Jazz Pharmaceuticals and Zymeworks Announce Jazz has Confirmed Opt-in and Advances Partnership for Zanidatamab

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Follows positive top-line clinical data readout from HERIZON-BTC-01 pivotal trial in biliary tract cancers

DUBLIN and VANCOUVER, BC, Dec. 21, 2022 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) and Zymeworks Inc. (Nasdaq: ZYME) today announced that Jazz has exercised its option to continue with its exclusive development and commercialization rights to Zymeworks' zanidatamab in key markets, including the U.S., Europe and Japan, pursuant to the license and collaboration agreement entered into in October 2022.

The decision to exercise this option follows positive top-line clinical data from HERIZON-BTC-01, a pivotal trial in previously treated HER2-amplified biliary tract cancers (BTC), which demonstrated that 41.3% (95% CI: 30.4, 52.8) of enrolled patients with HER2-amplified and expressing (IHC2+ and 3+) disease achieved an objective response as assessed by independent central review. The median duration of response was 12.9 months (95% CI: 5.95 to not reached). The safety profile of zanidatamab in this trial was consistent with that observed in previously reported monotherapy studies, with no new safety signals identified.

"The compelling top-line clinical data from the pivotal trial in patients with BTC highlight zanidatamab's potential to transform the current standard of care," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "This important milestone strengthens our confidence in advancing this therapy for cancer patients with significant unmet need. While our initial focus will be on the ongoing clinical programs in BTC and GEA, these data add to the growing body of evidence that zanidatamab has anti-tumor activity across multiple HER2-expressing cancers."

"We're pleased that our collaboration with Jazz is moving forward, enabling the global, rapid advancement of zanidatamab in multiple tumor types with the potential to provide a foundational HER2-targeted therapy for patients with difficult-to-treat cancers and limited treatment options," said Kenneth Galbraith, Chair & CEO of Zymeworks. "Jazz's track record of R&D and commercial success, combined with their deep relationships in the oncology community and shared passion for working to improve outcomes for cancer patients, make them the ideal development and commercialization partner for zanidatamab."

Transaction Terms
Pursuant to the terms of the agreement, Jazz will make a one-time payment of $325 million to Zymeworks, in the fourth quarter of 2022, to exercise its option to continue with its exclusive license to develop and commercialize zanidatamab in the United States, Europe, Japan and all other territories except for those Asia/Pacific territories that Zymeworks previously licensed to BeiGene, Ltd. Jazz previously made a separate $50 million up-front payment. Zymeworks is also eligible to receive up to $525 million upon the achievement of certain regulatory milestones and up to $862.5 million in potential commercial milestone payments, for total potential payments of up to $1.76 billion. Pending approval of zanidatamab, Zymeworks is eligible to receive tiered royalties between 10% and 20% on Jazz's net sales.

MTS Health Partners, L.P. acted as exclusive financial advisor and Wilson Sonsini Goodrich & Rosati P.C. acted as legal advisor to Zymeworks in connection with the license and collaboration agreement entered into in October 2022.

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, are developing zanidatamab in multiple Phase 1, Phase 2 and pivotal clinical trials globally as a targeted treatment option for patients with solid tumors that express HER2.

About Biliary Tract Cancers
Biliary tract cancers (BTC), including gallbladder cancer and cholangiocarcinoma, account for approximately 3% of all adult cancers and are often associated with a poor prognosis[1]. Globally, more than 210,000 people are diagnosed with BTC every year[2] and most patients (> 65%) are diagnosed with tumors that cannot be removed surgically. The human epidermal growth factor receptor 2 (HER2) is a well-validated target for anti-cancer therapy. About 5% to 19% of patients with BTC have tumors that express HER2[3] and may be positioned for potential benefit from HER2-targeted therapy. Currently no HER2-targeted therapy has been approved for the treatment of BTC.

About Gastroesophageal Adenocarcinoma
Gastroesophageal adenocarcinoma (GEA) is the fifth most common cancer worldwide and approximately 20% of patients are HER2–positive. 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 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 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™ technology. Zymeworks 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 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 the release of top-line data from the ongoing pivotal Phase III trial in GEA; zanidatamab's potential to transform the current standard of care in multiple HER2-expressing cancers and its potential in difficult-to-treat HER2-expressing cancers; the potential future development, manufacturing, regulatory and commercialization activities; potential future payments by Jazz Pharmaceuticals to Zymeworks for development, regulatory and commercial milestones as well as tiered royalties based on future net sales; 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: Jazz Pharmaceuticals' ability to achieve the expected benefits (commercial or otherwise) from the license agreement; 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 license agreement with Jazz; Zymeworks' ability to receive additional payments pursuant to the license agreement, including any future milestone payments and royalties; the timing of and results of the interactions with regulators; the timing and status of ongoing and future studies and the related data; the commercial potential of zanidatamab and Zymeworks' and Jazz's ability to obtain regulatory approval of and successfully commercialize zanidatamab; 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.

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[1]Valle JW, Lamarca A, Goyal L, Barriuso J, Zhu AX. New Horizons for precision medicine in biliary tract cancers. Cancer Discov. 2017;7(9):943-962.

[2]GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1789-1858.

[3]Galdy S, Lamarca A, McNamara MG, et al. HER2/HER3 pathway in biliary tract malignancies; systematic review and meta-analysis: a potential therapeutic target? Cancer Metastasis Rev. 2017;36(1):141-157.

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