Zanidatamab Granted Priority Review for HER2-Positive Metastatic Biliary Tract Cancer

May 29, 2024

Target Action (PDUFA) Date set for November 29, 2024

If approved, zanidatamab will be the first HER2-targeted treatment specifically indicated for patients with HER2+ locally advanced or metastatic biliary tract cancer

DUBLIN, May 29, 2024 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the U.S. Food and Drug Administration (FDA) has accepted and granted Priority Review of the Biologics License Application (BLA) for zanidatamab, the human epidermal growth factor receptor 2 (HER2)-targeted bispecific antibody, for the treatment of previously treated, unresectable, locally advanced, or metastatic HER2-positive biliary tract cancer (BTC). Under the Prescription Drug User Fee Act (PDUFA), FDA has set a target action date of November 29, 2024.

"The priority review designation for zanidatamab underscores the critical need for new treatment options for patients with locally advanced or metastatic HER2-positive BTC, a devastating disease with a poor prognosis," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "Upon approval, zanidatamab will be the first HER2-targeted treatment specifically indicated for these patients, and we look forward to the opportunity to deliver this new treatment option to the BTC community."

Jazz's BLA submission is based on results from Cohort 1 of the Phase 2b HERIZON-BTC-01 clinical trial (NCT04466891) of zanidatamab in previously treated patients with unresectable, locally advanced, or metastatic HER2-positive BTC (defined as in situ hybridization [ISH] positive and immunohistochemistry [IHC] 2+ or 3+). The trial demonstrated a primary endpoint of 41.3% [95% confidence interval (CI): 30.4, 52.8] confirmed objective response rate (cORR) by independent central review (ICR) and results were presented 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.Overall survival, updated duration of response and additional long-term follow-up data from the Phase 2b HERIZON-BTC-01 trial will be presented at the upcoming ASCO Annual Meeting 2024.

Additionally, the global, open-label, randomized HERIZON-BTC-302 Phase 3 trial (NCT06282575) to evaluate the efficacy and safety of zanidatamab in combination with standard-of-care therapy against standard-of-care therapy alone in first-line advanced or metastatic HER2-positive BTC is ongoing and is open for enrollment. HERIZON-BTC-302 is expected to serve as the confirmatory trial for zanidatamab in BTC.

About Zanidatamab
Zanidatamab is an investigational HER2-targeted bispecific antibody that can simultaneously bind two non-overlapping epitopes of the HER2 receptor, 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
BTC, including gallbladder cancer and intrahepatic and extrahepatic cholangiocarcinoma, account for <1% of all adult cancers globally and are often associated with a poor prognosis[1,2]. 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 HER2+ BTC annually[3,4,5,6].

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 opportunity to deliver this treatment option to the BTC community with the potential to be the first HER2-targeted treatment specifically indicated for HER2+ BTC 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, as supplemented by our Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, 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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References:

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

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

[3] BTC overall diagnosed patients as per SEER 22

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

[5] 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

[6] 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

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