Zymeworks Presents Initial Clinical Data from the Phase 1 trial of ZW191, an Antibody-Drug Conjugate Targeting Folate Receptor-α at AACR-NCI-EORTC Conference

October 23, 2025

- *Preliminary efficacy data, combined with a tolerable safety profile, reinforce the potential of ZW191 in patients with advanced solid tumors, including ovarian, endometrial, and non-small cell lung cancer*
- *64% overall response rate in gynecological cancers at doses ≥6.4mg/kg*
- *Responses observed at all doses evaluated at 3.2mg/kg and above demonstrating wide therapeutic index of Zymeworks' novel antibody-drug conjugate platform*
- *Dose optimization of ZW191 in ovarian cancer to initiate in 4Q-2025*
- *Investor and analyst call to be held today at 3:30 pm Eastern Time (ET)*

VANCOUVER, British Columbia, Oct. 23, 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 preliminary results from a Phase 1 study evaluating ZW191, an antibody-drug conjugate (ADC) targeting folate receptor-alpha (FRα), at the AACR-NCI-EORTC Conference on Molecular Targets and Cancer Therapeutics, being held October 22-26, 2025, in Boston, MA.

"These first clinical data from our Phase 1 study of ZW191 provide early validation of our innovative approach to designing novel ADCs, through combining a unique antibody design with our proprietary payload, ZD06519," said Sabeen Mekan, MD, Senior Vice President of Clinical Development of Zymeworks. "We are encouraged by the early signs of anti-tumor activity and favorable safety profile in a heavily pretreated population, which supports best-in-class potential and strengthens our confidence in this approach. With dose optimization planned to begin in the fourth quarter of this year and additional candidates such as ZW251 advancing in development, we remain focused on delivering meaningful new treatment options for patients with challenging cancers."

Key Findings

As of September 10, 2025, the study enrolled 41 patients from doses 1.6 to 11.2 mg/kg (which was ongoing as of this date) in a heavily pretreated patient population of platinum resistant ovarian cancer, metastatic endometrial cancer, and metastatic non-small cell lung cancer who were enrolled regardless of FRα expression levels. The majority of patients (85%) remain on study treatment.

- ZW191 exhibited promising preliminary anti-tumor activity:
  - For all response-evaluable participants (n=27) across dose levels, objective response rate (ORR) was 44%; across doses of 6.4 mg/kg to 9.6 mg/kg, ORR was 53%.
  - For response-evaluable gynecological cancer participants (n=24) across dose levels, ORR was 50%; across doses of 6.4 mg/kg to 9.6 mg/kg, ORR was 64%.
  - Responses were observed beginning at the 3.2 mg/kg dose and in tumors with low/negative levels of FRα expression.
- ZW191 demonstrated a manageable safety profile, with low rates of dose modifications, dose delays, and Grade ≥3 treatment-related adverse events (AE).
    - No serious treatment-related AEs, discontinuations due to AEs, or deaths were reported.
    - The most common ≥ Grade 3 treatment-related AEs were anemia (10%), neutropenia (5%) and thrombocytopenia (5%).

- These data represent a broad therapeutic window for ZW191 and provide the rationale for further investigation in advanced solid tumors.

Since this data-cut, 11.2 mg/kg has been determined as the maximum tolerated dose and based on safety, efficacy, and pharmacokinetic data, two dose levels – 6.4 mg/kg and 9.6 mg/kg – have been selected for dose optimization, with approximately 30 patients planned in each cohort. This next stage of development is designed to further evaluate ZW191's clinical activity and safety to inform a registrational strategy.

"It is rewarding to see the scientific promise behind ZW191, including its novel antibody and payload technology, begin to translate into meaningful observations in the clinic," said Patricia LoRusso, DO, PhD (hc), FAACR and lead author. "These early efficacy and safety findings represent an important step in exploring new treatment strategies for patients with advanced, aggressive cancers and I look forward to observing ZW191's continued progress."

Presentation Details

- **Title:** Preliminary Results From a Phase 1 First-in-Human Multicenter Open-Label Study Of ZW191, a Folate Receptor α–Targeting Antibody-Drug Conjugate, in Patients With Advanced Solid Tumors
- **Session:** Poster Session A
- **Date/Time:** Thursday, October 23, 2025 at 12:30-4:00 pm ET

Investor & Analyst Call
A live webcast will be held today at 3:30 pm ET with lead author Patricia LoRusso, DO, PhD (hc), FAACR and Zymeworks senior management to discuss the data presented. Dial-in details and webcast replay available on Zymeworks' website at https://ir.zymeworks.com/events-and-presentations.

About ZW191
ZW191 is an ADC engineered to target a protein called folate receptor-α (FRα), found in ~75% of high-grade serous ovarian carcinomas[1] and ~70% of lung adenocarcinomas[2]. ZW191's differentiated design strongly supports its ability to internalize into FR α-expressing cells with the potential to release bystander active topoisomerase-1 inhibitor (ZD06519), a novel proprietary payload developed by Zymeworks to kill tumor cells.

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. Zanidatamab has received accelerated approval from the U.S. FDA, conditional approval from the NMPA in China, and conditional marketing authorization from the European Commission for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer. It is the first and only dual HER2-targeted bispecific antibody approved for this indication in the U.S., Europe, and China. Zanidatamab is also 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. A Phase 1 study for ZW191 is actively recruiting and ZW251 is expected to enter clinical trials in 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 Zymeworks' data presentations and key findings; the timing and status of ongoing and future studies and the release of data; the potential therapeutic effects of and commercial potential of Zymeworks' product candidates; Zymeworks' preclinical pipeline; plans for product candidates' next stages of development; the ability to advance product candidates into later stages of development and the timing of such advancement; and other information that is not historical information. When used herein, words such as "plan", "believe", "expect", "may", "anticipate", "potential", "will", "on track", "continue", "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: 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 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.

Investor inquiries:
Shrinal Inamdar
Senior Director, Investor Relations

(604) 678-1388
ir@zymeworks.com

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

[1] Köbel, M., Madore, J., Ramus, S. et al., Br J Cancer 111, 2297–2307 (2014).
[2] O'Shannessy DJ, et al., Oncotarget. 2012 Apr; 3(4):414-25.

Source: Zymeworks Inc.