Ziihera® (zanidatamab-hrii) Combinations Achieve Unprecedented Results in First-Line HER2+ Locally Advanced or Metastatic GEA Including More Than Two Years Median Overall Survival Benefit

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Positive Phase 3 HERIZON-GEA-01 results support Ziihera *as the HER2-targeted agent-of-choice in HER2+ first-line metastatic GEA and* Ziihera *plus chemotherapy to replace trastuzumab as the new standard of care, with or without tislelizumab regardless of PD-L1 status*

Late-breaking results to be presented at the 2026 ASCO Gastrointestinal Cancers Symposium (ASCO GI) on January 8, 2026

For U.S. media and investors only

DUBLIN, Jan. 6, 2026 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced positive efficacy and safety results from the Phase 3 HERIZON-GEA-01 trial evaluating Ziihera® (zanidatamab-hrii) in combination with chemotherapy, with or without the PD-1 inhibitor Tevimbra® (tislelizumab), as first-line treatment for adults with HER2-positive (HER2+) locally advanced or metastatic gastroesophageal adenocarcinoma (GEA), including cancers of the stomach, gastroesophageal junction and esophagus.

The data will be presented as a late-breaking oral presentation at the 2026 ASCO Gastrointestinal Cancers Symposium (ASCO-GI) in San Francisco on January 8, 2026 from 8:57- 9:07 a.m. PST (abstract number: LBA285).

The study found:

- Both investigational arms, *Ziihera* plus tislelizumab and chemotherapy, and *Ziihera* plus chemotherapy, led to a statistically significant and clinically meaningful prolongation of progression-free survival (PFS) with approximately 35% reduction in the risk of disease progression or death versus trastuzumab plus chemotherapy. This resulted in a median PFS of more than one year, representing a greater than four-month improvement compared to the control arm.
- *Ziihera* plus tislelizumab and chemotherapy demonstrated a statistically significant and clinically meaningful overall survival (OS) benefit with a median OS of more than two years (26.4 months), the longest reported in a Phase 3 trial in GEA, representing a greater than seven-month improvement in median OS and a 28% reduction in the risk of death versus trastuzumab plus chemotherapy.
- At this first interim analysis, *Ziihera* plus chemotherapy showed a median OS of more than two years, with a strong trend toward statistical significance, favoring *Ziihera* plus chemotherapy versus trastuzumab plus chemotherapy. An additional planned OS interim analysis for *Ziihera* plus chemotherapy is currently expected in mid-2026.
- The OS and PFS benefits were generally consistent across major prespecified subgroups including geographic region and PD-L1 status for both investigational arms.

"Reaching more than two years of median overall survival in a global Phase 3 trial for HER2+ metastatic GEA is truly unprecedented," said Elena Elimova, M.D., Princess Margaret Cancer Centre, the presenting author of the late-breaking data. "The HERIZON-GEA-01 results represent the longest survival outcomes in a Phase 3 trial ever reported in this setting, with the zanidatamab plus tislelizumab and chemotherapy regimen improving median overall survival by more than seven months versus the control arm. The fact that both zanidatamab plus chemotherapy and zanidatamab plus tislelizumab and chemotherapy achieved median progression-free survival beyond one year further reinforces the depth and durability of benefit. These findings signal a meaningful step forward for patients who have historically faced very limited long-term outcomes."

"The results of the HERIZON-GEA-01 study are practice-changing," said Geoffrey Ku, M.D., associate attending physician on the Gastrointestinal Oncology Service in the Department of Medicine at Memorial Sloan Kettering Cancer Center and study co-author. "In addition to the progression-free survival and overall survival benefits, the remarkably long duration of response and consistent benefit across relevant subgroups, including PD-L1 positive and negative tumors, strongly suggest that zanidatamab plus chemotherapy, with or without tislelizumab, should become the new standard of care for patients with HER2+ first-line locally advanced unresectable or metastatic GEA."

Efficacy Summary from HERIZON-GEA-01

Primary Endpoints			
Endpoint	**Trastuzumab plus chemotherapy (control arm)**	***Ziihera* plus chemotherapy**	***Ziihera* plus tislelizumab and chemotherapy**
Median PFS (95% confidence interval [CI])	8.1 months (7.0–8.9)	12.4 months (9.8–14.5)	12.4 months (9.8–18.5)
PFS Hazard Ratio (HR) (95% CI)	—	0.65 (0.52–0.81) *P*<0.0001	0.63 (0.51–0.78) *P*<0.0001
Median OS (95% CI)	19.2 months (16.8–21.8)	24.4 months (20.4–30.0)	26.4 months (21.5–30.3)

