Zymeworks Announces NMPA Approval of Zanidatamab in China for Adults with Previously Treated, Unresectable or Metastatic HER2-high expression (IHC3+) Biliary Tract Cancer

May 30, 2025

- *Zanidatamab is the first and only dual HER2-targeted bispecific antibody approved for HER2+ biliary tract cancer in China; conditional approval based on the results of the HERIZON-BTC-01 clinical study*
- *$20 million milestone payment to be received from BeOne Medicines; Zymeworks remains eligible to receive up to $144 million in additional development and commercial milestones*

VANCOUVER, British Columbia, May 30, 2025 (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, including cancer, inflammation, and autoimmune disease, today announced that the National Medical Products Administration (NMPA) in China has approved zanidatamab for the treatment of patients with previously treated, unresectable or metastatic HER2-positive (HER2+) biliary tract cancer (BTC). The conditional approval marks the first and only[1] dual HER2-targeted bispecific antibody approved for HER2-high expression (IHC3+) BTC in China. Zymeworks' collaboration partner, BeOne Medicines Ltd. (formerly BeiGene, Ltd), obtained the conditional approval under the terms of its Asia Pacific license and collaboration agreement with Zymeworks. Continued approval of this indication will depend on the verification of clinical benefit in the patient population through ongoing confirmatory trials.

"Zanidatamab's conditional approval in China is a meaningful advancement for patients living with HER2-positive BTC, a population with historically high unmet need and poor prognoses," said Kenneth Galbraith, Chair and Chief Executive Officer of Zymeworks. "This milestone affirms the strength of zanidatamab's clinical potential and reflects our continued focus on translating innovation into real impact for patients around the globe. We are deeply grateful to our partners at BeOne Medicines, and to the patients, families, and clinical teams whose contributions have made this milestone a reality. As Zymeworks continues to advance our broader development programs and R&D pipeline, we remain committed to realizing zanidatamab's potential to transform the standard of care across HER2-expressing cancers."

Under the terms of its agreement with BeOne Medicines, Zymeworks has received $61 million in upfront and milestone payments, as well as certain co-development funding for zanidatamab clinical studies. Zymeworks is entitled to receive a $20 million milestone payment in connection with the NMPA approval of zanidatamab, and is eligible to receive up to $144 million in additional development and commercial milestones. Zymeworks is also eligible to receive tiered royalties of up to 19.5% of net sales in BeOne Medicine's territories.

Zanidatamab was approved by the U.S. Food and Drug Administration (FDA) in November 2024 for the treatment of adults with previously treated, unresectable or metastatic HER2+ (IHC 3+) BTC. In April 2025, Zymeworks' partner, Jazz Pharmaceuticals, announced that the European Medicines Agency (EMA) Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion recommending the approval of zanidatamab for the treatment of advanced HER2+ BTC.

About Biliary Tract Cancer

Biliary tract cancers (BTC), including gallbladder cancer and intrahepatic and extrahepatic cholangiocarcinoma, account for approximately 3% of all digestive system tumors and are often associated with a poor prognosis[2,3,4]. Approximately 11%-25.2% of patients with BTC are HER2-positive[5,6,7]. The human epidermal growth factor receptor 2 (HER2) is a well-validated target for antitumor therapy in other cancers[3,8]. The incidence rate of BTC is on the rise globally, in particular in Asian countries and regions.[9]

About zanidatamab

Zanidatamab is a dual HER2-targeted bispecific antibody that simultaneously binds extracellular domains 2 and 4 on separate HER2 monomers (binding in trans). Binding of zanidatamab with HER2 results in internalization leading to a reduction of the receptor on the cell surface. Zanidatamab induces complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP). These mechanisms result in tumor growth inhibition and tumor cell death.[10]

About Zymeworks Inc.

