Jazz Pharmaceuticals and Zymeworks Announce 84% Overall Survival at 18 Months from Phase 2 Trial Evaluating Zanidatamab in HER2-Expressing Metastatic Gastroesophageal Adenocarcinoma

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Results presented today at ASCO GI include first overall survival (OS) data for zanidatamab, overall confirmed objective response rate (cORR) of 79%, disease control rate (DCR) of 92%, and median progression-free survival (mPFS) of 12.5 months

Ongoing Phase 3 randomized clinical trial, HERIZON-GEA-01, has the potential to support regulatory submissions for zanidatamab in combination with chemotherapy as a therapeutic option for patients with advanced HER2-expressing metastatic gastroesophageal adenocarcinoma (mGEA)

DUBLIN and VANCOUVER, BC, Jan. 19, 2023 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) and Zymeworks Inc. (Nasdaq: ZYME) today announced tolerability and efficacy results, including the first overall survival (OS) data, from a Phase 2 trial examining zanidatamab, an investigational HER2-targeted bispecific antibody, in combination with chemotherapy, in first-line patients with HER2-expressing metastatic gastroesophageal adenocarcinoma (mGEA).

The preliminary results showed that, at the time of analysis, the median OS had not yet been reached with a median duration of study follow-up of 26.5 months. The 18-month overall survival rate was 84% [95% confidence interval (CI): 68%, 93%].

"Gastroesophageal adenocarcinoma represents one of the most frequent tumor types worldwide and, tragically, a leading cause of cancer-related deaths. Compared to what has historically been reported for OS with the current approved standard of care[1], the OS findings from the combination of zanidatamab and chemotherapy in this trial are very compelling," said Dr. Elena Elimova, lead trial investigator and a medical oncologist at Princess Margaret Cancer Centre. "HER2 has been recognized as a predictive biomarker for these cancers, and it is promising to see a treatment targeting this expression exhibit strong and durable anti-tumor activity when administered with chemotherapy."

"We are very encouraged by the data from this Phase 2 trial, which demonstrate zanidatamab administered with chemotherapy is a highly active treatment regimen and resulted in significant and durable tumor response in the first-line setting for patients with advanced HER2-expressing mGEA," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "These results showcase zanidatamab's potential as a foundational treatment for patients with HER2-positive mGEA, and we look forward to additional data in 2024 from the ongoing pivotal Phase 3 trial that may support U.S. and global regulatory filings."

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 advanced HER2-expressing mGEA, which is comprised of gastric, esophageal and gastroesophageal junction (GEJ) patients. Patients had not received prior HER2-targeted agents nor systemic treatment for mGEA. A total of 46 patients with 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 (standard first-line combination therapy).

The data demonstrated zanidatamab combined with standard chemotherapy is a highly active treatment regimen for first-line therapy of HER2-positive mGEA. In 42 patients evaluable for OS receiving zanidatamab in combination with chemotherapy, the 18-month OS rate was 84% (95% CI: 68%, 93%), the 12-month OS rate was 88% (95% CI: 73%, 95%), and the median overall survival had not yet been reached (with 26.5 months median duration of study follow-up). Treatment with zanidatamab resulted in a confirmed objective response rate (cORR) of 79% (95% CI: 63-90%), a disease control rate (DCR) of 92% (95% CI: 79-98%), with three patients achieving complete response among 38 response-evaluable patients.

The median duration of response was 20.4 months (95% CI: 8.3-NE) with a median progression-free survival (mPFS) of 12.5 months (95% CI: 7.1-NE) with 17 patients having an ongoing response at the time of data cutoff. The regimen was manageable, tolerable and consistent with the observed safety profiles reported for other standard combination regimens for patients with HER2-positive GEA.

Data were presented in a poster session entitled *Zanidatamab + Chemotherapy as First-Line Treatment for HER2-expressing Metastatic Gastroesophageal Adenocarcinoma (mGEA)* during the American Society of Clinical Oncology's Gastrointestinal Cancers Symposium (ASCO GI) taking place in San Francisco. The presentation is available to conference registrants on the ASCO GI conference website (Abstract Number 347), and will be available to the general public on Zymeworks' website.

Zymeworks 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.

About Zanidatamab
Zanidatamab is an investigational bispecific antibody, based on Zymeworks' Azymetric™ platform, that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. This unique design results in multiple mechanisms of action including dual HER2 signal blockade, increased binding and removal of HER2 protein from the cell surface, and potent effector function leading to encouraging antitumor activity in patients. Zymeworks, along with collaborators Jazz and BeiGene, Ltd. (BeiGene), are developing zanidatamab in multiple clinical trials as a targeted treatment option for patients with solid tumors that express HER2.

The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation for zanidatamab 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 first-line 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 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 are HER2–positive.[2,3,4] HER2–positive GEA has high morbidity and mortality, and patients are urgently in need of new treatment options.

