Jazz Pharmaceuticals and Zymeworks Announce Exclusive License Agreement to Develop and Commercialize Zanidatamab, a HER2-Targeted Bispecific Antibody

October 19, 2022

Jazz to obtain exclusive development and commercialization rights in key markets including the U.S., Europe and Japan

Zymeworks to receive $50 million upfront payment, a second payment of $325 million, at Jazz's option, and further potential regulatory and commercial milestones for total potential payments of up to $1.76 billion, plus royalties on net sales

Jazz continues to expand oncology portfolio with novel late-stage asset with compelling anti-tumor activity

Top-line clinical data for zanidatamab in biliary tract cancer (HERIZON-BTC-01) expected by end of 2022; potential to support first global regulatory filings

DUBLIN and VANCOUVER, Oct. 19, 2022 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) and Zymeworks Inc. (NYSE: ZYME) today announced that Jazz and Zymeworks' subsidiary, Zymeworks BC Inc., have entered into an exclusive licensing agreement under which Jazz will acquire development and commercialization rights to Zymeworks' zanidatamab across all indications in the United States, Europe, Japan and all other territories except for those Asia/Pacific territories previously licensed by Zymeworks.

"Zanidatamab is a novel HER2-targeted bispecific antibody with biparatopic binding and the potential to transform the current standard of care in multiple HER2 expressing cancers," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "This agreement reflects Jazz's strategic focus on opportunities where we can not only apply advanced technologies to address critical unmet patient needs, but where we can also leverage Jazz's existing integrated capabilities and global infrastructure to commercialize efficiently. Zanidatamab has the potential to deliver significant long-term value and meaningfully contribute to Vision 2025 as we aim to deliver at least five novel therapies to patients by the end of the decade. We are pleased to expand our growing oncology pipeline with a late-stage program, and today's announcement further demonstrates our commitment to delivering novel oncology therapies."

"In partnering with Jazz, we are thrilled to be working with a leading global biopharmaceutical team that brings a wealth of development and commercial experience in oncology and shares our vision and passion for working hard every day to improve outcomes for cancer patients around the world," said Kenneth Galbraith, Chair & CEO of Zymeworks. "Zymeworks and Jazz are committed to advancing the development of zanidatamab as rapidly as possible, with the potential to provide a foundational HER2-targeted therapy for patients with difficult-to-treat cancers who currently have limited treatment options."

Zanidatamab, a HER2-targeted bispecific antibody with novel mechanisms of action, has demonstrated compelling anti-tumor activity in several HER2-expressing cancers, both as monotherapy and in combination with chemotherapy and other agents. Zanidatamab is currently in pivotal trials as a second-line treatment for HER2-expressing biliary tract cancer (BTC) and as a first-line treatment for HER2-positive gastroesophageal adenocarcinoma (GEA). In BTC, where no HER2-targeted therapies are currently approved, the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation for zanidatamab, positioning it as a potential first-in-class therapy. In GEA, based on Phase 2 data, zanidatamab in combination with chemotherapy has the potential to be a best-in-class therapy.

Zanidatamab is based on Zymeworks' Azymetric™ platform and can simultaneously bind two non-overlapping epitopes of HER2, which is known as biparatopic binding. This innovative design results in multiple novel mechanisms of action including dual HER2 signal blockade, enhanced binding and removal of HER2 protein from the cell surface, and potent effector function leading to encouraging antitumor activity in patients.

FDA has granted Breakthrough Therapy designation for zanidatamab 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 first-line GEA. These designations mean zanidatamab is eligible for Accelerated Approval, Priority Review and Rolling Review, as well as FDA guidance on an efficient drug development program. Zanidatamab has also received Orphan Drug designations from FDA for the treatment of biliary tract and gastric cancers, as well as Orphan Drug designation from the European Medicines Agency for the treatment of gastric cancer.

Transaction Terms

Under the terms of the agreement, Jazz will receive an 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. Zymeworks is eligible to receive a $50 million upfront payment, following receipt of the clearance relating to the United States Hart-Scott Rodino Antitrust Improvements Act of 1976 (such clearance, the "HSR Clearance"), and should Jazz decide to continue the collaboration following readout of the top-line clinical data from HERIZON-BTC-01, a second, one-time payment of $325 million. 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, Zymeworks is eligible to receive tiered royalties between 10% and 20% on Jazz's net sales.

Closing of the agreement is subject to expiration or termination of the waiting period under the Hart-Scott-Rodino Act of 1976. The transaction is expected to close within the 2022 calendar year.

Zymeworks management will host a conference call and webcast for investors and analysts on October 19, 2022, at 8:00 a.m. ET. Interested parties should refer to the separate press release issued by Zymeworks for additional details.

About Zanidatamab

Zanidatamab is a 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 is 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. For more information, please visit www.jazzpharmaceuticals.com and follow @JazzPharma on Twitter.

About Zymeworks Inc.

Zymeworks is a clinical-stage biopharmaceutical company dedicated to the discovery, development and commercialization of next-generation multifunctional biotherapeutics. Zymeworks' suite of therapeutic platforms and its fully integrated drug development engine enable precise engineering of highly differentiated product candidates. Zymeworks' lead clinical candidate, zanidatamab, is a novel Azymetric™ HER2-targeted bispecific antibody currently being evaluated in multiple Phase 1, Phase 2, and pivotal clinical trials globally as a targeted treatment option for patients with solid tumors that express HER2. Zymeworks' second clinical candidate, zanidatamab zovodotin (ZW49), is a novel bispecific HER2 –targeted antibody-drug conjugate currently in Phase 1 clinical development and combines the unique design and antibody framework of zanidatamab with Zymeworks' proprietary ZymeLink™ linker and cytotoxin. Zymeworks is also advancing a deep preclinical pipeline in oncology (including immuno-oncology agents) and other therapeutic areas. In addition, its therapeutic platforms are being leveraged through strategic partnerships with global biopharmaceutical companies. For more information on our ongoing clinical trials visit www.zymeworksclinicaltrials.com. For additional 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 to be a best-in-class therapy in GEA and potential first-in-class therapy in BTC; zanidatamab's potential to deliver significant long-term value and meaningfully contribute to Vision 2025; 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 June 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, zanidatamab zovodotin and Zymeworks' other product candidates; the anticipated benefits of the license agreement with Jazz; Zymeworks' ability to receive the upfront $50 million payment following expiration or termination of the waiting period under the Hart-Scott-Rodino Act and the anticipated timing thereof; Zymeworks' ability to receive additional payments pursuant to the license agreement, including the additional $325 million following readout of the top-line clinical data from HERIZON-BTC-01, as well as any additional 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 our and Jazz Pharmaceutical's ability to obtain regulatory approval of and successfully commercialize zanidatamab the anticipated timing of closing of our agreement with Jazz Pharmaceuticals and satisfactions of closing conditions; 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, including the anticipated upfront payments from Zymeworks' agreement with Jazz; expiration or termination of the waiting period under the Hart-Scott-Rodino Act may be delayed or may not be received at all; 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; any of Zymeworks' or its partners' product candidates; Jazz may decide not to proceed with the collaboration following readout of the top-line clinical data from HERIZON-BTC-01; 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 June 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

[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.

SOURCE Jazz Pharmaceuticals plc