Ziihera® (zanidatamab-hrii) plus Chemotherapy Demonstrates Statistically Significant Overall Survival Benefit Versus Trastuzumab plus Chemotherapy in First-Line HER2+ Advanced GEA

August 31, 2026

HERIZON-GEA-01 results reinforce recently FDA-approved Ziihera *as the definitive HER2-targeted backbone therapy in first-line GEA*

Longer follow up of Ziihera *plus tislelizumab and chemotherapy shows improved OS hazard ratio, further supporting this regimen as the new standard of care*

Data submitted for presentation in fourth quarter 2026

For U.S. media and investors only

DUBLIN, Aug. 31, 2026 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced second interim top-line overall survival (OS) results from the Phase 3 HERIZON-GEA-01 trial showing that Ziihera® (zanidatamab-hrii) in combination with chemotherapy demonstrated statistically significant and clinically meaningful improvements in OS compared with trastuzumab plus chemotherapy as first-line treatment for adults with HER2-positive (HER2+) locally advanced or metastatic gastroesophageal adenocarcinoma (GEA). The *Ziihera* plus chemotherapy OS hazard ratio improved compared with the first interim analysis.

"Advanced HER2+ GEA remains an aggressive cancer with a poor prognosis, and trastuzumab plus chemotherapy has anchored first-line treatment for years. These HERIZON-GEA-01 results show that *Ziihera*-based regimens extend OS, demonstrating definitive superiority of *Ziihera* over trastuzumab and setting a new benchmark for what a first-line HER2-targeted therapy can achieve," said Dr. Kohei Shitara, director of the Department of Gastrointestinal Oncology, and principal trial investigator at the National Cancer Center Hospital East, Kashiwa, Japan.

The safety profile of *Ziihera* in combination with chemotherapy was generally consistent with the known safety profile of each agent and the previously reported data from HERIZON-GEA-01, with no new safety signals observed.

With longer follow up, the *Ziihera* plus Tevimbra® (tislelizumab-jsgr) and chemotherapy OS hazard ratio improved compared with the first interim analysis. These results build on the previous positive data, published in *The New England Journal of Medicine*, further demonstrating statistically significant, clinically meaningful and durable OS improvement for *Ziihera* plus tislelizumab and chemotherapy.

"These results reinforce our confidence that *Ziihera* is the new HER2-targeted backbone therapy in first-line HER2+ advanced GEA, replacing trastuzumab and extending survival beyond the current standard of care," 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. "Following the recent FDA approval, and further supported by these updated results, we are moving quickly to establish *Ziihera* as the HER2-targeted, first-line therapy of choice, with *Ziihera* plus tislelizumab and chemotherapy as the new standard of care in the United States."

On August 25, 2026, the FDA approved *Ziihera* in combination with tislelizumab and chemotherapy, for the first-line treatment of adults with HER2+ (IHC 3+ and IHC 2+/ISH+) unresectable locally advanced or metastatic GEA, and *Ziihera* in combination with chemotherapy in the same setting for patients with HER2+ (IHC 3+) disease.

Jazz has submitted these data for presentation at a major medical meeting in the fourth quarter 2026 and will also submit these data to global health authorities.

The U.S. Prescribing Information for *Ziihera* contains Boxed Warnings for diarrhea and embryo-fetal toxicity.

Additional Important Safety Information related to *Ziihera* use in GEA is provided below. Please see full Prescription, including Boxed Warnings at **https://pp.jazzpharma.com/pi/ziihera.en.USPI.pdf.**

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 zanidatamab plus chemotherapy, with and 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 225 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: zanidatamab in combination with chemotherapy and tislelizumab; zanidatamab in combination with chemotherapy; and trastuzumab plus chemotherapy. The trial evaluated 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.[1,2,3,4] 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 10% for patients with metastatic disease.[5,6]

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 CDC, ADCC, and

ADCP. These mechanisms result in tumor growth inhibition and cell death in vitro and in vivo.[7]

Gastroesophageal adenocarcinoma (GEA): In the United States, *Ziihera* is indicated for the first-line treatment of adults with HER2+ locally advanced or metastatic gastroesophageal adenocarcinoma (GEA), including cancers of the stomach, gastroesophageal junction and esophagus, in combination with tislelizumab-jsgr and fluoropyrimidine- and platinum-containing chemotherapy (HER2+ IHC 3+ and IHC 2+/ISH+ as detected by an FDA-authorized test); and in combination with fluoropyrimidine- and platinum-containing chemotherapy (HER2+ IHC 3+ as detected by an FDA-authorized test).

Biliary tract cancer (BTC): In the United States, *Ziihera* is also indicated for the treatment of adults with previously treated, unresectable or metastatic HER2+ (IHC 3+) biliary tract cancer (BTC), as detected by an FDA-approved test.[7] Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).[7] Ziihera is also approved in the European Union and other countries.

