Jazz Pharmaceuticals Announces FDA Acceptance and Priority Review of Supplemental Biologics License Application for Ziihera® (zanidatamab-hrii) Combinations in First-Line HER2+ Locally Advanced or Metastatic GEA

April 27, 2026

Prescription Drug User Fee Act (PDUFA) date set for August 25, 2026

For U.S. media and investors only

DUBLIN, April 27, 2026 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the U.S. Food and Drug Administration (FDA) accepted for filing with Priority Review the supplemental Biologics License Application (sBLA) for Ziihera® (zanidatamab-hrii) containing combinations for the first-line treatment of adult patients with HER2-positive (HER2+) unresectable locally advanced or metastatic gastric, gastroesophageal junction (GEJ), or gastroesophageal adenocarcinoma (GEA). The FDA has set a PDUFA target action date of August 25, 2026.

The sBLA is supported by data from the pivotal HERIZON-GEA-01 trial to investigate the efficacy and safety of zanidatamab in combination with standard-of-care chemotherapy with or without the PD-1 inhibitor Tevimbra® (tislelizumab) in patients with advanced or metastatic GEA, including gastric, GEJ and esophageal adenocarcinomas. The submission is under review via the Real-Time Oncology Review (RTOR) program, an initiative of FDA's Oncology Center of Excellence designed to provide a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible.

"The HERIZON-GEA-01 trial results are practice changing, supporting the potential of zanidatamab as the HER2-targeted agent-of-choice in HER2+ first-line locally advanced or metastatic GEA. Importantly, the results demonstrated adding tislelizumab to zanidatamab plus chemotherapy further enhanced clinical benefit and marked the first immuno-oncology combination to show efficacy across both PD-L1–positive and PD-L1–negative tumors in this clinical setting," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of R&D, and chief medical officer of Jazz Pharmaceuticals. "We look forward to continuing to work closely with FDA to obtain approval and quickly bring zanidatamab to market for GEA patients in need of new options."

The FDA granted Breakthrough Therapy designation to zanidatamab in combination with fluoropyrimidine- and platinum-containing chemotherapy, with or without tislelizumab, for the first-line treatment of patients with HER2+ unresectable locally advanced or metastatic gastric, GEJ, or esophageal adenocarcinoma. Breakthrough Therapy designation is intended to expedite the development and review of therapies that, based on preliminary clinical evidence, may offer substantial improvement over available therapies on one or more clinically significant endpoints, reflecting both the seriousness of the disease and the unmet medical need in this setting.

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 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: 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. Results from the trial were presented in January 2026 at the 2026 ASCO Gastrointestinal Cancers Symposium.

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-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.[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.[1] 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).[1]

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 under license agreements from Zymeworks, which first developed the molecule.

An sBLA for zanidatamab is being reviewed by the FDA under RTOR 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, GEJ or esophageal adenocarcinoma. 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/GEJ cancer and oesophageal 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 life-changing medicines for people with rare disease — often with limited or no therapeutic options. We have a diverse portfolio of marketed 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 Ziihera (zanidatamab-hrii) 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 and ability to obtain FDA approval under the RTOR program for zanidatamab in HER2+ first-line GEA 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.

Contacts:
Media:
CorporateAffairsMediaInfo@jazzpharma.com
Ireland +353 1 637 2141
U.S. +1 215 867 4948

Investor:
InvestorInfo@jazzpharma.com
Ireland +353 1 634 3211
U.S. +1 650 496 2717

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[4]Battaglin F, et al. Molecular biomarkers in gastro-esophageal cancer: recent developments, current trends and future directions. Cancer Cell International. 2018;18(99).
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