Jazz Pharmaceuticals Presents Updated Phase 2 Data for Zanidatamab Demonstrating Increased mPFS in HER2-Positive Metastatic Gastroesophageal Adenocarcinoma at ESMO 2024

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Phase 2 updated results for zanidatamab in HER2-positive mGEA included a confirmed objective response rate (cORR) of 84%, duration of response (DoR) of 18.7 months, median progression-free survival (mPFS) of 15.2 months and a Kaplan-Meier–estimated overall survival (OS) of 59% at 30 months

DUBLIN, Sept. 16, 2024 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced updated data, including median progression-free survival (mPFS) and overall survival (OS) findings, from the Phase 2 trial of zanidatamab, an investigational dual HER2-targeted bispecific antibody, in combination with chemotherapy as first-line treatment for patients with HER2-expressing advanced or metastatic gastroesophageal adenocarcinoma (mGEA).

Data from 41 patients with HER2-positive mGEA who were treated with zanidatamab in combination with physician's choice of chemotherapy treatment demonstrated a mPFS of 15.2 [95% CI: 9.5, 33.4] months. After a median duration of follow-up of 41.5 (range, 23.0-52.7) months, the median OS was not mature, a Kaplan-Meier–estimated 24-month OS was 65% [95% CI: 48.0, 78.0] and the 30-month overall survival was 59% [95% CI: 41.0, 73.0].

"Gastroesophageal adenocarcinoma (GEA) represents one of the most common tumor types worldwide; however, developing effective treatment options for GEA patients has been challenging," said Dr. Elena Elimova, lead trial investigator and a medical oncologist at Princess Margaret Cancer Centre, Toronto, Canada. "Despite recent advancements for patients, the sustained clinical antitumor activity seen in this trial demonstrates the potential for zanidatamab to address a significant unmet patient need in HER2-positive GEA."

"The updated results from this Phase 2 trial reaffirm zanidatamab's potential as a foundational treatment for patients with HER2-positive mGEA and showcase the promise of this HER2-targeted bispecific antibody to treat HER2-expressing cancers," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development, and chief medical officer of Jazz Pharmaceuticals. "We look forward to continuing to advance our broader clinical development program for zanidatamab in GEA, including the Phase 3 first-line clinical trial HERIZON-GEA-01 that is expected to read out in the second quarter of 2025, and other HER2-expressing solid tumors, with the goal of supporting more patients with HER2-positive cancers."

Phase 2 mGEA Trial Results
The data include efficacy and tolerability findings from an ongoing, open-label Phase 2 study (NCT03929666) evaluating zanidatamab in combination with chemotherapy as first-line treatment for patients with HER2-expressing mGEA, which comprises gastric, esophageal and gastroesophageal junction (GEJ) adenocarcinomas. Patients had not received prior HER2-targeted agents nor systemic treatment for mGEA. A total of 46 patients with HER2-expressing mGEA (41 patients with HER2-positive mGEA) were enrolled from 15 sites across the United States, Canada and South Korea, and patients were administered zanidatamab with physician's choice of chemotherapy treatment. Currently, chemotherapy-based regimens are the standard first-line combination therapy for 1L mGEA.

The longer-term data (median duration of follow-up of 41.5 [range, 23.0-52.7] months) demonstrates the promising antitumor activity of zanidamatab combined with chemotherapy as a first-line therapy for HER2-positive mGEA.

- Treatment with zanidatamab resulted in a cORR of 84% [95% CI: 68.0, 94.0], an increase of 5% from the cORR previously reported, and one additional patient achieved a complete response for a total of four patients achieving complete response among 37-response evaluable patients.
- The median duration of response was 18.7 months [95% CI: 8.3-NE] with 10 patients having an ongoing response at the time of data cutoff.
- The mPFS was 15.2 [95% CI: 9.5, 33.4] months.
- The Kaplan-Meier–estimated 24-month OS was 65% [95% CI: 48.0, 78.0] with a 30-month overall survival of 59% [95% CI: 41.0, 73.0].

With additional follow-up, the safety and tolerability profile of zanidatamab plus chemotherapy remained manageable with no new safety signals identified. Diarrhea was the most common Grade 3-4 treatment-related adverse events (TRAEs) (35%); the incidence of Grade 3-4 diarrhea was <15% for patients treated after the implementation of mandated antidiarrheal prophylaxis. Treatment discontinuation due to TRAEs were infrequent, and there were no treatment-related deaths.

These data were presented in a poster session entitled *Zanidatamab + Chemotherapy for First-Line Treatment for HER2+ Advanced or Metastatic Gastroesophageal Adenocarcinoma (mGEA)* during the European Society for Medical Oncology (ESMO) Annual Meeting taking place in Barcelona, Spain. The presentation is available to conference registrants on the ESMO conference website (Presentation Number 1423P).

Jazz continues to enroll patients in the Phase 3 randomized clinical trial, HERIZON-GEA-01 (NCT05152147), evaluating zanidatamab in combination with chemotherapy plus or minus tislelizumab as a first-line treatment for HER2-expressing mGEA. This is an events-based trial; top-line data from this trial is expected to read out in the second quarter of 2025.

Phase 2 Colorectal Cancer (CRC) Trial Results Presented as Mini-Oral at ESMO 2024
In addition to the mGEA trial presentation, a mini-oral was also presented at ESMO 2024 from another arm of the same Phase 2, open-label trial (NCT03929666) that includes a cohort of patients with metastatic CRC treated with first-line zanidatamab plus chemotherapy ± bevacizumab (bev). In

11 response-evaluable patients, there were 10 confirmed partial responses and 1 patient with stable disease as a best response. The cORR was 91% (95% CI: 58.7, 99.8) and median duration of response was not reached (2.9+,16.7+ months). All patients experienced TRAEs – Grade 3-4 TRAEs occurred in five (38%) patients, three (23%) of whom experienced diarrhea. No patients discontinued zanidatamab due to a TRAE and there were no treatment-related deaths. Zanidatamab plus chemotherapy ± bev demonstrated encouraging antitumor activity with a generally manageable safety profile as first-line treatment for patients with HER2-positive mCRC.

About Zanidatamab
Zanidatamab is an investigational dual HER2-targeted bispecific antibody that simultaneously binds to two distinct sites on HER2, known as biparatopic binding. This unique design and enhanced binding results in multiple mechanisms of action, including HER2 and HER3 signal blockade, removal of HER2 protein from the cell surface and enhanced immune effector functions, such as complement-dependent cytotoxicity (CDC), which leads to encouraging antitumor activity. 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 accepted and granted Priority Review of the Biologics License Application (BLA) for zanidatamab with a Prescription Drug User Fee Act (PDUFA) action date of November 29, 2024. Zanidatamab was also granted Breakthrough Therapy designation in patients with previously treated HER2 gene-amplified biliary tract cancers (BTC) and given two Fast Track designations: 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 Gastroesophageal Adenocarcinoma
Gastroesophageal adenocarcinoma (GEA) is the fifth most common cancer worldwide, and approximately 20% of patients have HER2–positive disease.[1,2,3] HER2–positive GEA has high morbidity and mortality, and patients are urgently in need of new treatment options.

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 zanidatamab's potential as a foundational treatment for patients with HER2-positive mGEA, the promise of HER2-targeted bispecific antibodies to treat HER2-expressing cancers and zanidatamab's potential to address a significant unmet patient need, growing our portfolio of innovative oncology products and investigational therapies, advancing our broader clinical development program for zanidatamab, including expectations with respect to the timing of the GEA Phase 3 clinical trial read out 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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