Zymeworks is a global clinical-stage 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 conditions such as cancer, inflammation, and autoimmune disease. 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 BeOne Medicines Ltd. (formerly BeiGene, Ltd.) and Jazz Pharmaceuticals Ireland Limited, granting each exclusive rights to develop and commercialize zanidatamab in different territories. The U.S. FDA granted accelerated approval and China's NMPA granted conditional approval for zanidatamab to treat adults with previously-treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer. Zanidatamab is the first and only dual HER2-targeted bispecific antibody approved for HER2-positive BTC in the U.S. and China. Zanidatamab is currently under regulatory review in the EU for second-line BTC and is being evaluated in multiple global clinical trials as a potential best-in-class treatment for patients with multiple HER2-expressing cancers. Zymeworks is rapidly advancing a robust pipeline of wholly-owned product candidates, leveraging its expertise in both antibody-drug conjugates and multispecific antibody therapeutics targeting novel pathways in areas of significant unmet medical need. Phase 1 studies for ZW171 and ZW191 are now actively recruiting with an investigational new drug application for ZW251 planned for mid-2025. In addition to Zymeworks' 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 the efficacy and safety of zanidatamab; ongoing clinical studies and regulatory reviews; the anticipated benefits of the collaboration agreement with BeOne Medicines, 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 and the timing thereof; potential safety profile and therapeutic effects of zanidatamab; the commercial potential of technology platforms and product candidates; Zymeworks' ability to satisfy potential regulatory and commercial milestones with existing and future partners and anticipated continued receipt of revenue from existing and future partners. When used herein, words such as "plan", "believe", "expect", "may", "anticipate", "potential", "will", "continues", 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: clinical trials, including any required confirmatory trials, may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; 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; conditional regulatory approval may be withdrawn or revoked if any of Zymeworks' or its partners' product candidates fail to satisfy the requirements of any such conditional regulatory approvals; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of new or changing laws and regulations; market conditions, including the impact of tariffs; potential negative impacts of FDA regulatory delays and uncertainty and new policies implemented under the current administration, including executive orders, changes in the leadership of federal agencies such as the FDA, staff layoffs, budget cuts to agency programs and research, and changes in drug pricing controls; 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 and any future clinical trials may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; 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.sedarplus.ca).

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] According to publicly available information, as of the approval announcement on May 29, 2025, zanidatamab is the only HER2-targeting bispecific antibody approved by the National Medical Products Administration (NMPA) for HER2-high-expression biliary tract cancer (BTC).

[2] Chinese Society of Clinical Oncology (CSCO). Diagnosis and Treatment Guidelines for Biliary Malignant Tumors (2024).

[3] Vogel A, Bridgewater J, Edeline J, et al. Biliary tract cancer: ESMO Clinical Practice Guideline for diagnosis, treatment, and follow-up. Ann Oncol. 2023;34(2):127-40. doi:10.1016/j.annonc.2022.10.506.

[4] Chakrabarti, S., Kamgar.doi.org/10.3390/cancers12082039.

[5] Choong-kun Lee, et al. 2025 ASCO GI Abstr. #629.

[6] Hiraoka N, et al. Hum Pathol. 2020 Nov:105:9-19.

[7] Vivaldi C, et al. Oncologist. 2020 Oct;25(10):886-893.

[8] Meric-Bernstam, F., Beeram, et al. Zanidatamab, a novel bispecific antibody, for the treatment of locally advanced or metastatic HER2-expressing or HER2-amplified cancers: a phase 1, dose-escalation and expansion study. The Lancet Oncology. 2022; doi: 10.1016/S1470-2045(22)00621-0.

[9] Chinese Society of Clinical Oncology (CSCO) Biliary Tumor Expert Committee Expert consensus on precise detection and molecular diagnosis of biliary malignant tumors [J]. Journal of Clinical Oncology, 2024, 29 (8): 797-804.

[10] Weisser NE, Sanches M, Escobar-Cabrera E et al. An anti-HER2 biparatopic antibody that induces unique HER2 clustering and complement-dependent cytotoxicity. Nature Communications. 2023 Mar 13;14(1):1394. doi: 10.1038/s41467-023-37029-3.

Source: Zymeworks Inc.