Jazz Pharmaceuticals Receives European Commission Marketing Authorization for Ziihera® (zanidatamab) for the Treatment of Advanced HER2-Positive Biliary Tract Cancer

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– Conditional approval based on positive results from the HERIZON-BTC-01 Phase 2b trial –

DUBLIN, July 1, 2025 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the European Commission (EC) has granted conditional marketing authorization[1] for Ziihera® (zanidatamab), a dual human epidermal growth factor receptor 2 (HER2)-targeted bispecific antibody, as monotherapy for the treatment of adults with unresectable locally advanced or metastatic HER2-positive (IHC 3+)† biliary tract cancer (BTC) previously treated with at least one prior line of systemic therapy.[2]

BTCs, which include gallbladder cancer (GBC) and cholangiocarcinoma (CCA), are a rare and aggressive group of cancers,[3] with most cases diagnosed at an advanced stage[4] when curative surgery is no longer an option.[5,6,7] Globally, approximately 26% of patients with BTC are HER2-positive,[8] a biomarker associated with poorer outcomes compared to HER2-negative disease.[9]

Ziihera is the first HER2-targeted therapy given conditional authorization for HER2-positive BTC in the European Union (EU). Continued approval for this indication is contingent upon verification and description of clinical benefit in the ongoing Phase 3 HERIZON-BTC-302 trial, which is evaluating zanidatamab in combination with standard-of-care therapy versus standard-of-care therapy alone in the first-line setting for patients with HER2-positive BTC.[10]

"People with HER2-positive biliary tract cancer who progress after first-line therapy face a challenging prognosis, with limited treatment options, poor tolerability, and median overall survival of only six to nine months," said Arndt Vogel, MD, managing senior consultant and professor in the Department of Gastroenterology, Hepatology and Endocrinology at Hannover Medical School, Germany. "Zanidatamab provides a much-needed targeted monotherapy for this population, and in the HERIZON-BTC-01 trial, it demonstrated clinically meaningful and durable responses with a manageable safety profile. These data represent a welcome advance for patients with historically poor outcomes and highlight the importance of HER2 testing in biliary tract cancer to ensure eligible patients are identified for biomarker-driven treatment."

The EC decision is based on data from the Phase 2b HERIZON-BTC-01 trial, which evaluated *Ziihera* in patients with previously treated, unresectable, locally advanced or metastatic HER2-positive BTC. This is the largest Phase 2b trial conducted to date specifically in this population.[11,12] The study enrolled 87 patients, including 80 in Cohort 1 with centrally confirmed HER2-positive tumors (IHC 2+/ISH+ [n=18] or IHC 3+/ISH+ [n=62]). The trial achieved its primary endpoint of confirmed objective response rate (cORR) in Cohort 1, as assessed by independent central review (ICR). At a median follow-up of 21.9 months, zanidatamab demonstrated a cORR of 41.3% (95% CI: 30.4, 52.8), including two complete responses.[11] The median duration of response (DOR) was 14.9 months (95% CI: (7.4, not reached), and the median overall survival (OS) was 15.5 months (95% CI: 10.4, 18.5).[11]

Findings from a pre-specified subgroup analysis in patients with IHC 3+ tumors (n=62) showed that *Ziihera* demonstrated a cORR of 51.6% (95% CI: 38.6, 64.5), with a median DOR of 14.9 months (95% CI: 7.4, 24.0).[2] The median OS in this subgroup was 18.1 months (95% CI: 12.2, 22.9).[2]

The recommended dose of *Ziihera* is 20 mg/kg, administered as an intravenous infusion every two weeks until disease progression or unacceptable toxicity.[2]

The safety profile for zanidatamab was evaluated in 87 patients with HER2-positive BTC (Cohorts 1 and 2) in HERIZON-BTC-01. The most common adverse reactions in this population were diarrhea (46%), infusion-related reaction (33.3%), abdominal pain (26.4%), anemia (25.3%) and fatigue (24.1%). Serious adverse reactions occurred in 16.1% of patients. The most frequent serious adverse reactions were diarrhea (2.3%), fatigue (2.3%), and increased alanine aminotransferase (2.3%).[2]

"This conditional approval represents significant progress for the patients we serve who have been diagnosed with advanced HER2-positive BTC," said Robert Iannone, MD., M.S.C.E., executive vice president, global head of research and development, and chief medical officer of Jazz Pharmaceuticals. "*Ziihera* is the first HER2-targeted therapy authorized in the European Union specifically for this population, and the European Commission's decision reflects both the strength of the HERIZON-BTC-01 data and the urgency for innovation in rare gastrointestinal cancers. This milestone reinforces our commitment to advancing biomarker-driven therapies that address serious unmet needs and improve patient outcomes. We are actively recruiting for our global Phase 3 trial in first-line HER2-positive BTC and continue to explore zanidatamab's potential in other HER2-expressing tumors."

