Jazz Pharmaceuticals Receives CHMP Positive Opinion for Zanidatamab for the Treatment of Advanced HER2-Positive Biliary Tract Cancer

April 25, 2025

DUBLIN, April 25, 2025 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending the conditional marketing authorization of zanidatamab, an investigational 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.[1]

"This positive CHMP opinion is a welcome step for physicians and patients in Europe who face a critical unmet need in HER2-positive biliary tract cancers, a rare and aggressive group of cancers with poor prognosis and limited treatment options," said Robert Iannone, MD., M.S.C.E., executive vice president, global head of research and development, and chief medical officer of Jazz Pharmaceuticals. "If approved, zanidatamab would be the first HER2-targeted therapy licensed for this difficult-to-treat cancer in the EU, marking an important milestone in addressing this unmet need. We look forward to the European Commission's decision and the opportunity to provide a new treatment option for patients."

The CHMP recommendation is based on data from the Phase 2b HERIZON-BTC-01 trial, which evaluated zanidatamab in previously treated, inoperable, and advanced or metastatic HER2-positive BTC.[2,3]

While biliary tract cancers (BTCs), which include gallbladder cancer (GBC) and cholangiocarcinoma (CCA),[4] account for less than 1% of all human cancers,[5] CCA is the second most common primary liver cancer after hepatocellular carcinoma (HCC).[5] It comprises approximately 10–15% of all primary liver cancers,[4,5] and its global mortality rate has risen in recent decades.[5]

Most BTC cases are diagnosed at an advanced stage due to the vague or nonspecific nature of early disease symptoms,[6] making curative surgery an option for only a minority of patients.[5,7,8] Although chemotherapy and, more recently, immunotherapy-based combinations are used in the first-line setting, disease progression is common, and second-line treatment options are, in the absence of molecular analysis, largely limited to chemotherapy.[5,7,9] HER2 overexpression or amplification has been identified as a distinct molecular subtype of BTC[10,11] and is associated with a worse prognosis compared to HER2-negative BTC.[12] Yet, no HER2-targeted therapies are currently approved for this indication in the European Union (EU).

The CHMP's recommendation will now be reviewed by the European Commission which has the authority to approve medicines in all EU Member States, Iceland, Norway, and Liechtenstein, and is expected to make a final decision.

About Zanidatamab

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.[13]

On November 20, 2024, in the United States, the U.S. Food and Drug Administration (FDA) granted accelerated approval of zanidatamab-hrii (*Ziihera*®) 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.[14] 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.[14]

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 BeiGene, Ltd. (BeiGene) 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), including gallbladder cancer and intrahepatic and extrahepatic cholangiocarcinoma, account for <1% of all adult cancers worldwide and are often associated with a poor prognosis.[5,7] Approximately 26% of patients with BTC are HER2-positive.[10] The human epidermal growth factor receptor 2 (HER2) is a well-validated target for antitumor therapy in other cancers.[7,15] Across the U.S., Europe, and Japan, approximately 12,000 people are diagnosed with HER2+ BTC annually.[16] Most patients (>65%) are diagnosed with tumors that cannot be removed surgically.[7]

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.

Jazz Pharmaceuticals plc Caution Concerning Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to the European Commission's potential approval of zanidatamab for the treatment of adults with BTC in the EU 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, 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, 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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† IHC3+ stands for ImmunoHistoChemistry 3+ and refers to the highest level of HER2 protein overexpression in cancer cells

References

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[1] Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 22-25 April 2025 | European Medicines Agency (EMA). European Medicines Agency (EMA). Published April 25, 2025. Accessed April 25, 2025. https://www.ema.europa.eu/en/news/meeting-highlights-committee-medicinal-products-human-use-chmp-22-25-april-2025

[2] Pant, S et al. Zanidatamab in Previously Treated HER2-Positive Biliary Tract Cancer: Overall Survival and Longer Follow-Up From the Phase 2b HERIZON-BTC-01 Study. *J Clin Oncol*. 2024; 42(16_suppl). Abstract 4091.

[3] Harding J, Fan J, Oh D-Y, et al. Zanidatamab for HER2-amplified, unresectable, locally advanced or metastatic biliary tract cancer (HERIZON-BTC-01): a multicentre, single-arm, phase 2b study. *Lancet Oncol*. 2023;24(7):772-82. doi:10.1016/S1470-2045(23)00242-5.

[4] Mirallas O, López-Valbuena D, García-Illescas D, et al. Advances in the systemic treatment of therapeutic approaches in biliary tract cancer. *ESMO Open*. 2022;7(3):100503. doi:10.1016/j.esmoop.2022.100503.

[5] Vogel A, Bridgewater J, Edeline J, et al. Biliary tract cancer: ESMO Clinical Practice Guideline for diagnosis, treatment, and follow-up. *Ann Oncol*. 2023;34(2):127-40. doi:10.1016/j.annonc.2022.10.506.

[6] Rimassa, L., Khan, S., Koerkamp, B. G., Roessler, S.,et al. Mapping the landscape of biliary tract cancer in Europe: challenges and controversies. *The Lancet Regional Health–Europe*. 2025; 50, 101171. doi.org/10.1016/j.lanepe.2024.101171

[7] Chakrabarti, S., Kamgar, M., Mahipal, A. Targeted therapies in advanced biliary tract cancer: an evolving paradigm. *Cancers*. 2020;*12*(8), 2039. doi.org/10.3390/cancers12082039

[8] Valle JW, Kelley RK, et al. Biliary tract cancer. *Lancet*. 2021;397(10272):428-44. doi:10.1016/S0140-6736(21)00153-7.

[9] Lamarca, A., Hubner, R. A., Ryder, W. D.,et al. Second-line chemotherapy in advanced biliary cancer: a systematic review. *Annals of Oncology*. 2025; *25*(12), 2328-2338. doi.org/10.1093/annonc/mdu162

[10] Galdy S, Lamarca A, et al. HER2/HER3 pathway in biliary tract malignancies; systematic review and meta-analysis: a potential therapeutic target? *Cancer Metastas Rev*. 2017; doi: 10.1007/s10555-016-9645-x

[11] Hechtman, J. F., Liu, W., Sadowska, J.,et al. Sequencing of 279 cancer genes in ampullary carcinoma reveals trends relating to histologic subtypes and frequent amplification and overexpression of ERBB2 (HER2). *Modern Pathology*. 2015;*28*(8), 1123-1129. doi: 10.1038/modpathol.2015.57

[12] Vivaldi, C. HER2 overexpression as a poor prognostic determinant in resected biliary tract cancer. *Oncologist*. 2020;25(10):886-893. doi:10.1634/theoncologist.2019-0922.

[13] Weisser NE, Sanches M, Escobar-Cabrera E et al. An anti-HER2 biparatopic antibody that induces unique HER2 clustering and complement-dependent cytotoxicity. *Nature Communications*. 2023 Mar 13;14(1):1394. doi: 10.1038/s41467-023-37029-3

[14] U.S. Food and Drug Administration. Ziihera® (zanidatamab-hrii) prescribing information. Accessdata.fda.gov. Updated November 2024. Accessed April 22, 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761416s000lbl.pdf
[15] Meric-Bernstam, F., Beeram, et al. Zanidatamab, a novel bispecific antibody, for the treatment of locally advanced or metastatic HER2-expressing or HER2-amplified cancers: a phase 1, dose-escalation and expansion study. *The Lancet Oncology*. 2022; doi: 10.1016/S1470-2045(22)00621-0
[16] Jazz Pharmaceuticals, Inc, Data on file.

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