Zymeworks Announces China NMPA Acceptance of Biologics License Application for Zanidatamab for Second-Line Treatment of Biliary Tract Cancer

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- Pursuant to the terms of the licensing agreement between Zymeworks and BeiGene, Zymeworks is entitled to receive an $8 million milestone payment from BeiGene and remains eligible to receive up to $164 million based on additional milestones plus royalties on product sales
- A Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) for zanidatamab as a treatment for previously-treated, unresectable, locally advanced, or metastatic HER2-positive biliary tract cancer (BTC) has also been recently accepted for Priority Review by the FDA with target action date of November 29, 2024

VANCOUVER, British Columbia, June 10, 2024 (GLOBE NEWSWIRE) -- Zymeworks Inc. (Nasdaq: ZYME), a clinical-stage biotechnology company developing a diverse pipeline of novel, multifunctional biotherapeutics to improve the standard of care for difficult-to-treat diseases, today announced that the Center for Drug Evaluation (CDE) of the National Medical Products Administration (NMPA) in China has accepted the BLA for zanidatamab for second-line treatment of HER2-positive BTC. Under the terms of Zymeworks' Asia Pacific license and collaboration agreement with BeiGene for the development and commercialization of zanidatamab, Zymeworks is entitled to receive an $8 million milestone payment. Zymeworks also remains eligible to receive up to $164 million based on additional milestones plus royalties on product sales in the Asia Pacific region.

This BLA is based on the data from the HERIZON-BTC-01 (NCT04466891, CTR20202607) clinical trial, which was published in *Lancet Oncology* in June 2023[1]. The trial is an open-label phase 2b study that evaluated the efficacy and safety of zanidatamab in previously treated patients with unresectable, locally advanced, or metastatic HER2-positive BTC. Zanidatamab demonstrated clinically meaningful anticancer activity and durable responses in subjects with previously treated HER2-positive BTC. As of October 10, 2022, the objective response rate (ORR), median duration of response (DOR), and median progression-free survival (PFS) assessed by independent central review (ICR) were 41.3% (95% CI: 30.4–52.8), 12.9 months (95% CI: 6.0–not estimable), and 5.5 months (95% CI: 3.7–7.2), respectively.

"Acceptance of this BLA in China represents a significant milestone in the global effort to bring effective, targeted treatment options to those affected by locally advanced or metastatic HER2-positive BTC," said Kenneth Galbraith, Chair and Chief Executive Officer of Zymeworks. "We are grateful to all of the stakeholders who have worked tirelessly to help us reach this milestone, including our dedicated teams in manufacturing, quality control, regulatory affairs, and clinical research at Zymeworks, and our collaboration partner in Asia Pacific, BeiGene, as well as the study investigators, patients, and families who have supported this development program for zanidatamab. We remain confident about zanidatamab's potential as a new treatment option for multiple HER2-expressing cancers, with ongoing Phase 3 trials in first-line advanced or metastatic HER2-positive BTC (HERIZON-BTC-302) and first-line HER2-positive gastroesophageal adenocarcinoma (HERIZON-GEA-01)."

"We further our mission by collaborating with other innovative companies to advance the development and delivery of impactful cancer medicines to more patients around the world," said Clare Fisher, Senior Vice President of Business Development at BeiGene. "We thank our partners at Zymeworks for their dedication and contributions toward achievement of this important milestone for zanidatamab. We look forward to continued partnership as we work to reach more patients in the Asia-Pacific region."

Under the terms of its collaboration with BeiGene regarding zanidatamab, Zymeworks has received $53 million in upfront and milestone payments as well as certain co-development funding for zanidatamab clinical studies, not including the $8 million milestone payment Zymeworks is eligible to receive in connection with the NMPA's acceptance of the BLA for zanidatamab for second-line treatment of HER2-positive BTC. Through our collaboration with BeiGene on zanidatamab, we remain eligible to receive up to $164 million in additional development and commercial milestones together with tiered royalties of up to 19.5% of net sales in BeiGene territories.

