated for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer (BTC), as detected by an FDA-approved test.[2] The U.S. Food and Drug Administration (FDA) granted accelerated approval for this indication based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).[2]

Zanidatamab is not yet approved outside of the United States.

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 FDA granted Breakthrough Therapy designation for zanidatamab development in patients with previously treated HER2 gene-amplified 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 1L 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 BTC and gastric cancer.

Important Safety Information for ZIIHERA

WARNING: EMBRYO-FETAL TOXICITY
Exposure to ZIIHERA during pregnancy can cause embryo-fetal harm. Advise patients of the risk and need for effective contraception.

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity
ZIIHERA can cause fetal harm when administered to a pregnant woman. In literature reports, use of a HER2-directed antibody during pregnancy resulted in cases of oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death.

Verify the pregnancy status of females of reproductive potential prior to the initiation of ZIIHERA. Advise pregnant women and females of reproductive potential that exposure to ZIIHERA during pregnancy or within 4 months prior to conception can result in fetal harm. Advise females of reproductive potential to use effective contraception during treatment with ZIIHERA and for 4 months following the last dose of ZIIHERA.

Left Ventricular Dysfunction

ZIIHERA can cause decreases in left ventricular ejection fraction (LVEF). LVEF declined by >10% and decreased to <50% in 4.3% of 233 patients. Left ventricular dysfunction (LVD) leading to permanent discontinuation of ZIIHERA was reported in 0.9% of patients. The median time to first occurrence of LVD was 5.6 months (range: 1.6 to 18.7). LVD resolved in 70% of patients.

Assess LVEF prior to initiation of ZIIHERA and at regular intervals during treatment. Withhold dose or permanently discontinue ZIIHERA based on severity of adverse reactions.
The safety of ZIIHERA has not been established in patients with a baseline ejection fraction that is below 50%.

Infusion-Related Reactions

ZIIHERA can cause infusion-related reactions (IRRs). An IRR was reported in 31% of 233 patients treated with ZIIHERA as a single agent in clinical studies, including Grade 3 (0.4%), and Grade 2 (25%). IRRs leading to permanent discontinuation of ZIIHERA were reported in 0.4% of patients. IRRs occurred on the first day of dosing in 28% of patients; 97% of IRRs resolved within one day.

Prior to each dose of ZIIHERA, administer premedications to prevent potential IRRs. Monitor patients for signs and symptoms of IRR during ZIIHERA administration and as clinically indicated after completion of infusion. Have medications and emergency equipment to treat IRRs available for immediate use.

If an IRR occurs, slow, or stop the infusion, and administer appropriate medical management. Monitor patients until complete resolution of signs and symptoms before resuming. Permanently discontinue ZIIHERA in patients with recurrent severe or life-threatening IRRs.

Diarrhea

ZIIHERA can cause severe diarrhea.
Diarrhea was reported in 48% of 233 patients treated in clinical studies, including Grade 3 (6%) and Grade 2 (17%). If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic tests as clinically indicated to exclude other causes of diarrhea. Withhold or permanently discontinue ZIIHERA based on severity.

ADVERSE REACTIONS

Serious adverse reactions occurred in 53% of 80 patients with unresectable or metastatic HER2-positive BTC who received ZIIHERA. Serious adverse reactions in >2% of patients included biliary obstruction (15%), biliary tract infection (8%), sepsis (8%), pneumonia (5%), diarrhea (3.8%), gastric obstruction (3.8%), and fatigue (2.5%). A fatal adverse reaction of hepatic failure occurred in one patient who received ZIIHERA.
The most common adverse reactions in 80 patients with unresectable or metastatic HER2-positive BTC who received ZIIHERA (≥20%) were diarrhea (50%), infusion-related reaction (35%), abdominal pain (29%), and fatigue (24%).

USE IN SPECIFIC POPULATIONS

Pediatric Use

Safety and efficacy of ZIIHERA have not been established in pediatric patients.

Geriatric Use

Of the 80 patients who received ZIIHERA for unresectable or metastatic HER2-positive BTC, there were 39 (49%) patients 65 years of age and older. Thirty-seven (46%) were aged 65-74 years old and 2 (3%) were aged 75 years or older.
No overall differences in safety or efficacy were observed between these patients and younger adult patients.

About Vyxeos® (daunorubicin and cytarabine)
Vyxeos is a liposomal combination of daunorubicin, an anthracycline topoisomerase inhibitor, and cytarabine, a nucleoside metabolic inhibitor, that is indicated for the treatment of newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC) in adults and pediatric patients 1 year and older. For more information about Vyxeos in the United States, please visit https://vyxeos.com.

Important Safety Information

WARNING: DO NOT INTERCHANGE WITH OTHER DAUNORUBICIN AND/OR CYTARABINE-CONTAINING PRODUCTS

VYXEOS has different dosage recommendations than daunorubicin hydrochloride injection, cytarabine injection, daunorubicin citrate liposome injection, and cytarabine liposome injection. Verify drug name and dose prior to preparation and administration to avoid dosing errors.

