Jazz Pharmaceuticals to Present Pivotal Phase 3 Results of Ziihera® (zanidatamab-hrii) Combinations in First-Line HER2-Positive Locally Advanced or Metastatic Gastroesophageal Adenocarcinoma at the 2026 ASCO Gastrointestinal Cancers Symposium

December 02, 2025

Late-breaking HERIZON-GEA-01 presentation highlights the expanding clinical profile of Ziihera across HER2-driven gastrointestinal cancers

Jazz to host investor webcast on Friday, January 9, 2026, to review data

For U.S. media and investors only

DUBLIN, Dec. 2, 2025 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced two abstracts featuring key data for Ziihera® (zanidatamab-hrii) have been accepted for presentation at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO GI) from January 8-10, 2026, in San Francisco. The Phase 3 HERIZON-GEA-01 trial results in first-line HER2-positive (HER2+) locally advanced or metastatic gastroesophageal adenocarcinoma (GEA) were accepted as a late-breaking presentation. Additionally, a new post-hoc overall survival (OS) analysis from the HERIZON-BTC-01 Phase 2b trial in previously treated HER2+ biliary tract cancer (BTC) will be presented, providing further information for this approved indication.

"We look forward to sharing the clinically meaningful results from the Phase 3 HERIZON-GEA-01 trial with the oncology community at ASCO GI," 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. "Advanced HER2+ GEA, which includes cancers of the stomach, gastroesophageal junction and esophagus, remains an aggressive cancer with a poor prognosis and continues to be an area with limited progress for patients. This trial was designed to evaluate whether *Ziihera* plus chemotherapy, with or without tislelizumab, could improve on the current standard of care in first-line therapy. We believe these positive results support *Ziihera* as the HER2-targeted agent-of-choice and the *Ziihera* combinations to become the new standard of care for patients with HER2+ first-line metastatic GEA regardless of PD-L1 status. Alongside new analyses from the HERIZON-BTC-01 Phase 2b trial, these presentations highlight the continued impact of our broad zanidatamab clinical program and our commitment to advancing innovation across HER2-targeted cancers."

The Phase 3 HERIZON-GEA-01 trial, conducted jointly with BeOne Medicines, is evaluating *Ziihera* in combination with chemotherapy, with or without the PD-1 inhibitor Tevimbra® (tislelizumab), as first-line treatment for HER2+ locally advanced or metastatic GEA. As previously announced, both *Ziihera* plus chemotherapy and *Ziihera* plus tislelizumab and chemotherapy demonstrated highly statistically significant and clinically meaningful improvements in progression-free survival (PFS) compared to the control arm, trastuzumab plus chemotherapy. *Ziihera* plus tislelizumab and chemotherapy also demonstrated clinically meaningful and statistically significant improvements in overall survival (OS), and *Ziihera* plus chemotherapy demonstrated a clinically meaningful effect with a strong trend toward statistical significance for OS compared to the control arm at the time of this first analysis.

Jazz Pharmaceuticals will host an investor webcast on Friday, January 9, at 6:30 a.m. PT/ 9:30 a.m. ET to review the *Ziihera* data presented at the meeting. The webcast will include commentary from the company's senior management and Dr. Geoffrey Ku, Associate Attending physician on the Gastrointestinal Oncology Service in the Department of Medicine at Memorial Sloan Kettering Cancer Center. The webcast may be accessed from the Investors section of the Jazz Pharmaceuticals website at www.jazzpharmaceuticals.com. To ensure a timely connection, it is recommended that participants register at least 15 minutes prior to the scheduled webcast.

A replay of the webcast will be available via the Investors section of the Jazz Pharmaceuticals website.

Details for both presentations can be found online and below:

Presentation Title	Authors	Presentation Details
Zanidatamab (zani) + chemotherapy (chemo) ± tislelizumab (tisle) for first-line (1L) HER2-positive (HER2+) advanced/metastatic gastroesophageal adenocarcinoma (mGEA): first results from the phase 3 HERIZON-GEA-01 study	Elena Elimova, Sun Young Rha, Kohei Shitara, Tianshu Liu, Josep Tabernero, Keun-Wook Lee, Michael Schenker, Niall Tebbutt, Jaffer Ajani, Norhidayu Bt Salimin, Geoffrey Ku, Jong Gwang Kim, Inmaculada Ales Diaz, Jingdong Zhang, Filippo Pietrantonio, Li-Yuan Bai, Samuel Le Sourd, Ye Chen, Jonathan Grim, Lin Shen, on behalf of the HERIZON-GEA-01 study group	**Type:** Late-Breaking Abstract Oral Presentation **Session:** Oral Abstract Session A: Cancers of the Esophagus and Stomach **Date:** Thursday, Jan. 8, 8:57-9:07 a.m. PST **Abstract number:** LBA285
Landmark analysis of overall survival (OS) by objective response in patients (pts) with previously treated, advanced HER2-	James J Harding, Jia Fan, Do-Youn Oh, Hye Jin Choi, Jin Won Kim, Heung-Moon Chang, Lequn Bao, Hui-Chuan Sun, Teresa Macarulla, Feng Xie, Jean-Philippe Metges, Jie'er Ying, John Bridgewater, Harpreet Singh Wasan,	**Type:** Poster Session **Session:** Poster Session B: Cancers of the Pancreas, Small Bowel, and Hepatobiliary Tract

positive biliary tract cancer (BTC): post hoc analysis of the HERIZON-BTC-01 trial	Michel Pierre Ducreux, Zinan Bao, Phillip M Garfin, Douglas S Fuller, Parveen Jayia, Shubham Pant	**Date:** Friday, Jan. 9, 11:30 a.m.-1:00 p.m. PST **Abstract number:** 545

The majority of abstracts accepted to ASCO GI will be released at 2:00 p.m. PT/ 5:00 p.m. ET on January 5, 2026. Late-breaking abstracts will be released at 7:00 a.m. PT / 10:00 a.m. ET on their day of presentation at the Symposium and made publicly available online at that time.

About Gastroesophageal Adenocarcinoma
GEA, including cancers of the stomach, gastroesophageal junction, and esophagus, is the fifth most common cancer worldwide, and approximately 20% of patients have HER2+ disease.[1,2,3] HER2+ GEA has high morbidity and mortality, and patients are urgently in need of new treatment options. The overall prognosis for patients with GEA remains poor, with a global five-year survival rate of less than 30% for gastric cancer and about 19% for GEA.[4]

About Biliary Tract Cancer
BTC, which includes gallbladder cancer and intrahepatic and extrahepatic cholangiocarcinoma, are rare and aggressive epithelial tumors often associated with poor prognosis.[5,6] Although they account for less than 1% of all human cancers, cholangiocarcinoma is the second most common primary liver cancer after hepatocellular carcinoma and comprises approximately 10–15% of all primary liver cancers. Global mortality from BTC has risen in recent decades.[7]

Because early symptoms are often vague or nonspecific, most BTCs are diagnosed at an advanced stage,[8] when curative surgery is not an option.[6,9,10] While chemotherapy and, more recently, immunotherapy-based combinations are used in the first-line setting, disease progression is common. In the absence of molecular profiling, treatment options following first-line therapy are largely limited to chemotherapy.[7,9,11]

HER2 overexpression or amplification defines a distinct molecular subtype of BTC[12] and is observed in approximately 26% of patients globally.[13] HER2-positive BTC is associated with worse prognosis than HER2-negative disease.[14] Across the U.S., Europe, and Japan, an estimated 12,000 people are diagnosed with HER2-positive BTC each year.[15]

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.[16] In the United States, *Ziihera* is indicated for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) BTC, as detected by an FDA-approved test.16 The U.S. 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).[16]

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 Pharmaceuticals and BeOne Medicines under license agreements from Zymeworks Inc., which first developed the molecule.

The FDA granted Breakthrough Therapy designation for zanidatamab's 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 first-line GEA. Additionally, zanidatamab has received Orphan Drug designations from the 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.

The full U.S. Prescribing Information for ZIIHERA, including BOXED Warning, is available at: https://pp.jazzpharma.com/pi/ziihera.en.USPI.pdf

® TEVIMBRA (tislelizumab) is a registered trademark of BeOne Medicines.

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.

Cautionary Note Concerning Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to the potential therapeutic benefits of Ziihera, Ziihera's potential as a new standard of care in HER2+ first-line GEA and other HER2-expressing cancers, 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, risks related to failure or delays in successfully initiating or completing clinical trials and assessing patients 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'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, as supplemented by Jazz Pharmaceuticals' Quarterly Report on Form 10-Q for the quarter ended September 30, 2025, 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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