About Zanidatamab
Zanidatamab is an investigational HER2-targeted bispecific antibody that can simultaneously bind two non-overlapping epitopes of the HER2 receptor, known as biparatopic binding. This unique design and increased binding results in multiple mechanisms of action, including dual HER2 signal blockade, removal of HER2 protein from the cell surface, and immune-mediated cytotoxicity leading to encouraging antitumor activity in patients. 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 Pharmaceuticals and 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 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 first-line 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 HERIZON-BTC-01
HERIZON-BTC-01 (NCT04466891, CTR20202607) is a global, multicenter, open-label, single-arm phase 2b trial to evaluate the efficacy and safety of zanidatamab in patients with previously treated advanced or metastatic HER2-amplified BTC. The primary endpoint was objective response rate (ORR) assessed by independent central review (ICR) in HER2-positive patients. Secondary endpoints included ICR-assessed duration of response (DOR), progression-free survival (PFS), and overall survival (OS).

About Biliary Tract Cancer
Biliary tract cancer (BTC), including gallbladder cancer and intrahepatic and extrahepatic cholangiocarcinoma, account for <1% of all adult cancers and are often associated with a poor prognosis[2,3]. The human epidermal growth factor receptor 2 (HER2) is a well-validated target for antitumor therapy in other cancers. Across the U.S., Europe, and Japan, approximately 12,000 people are diagnosed with BTC annually[4,5,6,7] and most patients (> 65%) are diagnosed with tumors that cannot be removed surgically.

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 in the lives of people impacted by difficult-to-treat cancers and other diseases. The Company's 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 the Company's proprietary Azymetric™ technology.Zymeworks has entered into separate agreements with BeiGene, Ltd. (BeiGene) and Jazz Pharmaceuticals Ireland Limited (Jazz), granting each exclusive rights to develop and commercialize zanidatamab in different territories. Zanidatamab is currently being evaluated in multiple global clinical trials as a potential best-in-class treatment for patients with HER2-expressing cancers. A Biologics License Application (BLA) to the U.S. Food and Drug Administration (FDA) seeking accelerated approval for zanidatamab as a treatment for previously-treated, unresectable, locally advanced, or metastatic HER2-positive biliary tract cancer (BTC) has been accepted and granted Priority Review. A BLA has also been accepted for review by the Center for Drug Evaluation (CDE) of the National Medical Products Administration (NMPA) in China. If approved, zanidatamab would be the first HER2-targeted treatment specifically approved for BTC in the U.S. and China. Zymeworks is rapidly advancing a deep pipeline of product candidates based on its experience and capabilities in both antibody-drug conjugates and multispecific antibody therapeutics across multiple novel targets in indications that represent areas of significant unmet medical need. 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 X.

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 Zymeworks' expectations regarding implementation of its strategic priorities; the anticipated benefits of the licensing agreement with BeiGene and agreements with other partners, including Zymeworks' ability to receive any future milestone payments and royalties thereunder; the potential addressable market of zanidatamab; the timing of and results of interactions with regulators; Zymeworks' clinical development of its product candidates and enrollment in its clinical trials; the timing and status of ongoing and future studies and the related data; expectations regarding future regulatory filings and approvals; the timing of and results of interactions with regulators; potential safety profile and therapeutic effects of zanidatamab and Zymeworks' other product candidates; the commercial potential of technology platforms and product candidates and other information that is not historical information. When used herein, words such as "plan", "believe", "expect", "may", "continue", "anticipate", "potential", "will", "progress", 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 pandemics and other health crises 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; clinical trials may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; Zymeworks' assumptions and estimates regarding its financial condition, future financial performance and estimated cash runway may be incorrect; inability 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 (copies 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] Harding JJ, 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):772-782.

[2] Valle JW, et al. Lancet 2021; 397:428-44

[3] Siegel RL, et al. CA Cancer J Clin 2022; 72;7-33

[4] BTC overall diagnosed patients as per SEER 22;

[5] Assumes anatomic subsites intrahepatic CCA, extrahepatic CCA, gallbladder cancer, and BTC unspecified;

[6] Assumes HER2 positivity rates per anatomical subsite from: Galdy, S., Lamarca, A., McNamara, M.G. et al. Cancer Metastasis Rev 36, 141–157 (2017), Nobuyoshi Hiraoka, et al. Human Pathology, Volume 105, 2020, Pages 9-19

[7] Major markets: U.K, France, Germany, Spain, Italy. Note: HER2+ BTC patients in Jazz-controlled commercial territories, which includes Japan, and excludes other certain Asia Pacific countries licensed to BeiGene, Ltd

Source: Zymeworks Inc.