Contraindications

VYXEOS is contraindicated in patients with a history of serious hypersensitivity reactions to cytarabine, daunorubicin, or any component of the formulation.

Warnings and Precautions

Hemorrhage

Serious or fatal hemorrhage events, including fatal CNS hemorrhages, associated with prolonged thrombocytopenia, have occurred with VYXEOS. The overall incidence (grade 1-5) of hemorrhagic events was 74% in the VYXEOS arm and 56% in the control arm. The most frequently reported hemorrhagic event was epistaxis (36% in VYXEOS arm and 18% in control arm). Grade 3 or greater events occurred in 12% of VYXEOS-treated patients and in 8% of patients in the control arm. Fatal treatment-emergent CNS hemorrhage not in the setting of progressive disease occurred in 2% of patients in the VYXEOS arm and in 0.7% of patients in the control arm. Monitor blood counts regularly and administer platelet transfusion support as required.

Cardiotoxicity

VYXEOS contains daunorubicin, which has a known risk of cardiotoxicity. This risk may be increased in patients with prior anthracycline therapy, preexisting cardiac disease, previous radiotherapy to the mediastinum, or concomitant use of cardiotoxic drugs. Assess cardiac function prior to VYXEOS treatment and repeat prior to consolidation and as clinically required. Discontinue VYXEOS in patients with impaired cardiac function unless the benefit of initiating or continuing treatment outweighs the risk. VYXEOS is not recommended in patients with cardiac function that is less than normal.

Total cumulative doses of non-liposomal daunorubicin greater than 550 mg/m^2 have been associated with an increased incidence of drug-induced congestive heart failure. The tolerable limit appears lower (400 mg/m^2) in patients who received radiation therapy to the mediastinum. Calculate the lifetime cumulative anthracycline exposure prior to each cycle of VYXEOS. VYXEOS is not recommended in patients whose lifetime anthracycline exposure has reached the maximum cumulative limit.

Hypersensitivity Reactions

Serious or fatal hypersensitivity reactions, including anaphylactic reactions, have been reported with daunorubicin and cytarabine. Monitor patients for hypersensitivity reactions. If a mild or moderate hypersensitivity reaction occurs, interrupt or slow the rate of infusion with VYXEOS and manage symptoms. If a severe or life-threatening hypersensitivity reaction occurs, discontinue VYXEOS permanently, treat the symptoms, and monitor until symptoms resolve.

Copper Overload

VYXEOS contains copper. Consult with a hepatologist and nephrologist with expertise in managing acute copper toxicity in patients with Wilson's disease treated with VYXEOS. Monitor total serum copper, serum non-ceruloplasmin-bound copper, 24-hour urine copper levels, and serial neuropsychological examinations during VYXEOS treatment in patients with Wilson's disease or other copper-related metabolic disorders. Use only if the benefits outweigh the risks. Discontinue in patients with signs or symptoms of acute copper toxicity.

Tissue Necrosis

Daunorubicin has been associated with severe local tissue necrosis at the site of drug extravasation. Administer VYXEOS by the intravenous route only. Confirm patency of intravenous access before administration. Do not administer by intramuscular or subcutaneous route.

Embryo-Fetal Toxicity

VYXEOS can cause embryo-fetal harm when administered to a pregnant woman. Patients should avoid becoming pregnant while taking VYXEOS. If VYXEOS is used during pregnancy or if the patient becomes pregnant while taking VYXEOS, apprise the patient of the potential risk to a fetus. Advise females and males of reproductive potential to use effective contraception during treatment and for 6 months following the last dose of VYXEOS.

MOST COMMON ADVERSE REACTIONS

The most common adverse reactions (incidence ≥25%) are hemorrhagic events (74%), febrile neutropenia (70%), rash (56%), edema (55%), nausea (49%), mucositis (48%), diarrhea (48%), constipation (42%), musculoskeletal pain (43%), fatigue (39%), abdominal pain (36%), dyspnea (36%), headache (35%), cough (35%), decreased appetite (33%), arrhythmia (31%), pneumonia (31%), bacteremia (29%), chills (27%), sleep disorders (26%), and vomiting (25%).

Please see full Prescribing Information, including BOXED Warning

About Dordaviprone
Dordaviprone (ONC201) is a novel first-in-class small molecule imipridone that selectively targets the mitochondrial protease ClpP and dopamine

receptor D2 (DRD2). Dordaviprone's unique mechanism of action includes alterations of key epigenetic modifications such as reversal of H3 K27me3-loss, which is the hallmark of H3 K27M-mutant gliomas.

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 potentially 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.

Jazz Pharmaceuticals plc Caution Concerning Forward-Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements related to Zepzelca's potential as a first-line maintenance therapy for extensive-stage small cell lung cancer, zanidatamab's promise in reshaping treatment paradigms for HER2+ gastroesophageal cancer 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 the successful completion of regulatory activities and uncertain regulatory approval, 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, 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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[1] ZEPZELCA (lurbinectedin) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.
[2] ZIIHERA (zanidatamab-hrii) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

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