About Jazz Pharmaceuticals plc
Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharmaceutical 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 and novel product candidates, from early- to late-stage development, in neuroscience and oncology. Within these therapeutic areas, we are identifying new options for patients by actively exploring small molecules and biologics, and through innovative delivery technologies and cannabinoid science. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in nearly 75 countries. Please visit www.jazzpharmaceuticals.com for more information.

About Zymeworks Inc.
Zymeworks Inc. (Nasdaq: ZYME) is a global biotechnology company committed to the discovery, development, and commercialization of novel, multifunctional biotherapeutics. Zymeworks' mission is to make a meaningful difference for people impacted by difficult-to-treat cancers and other serious diseases. Zymeworks' complementary therapeutic platforms and fully integrated drug development engine provide the flexibility and compatibility to precisely engineer and develop highly differentiated antibody-based therapeutic candidates. Zymeworks engineered and developed zanidatamab, a HER2-targeted bispecific antibody using Zymeworks' proprietary Azymetric™ technologyZymeworks has entered into separate agreements with BeiGene, Ltd. (BeiGene) and Jazz Pharmaceuticals Ireland Limited (Jazz), granting each of BeiGene and Jazz with exclusive rights to develop and commercialize zanidatamab in different territories. Zanidatamab is currently being evaluated in global Phase 1, Phase 2, and pivotal clinical trials as a treatment for patients with HER2-expressing cancers. Zymeworks' next clinical candidate, zanidatamab zovodotin (ZW49), is a HER2-targeted bispecific antibody-drug conjugate (ADC) developed using Zymeworks' proprietary Azymetric™ and ZymeLink™ Auristatin technologies. Zanidatamab zovodotin is currently being evaluated in a Phase 1 clinical trial for patients with a variety of HER2-expressing, HER2-amplified or HER2-mutant cancers. Zymeworks is also advancing a deep pipeline of product candidates based on its experience and capabilities in both ADC and multispecific antibodies (MSAT). In addition to Zymeworks' wholly-owned pipeline, its therapeutic platforms have been further leveraged through strategic partnerships with global biopharmaceutical companies. For information about Zymeworks, visit www.zymeworks.com and follow @ZymeworksInc on Twitter.

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 option for patients with HER2-positive mGEA; potential U.S. and global regulatory filings; the potential future development, manufacturing, regulatory and commercialization activities; 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 clinical success thereof; the regulatory approval process; effectively commercializing any product candidates; and other risks and uncertainties affecting Jazz Pharmaceuticals, 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' Quarterly Report on Form 10-Q for the quarter ended September 30, 2022 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.

Zymeworks Cautionary Note Regarding Forward-Looking Statements
This press release includes "forward-looking statements" or information within the meaning of the applicable securities legislation, including Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements in this press release include, but are not limited to, statements that relate to the potential therapeutic effects and commercial potential of zanidatamab and Zymeworks' other product candidates; the anticipated benefits of the partnerships with Jazz and BeiGene; the timing and status of ongoing and future studies and the related data; the commercial potential of zanidatamab and Zymeworks' and its collaborators' ability to obtain regulatory approval of and successfully commercialize zanidatamab; anticipated interactions and filings with regulators and the results thereof; and other information that is not historical information. When used herein, words such as "subject to", "believes", "future", "anticipate", "approximately", "will", "plans", "may", "potential", and similar expressions are intended to identify forward-looking statements. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements are based upon Zymeworks' current expectations and various assumptions. Zymeworks believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. Zymeworks may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various factors, including, without limitation: any of Zymeworks' or its partners' product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; Zymeworks may not achieve milestones or receive additional payments under its collaborations; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of new or changing laws and regulations; market conditions; the impact of the COVID-19 pandemic on Zymeworks' business, research and clinical development plans and timelines and results of operations, including impact on its clinical trial sites, collaborators, and contractors who act for or on Zymeworks' behalf, may be more severe and more prolonged than currently anticipated; clinical trials may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; Zymeworks may be unable to maintain or enter into new partnerships or strategic collaborations and the factors described under "Risk Factors" in Zymeworks' quarterly and annual reports filed with the Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for its quarter ended September 30, 2022 (a copy of which may be obtained at www.sec.gov and www.sedar.com).

Although Zymeworks believes that such forward-looking statements are reasonable, there can be no assurance they will prove to be correct. Investors should not place undue reliance on forward-looking statements. The above assumptions, risks and uncertainties are not exhaustive. Forward-looking statements are made as of the date hereof and, except as may be required by law, Zymeworks undertakes no obligation to update, republish, or revise any forward-looking statements to reflect new information, future events or circumstances or to reflect the occurrences of unanticipated events.

Jazz Media Contact:
Kristin Bhavnani
Head of Global Corporate Communications
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

Zymeworks Media Contact:
Diana Papove
Senior Manager, Corporate Communications
media@zymeworks.com
(604) 678-1388

Zymeworks Investor Contact:
Jack Spinks
Associate Director, Investor Relations
ir@zymeworks.com
(604) 678-1388

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