Jazz Pharmaceuticals Completes Zanidatamab Biologics License Application for Previously Treated HER2-Positive Metastatic Biliary Tract Cancer

April 02, 2024

Submission based on data from Phase 2b HERIZON-BTC-01 trial, which met its primary endpoint in patients receiving zanidatamab for previously treated HER2-positive biliary tract cancer (BTC)

Confirmatory Phase 3 trial in first-line (1L) BTC open for enrollment at multiple global sites

DUBLIN, April 2, 2024 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the company has completed the rolling submission of a Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) seeking accelerated approval for the HER2-targeted bispecific antibody zanidatamab as a treatment for previously-treated, unresectable, locally advanced, or metastatic HER2-positive biliary tract cancer (BTC). If approved, zanidatamab would be the first HER2-targeted treatment specifically approved for BTC in the U.S.

"This important milestone brings us one step closer to delivering zanidatamab, a targeted treatment option, to patients living with HER2-positive BTC, a type of cancer that is associated with a five-year overall survival rate of less than 5%," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "Zanidatamab is a biparatopic HER2-targeted bispecific antibody that simultaneously binds two non-overlapping epitopes of HER2 resulting in multiple mechanisms of action. Second-line (2L) BTC represents the first of multiple indications we are evaluating and we are excited about zanidatamab's potential as a new option for multiple HER2-expressing cancers, with ongoing Phase 3 trials in 1L BTC, 1L gastroesophageal adenocarcinoma (GEA), and previously treated breast cancer."

The BLA includes data from the Phase 2b HERIZON-BTC-01 trial of zanidatamab in previously treated HER2-positive BTC. The primary endpoint was confirmed objective response rate (cORR) by independent central review (ICR) in Cohort 1. Data as of Oct. 10, 2022, from the 80 HER2-positive BTC patients enrolled in Cohort 1 of the trial demonstrated a cORR of 41.3% [95% confidence interval (CI): 30.4, 52.8] with a Kaplan Meier (KM) estimated median duration of response (DOR) of 12.9 months [95% CI: 6.0-not estimable] by ICR. Historical response rates for 2L standard-of-care chemotherapy in patients with BTC are reported to be 5 to 15%[1,2]. The KM estimated median progression-free survival (PFS) was 5.5 months [95% CI: 3.7, 7.2] with a range of 0.3 to 18.5 months.

Zanidatamab demonstrated a manageable and tolerable safety profile, with only two patients (2.3%) in HERIZON-BTC-01 experiencing adverse events (AEs) leading to treatment discontinuation. There were no Grade 4 AEs, and no deaths were considered treatment-related. The most common AEs were diarrhea and infusion-related reactions, which were predominately low-grade, reversible and manageable prophylactically with routine supportive care.

These data were featured as an oral presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting 2023, published in *The Lancet Oncology*, and included in the 2023 Best of ASCO® program. Quality-of-life data from this trial were also presented at the European Society for Medical Oncology (ESMO) Congress 2023 and at the 2024 ASCO Gastrointestinal Cancers Symposium.

The HERIZON-BTC-302 Phase 3 trial (NCT06282575) of zanidatamab in 1L advanced or metastatic HER2-positive BTC was recently initiated and is open for enrollment. The global, open-label, randomized trial will evaluate the efficacy and safety of zanidatamab in combination with standard-of-care therapy against standard-of-care therapy alone. The primary objective of the study is to compare the efficacy of zanidatamab and chemotherapy (cisplatin plus gemcitabine) with or without the addition of a programmed death protein 1/ligand 1 (PD-1/L-1) inhibitor versus chemotherapy with or without a PD-1/L1 inhibitor in patients. HERIZON-BTC-302 is proposed as the confirmatory trial for zanidatamab in BTC.

About Zanidatamab
Zanidatamab is an investigational bispecific antibody that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. This unique design and increased binding results in multiple mechanisms of action, including dual HER2 signal blockade, removal of HER2 protein from the cell surface, and immune-mediated cytotoxicity leading to encouraging antitumor activity in patients. 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 BeiGene, Ltd. (BeiGene) under license agreements from Zymeworks, which first developed the molecule.

The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation for zanidatamab development in patients with previously treated HER2 gene-amplified biliary tract cancers (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. Zanidatamab was also granted Breakthrough Therapy designation from the Center for Drug Evaluation (CDE) in China.

About Biliary Tract Cancer
Biliary tract cancer (BTC), including gallbladder cancer and intrahepatic and extrahepatic cholangiocarcinoma, account for <1% of all adult cancers and are often associated with a poor prognosis[3,4]. The human epidermal growth factor receptor 2 (HER2) is a well-validated target for antitumor therapy in other cancers. Across the U.S., Europe, and Japan, approximately 12,000 people are diagnosed with BTC annually[5,6,7,8] and most patients (> 65%) are diagnosed with tumors that cannot be removed surgically.

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 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.

Jazz Pharmaceuticals plc Caution Concerning Forward-Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements related to our goal of bringing to market the first HER2-targeted treatment specifically approved for BTC, leading the development of a HER2-targeted therapy with a unique bispecific antibody with potential to treat multiple 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 pharmaceutical product development, 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 plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2023, 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:

Jazz Media Contact:
Kristin Bhavnani
Head of Global Strategic Brand Engagement
Jazz Pharmaceuticals plc
CorporateAffairsMediaInfo@jazzpharma.com
Ireland +353 1 637 2141
U.S. +1 215 867 4948

Jazz Investor Contact:
Andrea N. Flynn, Ph.D.
Vice President, Head, Investor Relations
Jazz Pharmaceuticals plc
investorinfo@jazzpharma.com
Ireland +353 1 634 3211
U.S. +1 650 496 2717

References:

[1] Lamarca A, et al. Second-line FOLFOX chemotherapy versus active symptom control for advanced biliary tract cancer ABC-06): a phase 3, open-label, randomised, controlled trial. Lancet Oncol 2021;22:690–701

[2] Yoo C, et al. Liposomal irinotecan plus fluorouracil and leucovorin versus fluorouracil and leucovorin for metastatic biliary tract cancer after progression on gemcitabine plus cisplatin (NIFTY): a multicentre, open-label, randomised, phase 2b study. Lancet Oncol 2021;22:1560–72

[3] Valle JW, et al. Lancet 2021; 397:428-44

[4] Siegel RL, et al. CA Cancer J Clin 2022; 72;7-33

[5] BTC overall diagnosed patients as per SEER 22;

[6] Assumes anatomic subsites intrahepatic CCA, extrahepatic CCA, gallbladder cancer, and BTC unspecified;

[7] Assumes HER2 positivity rates per anatomical subsite from: Galdy, S., Lamarca, A., McNamara, M.G. et al. Cancer Metastasis Rev 36, 141–157 (2017), Nobuyoshi Hiraoka, et al. Human Pathology, Volume 105, 2020, Pages 9-19

[8] Major markets: U.K, France, Germany, Spain, Italy. Note: HER2+ BTC patients in Jazz-controlled commercial territories, which includes Japan, and excludes other certain Asia Pacific countries licensed to BeiGene, Ltd

View original content to download multimedia:https://www.prnewswire.com/news-releases/jazz-pharmaceuticals-completes-zanidatamab-biologics-license-application-for-previously-treated-her2-positive-metastatic-biliary-tract-cancer-302105018.html

SOURCE Jazz Pharmaceuticals plc