Phase 3 HERIZON-GEA-01 Results Published in The New England Journal of Medicine Show Durable and Consistent Survival Benefit with Ziihera® (zanidatamab-hrii) Combinations in First-Line HER2+ Locally Advanced or Metastatic GEA

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Expanded safety, subgroup, progression-free survival sensitivity and subsequent therapy analyses further characterize the consistency and durability of outcomes observed with zanidatamab-containing combinations in the first-line setting

Additional subgroup analyses to be presented at the 2026 ASCO Annual Meeting show improved clinical outcomes with zanidatamab-containing combinations regardless of PD-L1 expression, including in PD-L1-negative patients

For U.S. media and investors only

DUBLIN, May 27, 2026 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the *New England Journal of Medicine* has published the Phase 3 HERIZON-GEA-01 trial results, further characterizing the efficacy and safety profile of Ziihera® (zanidatamab-hrii) in combination with chemotherapy, with and 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 manuscript builds on the late-breaking oral presentation of the HERIZON-GEA-01 trial results at the 2026 ASCO Gastrointestinal Cancers Symposium (ASCO GI), where zanidatamab-containing combinations demonstrated unprecedented progression-free survival (PFS) and overall survival (OS) outcomes in a global Phase 3 trial.

- As previously reported, both zanidatamab-containing combinations significantly improved PFS compared with trastuzumab plus chemotherapy (median PFS 12.4 months versus 8.1 months; Hazard Ratio (HR) 0.63-0.65), and zanidatamab plus tislelizumab and chemotherapy demonstrated a statistically significant OS benefit (median OS 26.4 versus 19.2 months; HR 0.72).
- At the first interim analysis, zanidatamab plus chemotherapy also demonstrated a median OS of more than two years. The OS for zanidatamab plus chemotherapy will be assessed at a second interim analysis expected in mid-2026.
- The publication includes expanded prespecified subgroup analyses showing that PFS and OS results were generally consistent across clinically relevant patient characteristics, including PD-L1 status, geographic region, and Eastern Cooperative Oncology Group performance status, as well as PFS sensitivity analyses supporting the robustness of the findings.
- Expanded safety analyses further characterize the safety profile of zanidatamab-containing regimens.

"The additional analyses from HERIZON-GEA-01 provide further support for using zanidatamab in clinical practice," said Kohei Shitara, M.D., director of the Department of Gastrointestinal Oncology, co-lead author of the *New England Journal of Medicine* publication, and principal investigator of the HERIZON-GEA-01 trial at the National Cancer Center Hospital East in Kashiwa, Japan. "For patients with HER2+ locally advanced or metastatic GEA, long-term outcomes have historically been limited. The expanded subgroup and sensitivity analyses indicate the durability and consistency of benefit observed with zanidatamab-containing regimens. Importantly, survival benefit with the addition of tislelizumab was suggested across PD-L1-defined subgroups, including in patients with PD-L1-negative tumors, a population that has historically derived limited benefit from PD-1-based approaches."

"We believe the HERIZON-GEA-01 results, together with the additional analyses now published, establish zanidatamab's differentiated clinical profile in first-line HER2+ locally advanced or metastatic GEA," 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. "In this global Phase 3 trial, zanidatamab demonstrated superior efficacy compared with trastuzumab-based standard of care, and the addition of tislelizumab enhanced overall survival. Taken together, these findings support the potential for zanidatamab-containing regimens to become a HER2-targeted agent of choice in this setting. Additionally, this marks the first immuno-oncology combination to show efficacy across both PD-L1–positive and PD-L1–negative tumors in this clinical setting, consistent with zanidatamab's unique mechanism of action that enhances immune activation through complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC), and antibody-dependent cellular phagocytosis (ADCP). These results are reshaping expectations for first-line treatment in this disease, and we continue to work with urgency to deliver this treatment option for patients."

Results of additional safety analyses of zanidatamab plus chemotherapy, with and without tislelizumab, were consistent with the known safety profiles of the individual components. Gastrointestinal events, including diarrhea, most commonly occurred early in treatment, were generally time-limited, and infrequently led to discontinuation of HER2-targeted therapy.

Analyses of subsequent anticancer therapies showed greater use of immune checkpoint inhibitors and HER2-targeted therapies in the trastuzumab plus chemotherapy group than in the zanidatamab-containing groups, reflecting that a higher proportion of patients in that arm experienced disease progression and subsequently received additional therapy. These analyses provide important context for interpreting OS outcomes.

Jazz has submitted the Phase 3 HERIZON-GEA-01 data, including this manuscript, to the National Comprehensive Cancer Network® (NCCN®) for inclusion in the NCCN Clinical Practice Guidelines in Oncology® (NCCN Guidelines®).

PD-L1 Subgroup Oral Presentation at ASCO 2026

In addition, prespecified PD-L1 subgroup analyses from the Phase 3 HERIZON-GEA-01 trial to be presented at the 2026 American Society of Clinical Oncology (ASCO) Annual Meeting (May 29-June 2, 2026, in Chicago) provide further insight into the impact of zanidatamab-containing combinations across PD-L1-defined subgroups.

- Zanidatamab in combination with tislelizumab and chemotherapy demonstrated meaningful improvements in PFS and OS in both PD-L1-positive and PD-L1-negative patients as determined by tumor area positivity (TAP) score and combined positive score (CPS).
- With 26 months of follow-up, similarly prolonged PFS and OS were observed in both PD-L1-positive and PD-L1-negative patients compared with the control arm.
- Notably, in PD-L1-negative patients (TAP <1%), median OS was 29.7 months with zanidatamab in combination with tislelizumab and chemotherapy compared with 15.8 months with trastuzumab plus chemotherapy, with findings consistent across PD-L1 assessment methods.
- In PD-L1-positive patients (TAP≥1%), median OS was 26.4 months with zanidatamab in combination with tislelizumab and chemotherapy compared with 21.2 months with trastuzumab plus chemotherapy, with findings consistent across PD-L1 assessment methods.

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 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 CDC, ADCC, and 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 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.

A supplemental biologics license application for zanidatamab is under FDA Real-Time Oncology Review in first-line HER2+ locally advanced or metastatic GEA. The FDA granted two Breakthrough Therapy designations for zanidatamab's development: one as a single agent for previously treated HER2 gene-amplified BTC, and 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. 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.

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 patients 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 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 the potential therapeutic benefits of zanidatamab and of combination therapies with zanidatamab, zanidatamab'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, 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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