OS HR (95% CI)	—	0.80 (0.64–1.01)* *P*=0.0564	0.72 (0.57–0.90) *P*=0.0043
Key Secondary Endpoints			
Endpoint	**Trastuzumab plus chemotherapy (control arm)**	***Ziihera* plus chemotherapy**	***Ziihera* plus tislelizumab and chemotherapy**
Objective Response Rate (ORR)	65.7 %	69.6 %	70.7 %
Median Duration of Response (DoR)	8.3 months	14.3 months	20.7 months
18-Month PFS Rate	20.9 %	38.0 %	43.9 %
30-Month OS Rate	30.0 %	42.2 %	43.8 %
Subgroup Findings	—	Consistent PFS benefit across PD-L1 status, geographic region, and ECOG performance status	Consistent PFS and OS benefit across PD-L1 status, geographic region, and ECOG performance status

** Did not reach statistical significance at the first interim OS analysis*

The safety profile of *Ziihera* in combination with chemotherapy, with or without tislelizumab, was consistent with the known effects of HER2-directed therapy and immunotherapy, and no new safety signals were identified. Duration of treatment was longest on the *Ziihera* plus tislelizumab and chemotherapy arm. Rates of Grade ≥3 treatment-related adverse events (TRAEs) were 71.8% with *Ziihera* plus tislelizumab and chemotherapy, 59.0% with *Ziihera* plus chemotherapy, and 59.6% with trastuzumab plus chemotherapy. Discontinuations due to *Ziihera*- or trastuzumab-related and treatment discontinuations due to adverse events were 11.9% with *Ziihera* plus tislelizumab and chemotherapy, 8.5% with *Ziihera* plus chemotherapy, and 2.3% in the trastuzumab plus chemotherapy arm. The most common Grade ≥3 TRAE was diarrhea (24.5% of patients with *Ziihera* plus tislelizumab and chemotherapy; 20.0% with *Ziihera* plus chemotherapy; and 12.9% of patients in the trastuzumab plus chemotherapy arm). Importantly, discontinuation of either *Ziihera* or trastuzumab due to treatment-related diarrhea was uncommon (4.1% of patients with *Ziihera* plus tislelizumab and chemotherapy, 1.3% with *Ziihera* plus chemotherapy, and 0% of patients in the trastuzumab plus chemotherapy arm). Treatment-emergent diarrhea generally occurred early in treatment and resolved within three weeks. The manageable safety profile supports the feasibility of these combinations in the first-line metastatic setting.

"The strength of the HERIZON-GEA-01 data firmly positions *Ziihera* as the HER2-targeted agent-of-choice capable of reshaping first-line treatment for HER2+ metastatic GEA patients," 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. "These results signal a clear evolution beyond the current standards and give us strong conviction as we move rapidly toward FDA submission. We are equally energized by the momentum we see across our broader development program, and we continue to evaluate *Ziihera* in multiple HER2-driven tumor types, including in HER2+ metastatic breast cancer with the ongoing Phase 3 EmpowHER-303 trial. This is the kind of scientific advancement that can redefine outcomes for patients, and we are committed to delivering it with urgency."

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. 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.

About the Phase 3 HERIZON-GEA-01 Trial

HERIZON-GEA-01 (NCT05152147) is a global, randomized, open-label Phase 3 trial, conducted jointly with BeOne Medicines, to evaluate and compare the efficacy and safety of *Ziihera* plus chemotherapy, with or without tislelizumab, to trastuzumab plus chemotherapy as first-line treatment for adult patients with advanced/metastatic HER2+ GEA. The trial randomized 914 patients from approximately 300 trial sites in more than 30 countries. Appropriate patients for this trial had unresectable locally advanced, recurrent or metastatic HER2+ GEA (adenocarcinomas of the stomach or esophagus, including the gastroesophageal junction), defined as 3+ HER2 expression by IHC or 2+ HER2 expression by IHC with ISH positivity per central assessment. Patients were randomized to the three trial arms: *Ziihera* in combination with chemotherapy and tislelizumab; *Ziihera* in combination with chemotherapy; and trastuzumab plus chemotherapy. The trial is evaluating dual primary endpoints, PFS per blinded independent central review (BICR) and OS.

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 Ziihera® (zanidatamab-hrii)

Ziihera (zanidatamab-hrii) is a bispecific HER2-directed antibody that binds to two extracellular sites on HER2. Binding of zanidatamab with HER2 results in internalization leading to a reduction in HER2 expression of the receptor on the tumor cell surface. Zanidatamab 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.[5] 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.5 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).[5]

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 BeOne under license agreements from Zymeworks, 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.

Dr. Ku has financial interests related to Jazz Pharmaceuticals.

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 and of combination therapies with Ziihera, Ziihera's potential as a new standard of care in HER2+ first-line GEA and other HER2-expressing cancers, expected timing of OS data from the pivotal Phase 3 HERIZON-GEA-01 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 Securities and Exchange Commission filings and reports, 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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