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 three Breakthrough Therapy designations for zanidatamab's development: one as a single agent for previously treated HER2 gene-amplified BTC; one in combination with fluoropyrimidine- and platinum-containing chemotherapy, with or without tislelizumab for first-line HER2+ unresectable locally advanced or metastatic gastric, gastroesophageal junction (GEJ), or esophageal GEA; and one for the treatment of adults with previously treated, locally advanced, unresectable, or metastatic HER2+ colorectal cancer (CRC). The FDA also granted 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, gastric (including GEJ) cancer, and esophageal cancer, as well as Orphan Drug designations from the European Medicines Agency for the treatment of BTC, gastric/gastroesophageal junction cancer, and esophageal cancer. Jazz continues to pursue additional regulatory approvals for zanidatamab in markets worldwide.

Important Safety Information for ZIIHERA

WARNING: DIARRHEA and EMBRYO-FETAL TOXICITY

ZIIHERA, in combination with fluoropyrimidine- and platinum-containing chemotherapy, with or without tislelizumab-jsgr, can cause severe diarrhea, including life threatening and fatal cases. Use antidiarrheal prophylaxis during the first cycle when ZIIHERA is given in combination with these drugs. Manage with antidiarrheals and supportive measures as clinically indicated. Interrupt, reduce the dose or discontinue ZIIHERA based on severity.

Embryo-Fetal Toxicity: Exposure to ZIIHERA during pregnancy can cause embryo-fetal harm. Advise patients of the risk and need for effective contraception.

Diarrhea: ZIIHERA can cause severe diarrhea.

When ZIIHERA is used in combination with fluoropyrimidine- and platinum-containing chemotherapy with or without tislelizumab-jsgr, severe, life threatening, and fatal cases of diarrhea can occur despite loperamide prophylaxis. The risk of severe and life threatening diarrhea is higher when ZIIHERA is administered with chemotherapy and tislelizumab-jsgr, with a higher risk in patients aged ≥ 65 years compared to younger patients. Advise patients to increase oral fluids, begin antidiarrheals, and notify their healthcare provider immediately if diarrhea occurs.

Administer antidiarrheal prophylaxis with loperamide in cycle 1 for all patients receiving ZIIHERA in combination with fluoropyrimidine- and platinum-containing chemotherapy with or without tislelizumab-jsgr. Begin loperamide at the first loose stool when ZIIHERA is administered in combination with chemotherapy. Administer fluids, electrolytes, and additional antidiarrheal agents as necessary. Before modifying the dose of ZIIHERA, evaluate, modify or discontinue drug(s) contributing to diarrhea in accordance with their respective prescribing information. Withhold, reduce the dose, or permanently discontinue ZIIHERA based on severity.

If treating patients with ZIIHERA in combination with FOLFOX, do not administer the fluorouracil bolus.

ZIIHERA in combination with chemotherapy and tislelizumab-jsgr
Diarrhea was reported in 85% of 330 patients in clinical studies, including Grade 4 (2.1%), Grade 3 (24%), and Grade 2 (31%) events. Fatal outcomes resulting from diarrhea occurred in 1.5% of patients. Diarrhea leading to dose reduction of ZIIHERA occurred in 10% of patients, and permanent discontinuation of ZIIHERA occurred in 3.9% of patients.

In cycle 1, diarrhea at Grade 4 severity occurred in 1.5% and Grade 3 severity occurred in 15% of patients despite use of loperamide prophylaxis. The median time to onset for cycle 1 diarrhea was 6 days and median time to resolution was 18 days.

ZIIHERA in combination with chemotherapy
Diarrhea was reported in 81% of 395 patients in clinical studies, including Grade 4 (1.3%), Grade 3 (20%) and Grade 2 (33%). Diarrhea leading to dose reduction of ZIIHERA occurred in 10% of patients, and permanent discontinuation of ZIIHERA occurred in 1.8% of patients.

In cycle 1, diarrhea at Grade 4 severity occurred in 0.8% and Grade 3 severity occurred in 14% of patients despite use of loperamide prophylaxis. The median time to onset for cycle 1 diarrhea was 6 days and median time to resolution was 18 days.

Embryo-Fetal Toxicity: Based on the mechanism of action, ZIIHERA can cause fetal harm when administered to a pregnant woman. There are no human or animal data on the use of ZIIHERA in pregnancy. 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 while receiving ZIIHERA and for 4 months following the last dose of ZIIHERA.

Left Ventricular Dysfunction (LVD): ZIIHERA can cause decreases in left ventricular ejection fraction (LVEF).

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 < 50%.

ZIIHERA in combination with chemotherapy and tislelizumab-jsgr
LVEF decrease (an absolute decline in LVEF of > 10%, resulting in a final value of < 50%) was observed in 9% of 330 patients in clinical studies. LVD leading to permanent discontinuation of ZIIHERA was reported in 3% of patients. Fatal outcomes due to LVD occurred in one patient (0.3%). The median time to first occurrence of LVD was 6.9 months (range: 1.2 to 29.1 months). LVD resolved in 78% of patients.