"Biliary tract cancers are becoming more common worldwide and are increasingly affecting people under the age of 60, resulting in a significant social and economic burden," said Zorana Maravic, chief executive officer at Digestive Cancers Europe (DiCE). "These cancers are typically diagnosed late, when patients have limited treatment options available and, unfortunately, their disease often progresses. *Ziihera* provides a much-needed alternative to chemotherapy for patients with HER2-positive BTC at this stage. It also brings hope to the digestive cancer patient community as another step in expanding the availability of targeted therapies."

The European Commission authorization extends to all European Union Member States, as well as Iceland, Norway, and Liechtenstein.

For a full list of side effects and information on dosage and administration, contraindications, and other precautions when using *Ziihera*, please refer to the Summary of Product Characteristics for further information.

About Ziihera® (zanidatamab)

Ziihera (zanidatamab) is a dual HER2-targeted bispecific antibody that simultaneously binds extracellular domains 2 and 4 on separate HER2 monomers (binding in trans). Binding of zanidatamab with HER2 results in internalization leading to a reduction of the receptor on the 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 tumor cell death.[2]

On November 20, 2024, in the United States, the U.S. Food and Drug Administration (FDA) granted accelerated approval of *Ziihera* (zanidatamab-hrii) 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.[13] This accelerated approval was granted based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the ongoing Phase 3 HERIZON-BTC-302 confirmatory trial.[13] It also received conditional approval from China's National Medical Products Administration (NMPA) in May 2025 for the treatment of patients with previously treated, unresectable or metastatic HER2+BTC. Continued approval of this indication will depend on the verification of clinical benefit in the patient population through an ongoing confirmatory trial.

Zanidatamab is also being investigated in multiple other clinical trials as a targeted treatment option for patients with solid tumors that express HER2. Zanidatamab is being developed by Jazz and BeOne Medicines Ltd. (formerly BeiGene, Ltd) under license agreements from Zymeworks, which first developed the molecule. Jazz has rights to commercialize zanidatamab in the U.S., Europe, Japan and all other territories except for those Asia/Pacific territories that Zymeworks previously licensed to BeiGene, Ltd. [which are Asia (excluding Japan), Australia and New Zealand].

The FDA granted Breakthrough Therapy designation for zanidatamab 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 1L gastroesophageal adenocarcinoma (GEA). Additionally, zanidatamab has received Orphan Drug designations from 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.

About Biliary Tract Cancer

Biliary tract cancers (BTC), which include gallbladder cancer and intrahepatic and extrahepatic cholangiocarcinoma, are rare and aggressive epithelial tumors often associated with poor prognosis.[3,14] 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.[5]

Because early symptoms are often vague or nonspecific, most BTCs are diagnosed at an advanced stage,[4] when curative surgery is not an option.[5,6,7] 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.[5,6,15]

HER2 overexpression or amplification defines a distinct molecular subtype of BTC[16] and is observed in approximately 26% of patients globally.[8] HER2-positive BTC is associated with worse prognosis than HER2-negative disease.[9] Across the U.S., Europe, and Japan, an estimated 12,000 people are diagnosed with HER2-positive BTC each year.[17]

About Jazz Pharmaceuticals plc

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.

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† IHC3+ stands for ImmunoHistoChemistry 3+ and refers to the highest level of HER2 protein overexpression in cancer cells

1 European Medicines Agency. Conditional marketing authorisation. European Medicines Agency website. Accessed July 1, 2025. Available at: https://www.ema.europa.eu/en/human-regulatory-overview/marketing-authorisation/conditional-marketing-authorisation

2 Ziihera Summary of Product Characteristics (SmPC).

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[17] Jazz Pharmaceuticals, Inc, Data on file.

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