# Zymeworks Presents New Preclinical Data on Antibody-Drug Conjugate Programs at EORTC-NCI-AACR Conference

October 25, 2024

- Presentations highlight key preclinical data that support investigational new drug application (IND) submissions for ZW220 in 1H and ZW251 in 2H in 2025

VANCOUVER, British Columbia, Oct. 25, 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 new preclinical data for Zymeworks' antibody-drug conjugate (ADC) candidates ZW220 and ZW251 in presentations at the European Organisation for Research and Treatment of Cancer-National Cancer Institute-American Association for Cancer Research (EORTC-NCI-AACR) Conference taking place in Barcelona on October 23-25, 2024.

"We are thrilled to present preclinical data for ZW220 and ZW251 at the EORTC-NCI-AACR Conference," said Paul Moore, Ph.D., Chief Scientific Officer at Zymeworks. "These innovatively designed molecules, incorporating our proprietary payload, ZD06519, show significant potential to address critical unmet needs in oncology. The preclinical data presented this week supports our belief that these programs could advance treatment options beyond current standards of care, offering renewed hope for patients battling challenging cancers where therapeutic progress has been limited."

**Oral Presentation Details**

An oral presentation titled "Z *W220, a NaPi2b-directed topoisomerase I inhibitor Antibody-Drug Conjugate, demonstrates compelling preclinical activity in NSCLC, ovarian and uterine cancer models, with a favorable toxicology profile in non-human primate*" highlights preclinical data that continue to support an IND submission in the first half of 2025.

Results demonstrate that ZW220 has the potential for improvement over previous NaPi2b ADCs and on the basis of efficacy, tolerability and payload mechanism. ZW220 features a novel, moderate potency TOPO1i payload with strong bystander activity, beneficial for tumors with low and heterogeneous NaPi2b expression. We believe it offers a differentiated safety profile compared to other ADCs currently in the clinic, demonstrating high tolerability in animal studies with MTD ≥90 mg/kg in non-human primates (NHP) and ≥200 mg/kg in rats, suggesting potential for high doses in humans. The low drug-antibody ratio (DAR) and moderate stability of the antibody-linker provide a good balance of stability, tolerability, and anti-tumor activity, while potentially minimizing antibody-driven toxicities. ZW220's strong internalizing antibody enables efficient cellular trafficking and tissue penetration, potentially improving anti-tumor activity even at lower NaPi2b levels.

**Poster Presentation Details**

A poster titled "*ZW251, a novel glypican-3-targeting antibody-drug conjugate bearing a topoisomerase I inhibitor payload*, *demonstrates compelling preclinical activity in hepatocellular carcinoma models*" highlights preclinical data that continue to support an IND submission in the second half of 2025.

Results demonstrate that ZW251 shows promise as a new treatment option for patients, potentially improving upon the current standard of care (SOC). Demonstrating strong anti-tumor activity across a wide range of hepatocellular carcinoma (HCC) models, including those with lower and heterogenous GPC3 expression, ZW251 was designed with a DAR of four, striking a balance between tolerability and broad anti-tumor effectiveness. In NHP studies, ZW251 displayed significant tolerability at doses up to 120 mg/kg. As an ADC, ZW251 offers flexibility in treatment strategies, potentially serving as either a standalone therapy or in combination with existing SOC treatments.

**About ZW220**

ZW220 is an ADC that targets NaPi2b-expressing NSCLC and ovarian cancers, and is built, like ZW191, using our proprietary TOPO1i- payload technology. The NaPi2b-targeting monospecific antibody incorporated in ZW220 was developed in-house and selected based on a favorable binding profile and enhanced internalization properties to enable targeting of both high- and low- NaPi2b-expressing tumors. The antibody in ZW220 is Fc-silenced, containing mutations in its Fc region which abolish FcγR (Fc gamma receptor) binding in normal cells, with the goal of minimizing potential off-target toxicities. A DAR of four and a moderate stability antibody-linker were selected to balance tolerability and efficacy. NaPi2b is reported to be expressed in approximately 96% of ovarian serous adenocarcinoma and 87% of non-small cell lung cancer (NSCLC) adenocarcinoma[1], and ZW220 has demonstrated anti-tumor activity in patient-derived xenograft models and robust growth inhibition in 3D spheroid models of these cancers. The bystander effect of the TOPO1i payload may help address NaPi2b heterogeneity across these cancers. ZW220 is well-tolerated in non-human primates (NHP) and rats, reaching maximum tolerated doses (MTDs) of ≥ 90 mg/kg and ≥ 200 mg/kg, respectively. We expect to submit an investigational new drug application (IND) and non-U.S. applications for ZW220 in the first half of 2025.

**About ZW251**

ZW251, a potential first-in-class ADC molecule designed for the treatment of glypican 3 (GPC3)-expressing HCC, incorporates the same Zymeworks proprietary bystander-active TOPO1i payload utilized in ZW191 (anti-FRα) and ZW220 (anti-NaPi2b). A DAR of four and a moderate stability antibody-linker were selected to balance tolerability and efficacy. In preclinical studies, anti-tumor activity for ZW251 was observed in multiple patient-derived xenograft models of HCC reflecting a range of GPC3 over-expression. GPC3, a glycosylphosphatidylinositol (GPI)-anchored cell surface oncofetal antigen, is over-expressed in most HCC patients (>75%[2]), and displays minimal normal adult tissue expression, making it an appealing ADC target. In NHP studies, ZW251 displayed significant tolerability at doses up to 120 mg/kg, suggesting the possibility of high initial dosing in human trials. We are encouraged by published research demonstrating the potential of GPC3-targeting antibody in HCC patients as evidenced by tumor localization of iodine radiolabeled condrituzumab, a prior clinical-stage anti-GPC3 mAb, and believe that ADC-based targeting of GPC3 could enable a novel and effective approach to treatment of HCC. We expect to submit an IND and non-U.S. applications for ZW251 in the second half of 2025.

**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 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 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. 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.

**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 anticipated preclinical data presentations; the timing and status of ongoing and future studies and the release of data; expectations regarding future regulatory filings and approvals and the timing thereof; the timing of and results of interactions with regulators; Zymeworks' preclinical pipeline; the anticipated benefits of the collaboration agreements with Jazz and BeiGene; the commercial potential of technology platforms and product candidates; Zymeworks' clinical development of its product candidates and enrollment in its clinical trials; the potential addressable market of zanidatamab; potential safety profile and therapeutic effects of zanidatamab and Zymeworks' other product candidates; the ability to advance product candidates into later stages of development; and other information that is not historical information. 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 and any future 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 may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; 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; the impact of new or changing laws and regulations; market conditions; 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.

**Contacts:**

Investor Inquiries:

Shrinal Inamdar
Director, Investor Relations
(604) 678-1388
ir@zymeworks.com

Media Inquiries:

Diana Papove
Senior Director, Corporate Communications
(604) 678-1388
media@zymeworks.com

[1]Lin *et al*. 2015. *Clin Cancer Res*

[2]Wang HL et al., Arch Pathol Lab Med 2008




Source: Zymeworks Inc.