ZIIHERA in combination with chemotherapy
LVEF decrease was observed in 5% of 395 patients. LVD leading to permanent discontinuation of ZIIHERA was reported in 1.0% of patients. The median time to first occurrence of LVD was 6.0 months (range: 1.4 to 15.0 months). LVD dysfunction resolved in 70% of patients.

Infusion-Related Reactions: ZIIHERA can cause infusion-related reactions (IRRs).

Prior to each dose of ZIIHERA, administer premedication 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.

ZIIHERA in combination with chemotherapy and tislelizumab-jsgr
An IRR was reported in 22% of 330 patients in clinical studies, including Grade 4 (0.3%), Grade 3 (1.2%), and Grade 2 (16%) despite use of prophylaxis. IRRs leading to permanent discontinuation of ZIIHERA were reported in 0.3% of patients. IRRs occurred on the first day of dosing in 17% of patients. Of all patients who experienced IRRs, 60% of reactions resolved within the first day.

ZIIHERA in combination with chemotherapy
An IRR was reported in 24% of 395 patients in clinical studies, including Grade 4 (0.3%), Grade 3 (1.5%), and Grade 2 (18%) despite use of prophylaxis. IRRs leading to permanent discontinuation of ZIIHERA were reported in 1.3% of patients. IRRs occurred on the first day of dosing in 22% of patients. Of all patients who experienced IRRs, 83% of reactions resolved within the first day.

Adverse Reactions
ZIIHERA in combination with chemotherapy and tislelizumab-jsgr
Serious adverse reactions occurred in 59% of 294 patients in HERIZON-GEA-01. Serious adverse reactions in > 2% of patients included diarrhea (17%), IRR (5%), vomiting (4.8%), hypokalemia (4.4%), acute kidney injury (3.7%), pneumonia (3.7%), nausea (2.4%), decreased appetite (2.4%), and anemia (2.4%). Fatal adverse reactions occurred in 2.4% of patients and included acute kidney injury (N=2), cardiac failure, diarrhea, dehydration, hypovolemic shock and intestinal obstruction (all N=1).

Permanent discontinuation of ZIIHERA occurred in 13% of patients. Adverse reactions that resulted in permanent discontinuation of ZIIHERA in ≥ 1% of patients included diarrhea (4.4%) and ejection fraction decreased (2.7%).

The most common adverse reactions (≥ 20%) were diarrhea (83%), nausea (56%), decreased appetite (46%), vomiting (44%), hypokalemia (39%), fatigue (37%), rash (36%), peripheral neuropathy (27%), and IRR (25%).

ZIIHERA in combination with chemotherapy
Serious adverse reactions occurred in 49% of 305 patients in HERIZON-GEA-01. Serious adverse reactions in > 2% of patients included diarrhea (11%), vomiting (3.3%), decreased appetite (2.6%), pneumonia (2.6%), sepsis (2.6%), hypokalemia (2.3%), and nausea (2.3%).

Permanent discontinuation of ZIIHERA occurred in 10% of patients. Adverse reactions that resulted in permanent discontinuation of ZIIHERA in ≥ 1% of patients included ejection fraction decreased (2.0%), IRR (1.6%), and diarrhea (1.6%).

The most common adverse reactions (≥ 20%) were diarrhea (79%), nausea (54%), vomiting (44%), decreased appetite (40%), fatigue (36%), hypokalemia (33%), peripheral neuropathy (32%), IRR (25%), and rash (22%).

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

Geriatric Use
ZIIHERA in combination with chemotherapy and tislelizumab-jsgr
Of 302 patients randomized to ZIIHERA in combination with chemotherapy and tislelizumab-jsgr in HERIZON-GEA-01, there were 139 (46%) patients aged ≥ 65 years. One hundred and six (35%) were aged 65-74 years and 33 (11%) were aged ≥ 75 years.

There was a higher incidence of Grade ≥ 3 adverse reactions observed in patients aged ≥ 65 years (87%) as compared to younger patients (80%). The incidence of Grade 3 or 4 diarrhea was higher in patients aged ≥ 65 years (32%) compared to younger patients (20%).

There was an increased incidence of fatal adverse reactions in patients aged ≥ 65 years (4.4%); including acute kidney injury (N=2), cardiac failure, dehydration, hypovolemic shock and intestinal obstruction (all N=1), compared to younger patients (0.6%), including diarrhea (N=1).

ZIIHERA in combination with chemotherapy
Of 304 patients randomized to ZIIHERA in combination with chemotherapy in HERIZON-GEA-01, there were 130 (43%) patients aged ≥ 65 years. One hundred (33%) were aged 65-74 years and 30 (10%) were aged ≥ 75 years.

No overall differences in safety were observed between patients aged ≥ 65 years and younger adult patients.

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 life-changing medicines for people with rare disease — often with limited or no therapeutic options. We have a diverse portfolio of medicines, including leading therapies addressing epilepsies, cancers and sleep disorders. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics. 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 Ziihera's potential to extend survival, 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' Securities and Exchange Commission filings and reports, including Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 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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