Zymeworks Announces Decision to Discontinue Clinical Development of ZW171, a Mesothelin-directed T cell Engager

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VANCOUVER, British Columbia, Sept. 02, 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 its decision to voluntarily discontinue clinical development of ZW171, a T cell engager designed to target gynecological, thoracic, and digestive system cancers.

ZW171 is designed to address cancers driven by mesothelin, a well-recognized but historically challenging target.

The decision to discontinue clinical development of ZW171 was based on completion of the planned cohorts of the dose escalation portion of the Phase 1 trial of ZW171 in patients with ovarian cancer and non-small cell lung cancer. After completing the planned dose escalation cohorts and establishing a maximum tolerated dose, Zymeworks determined that further dose evaluation in the current trial would be unlikely to support a benefit-risk profile consistent with the desired monotherapy target product profile. While cytokine release syndrome was well-managed in the Phase 1 study, dose-limiting toxicities were consistent with mesothelin-related on-target off-tumor toxicity. Ongoing participants in the Phase 1 trial will continue treatment at the discretion of their investigator, and participants who have discontinued treatment will continue safety follow-up as per the study protocol.

“While this is a disappointing outcome given the promising preclinical activity observed with ZW171, we are deeply grateful to the patients, providers, and caregivers for their support and participation in the ZW171 Phase 1 study,” said Kenneth Galbraith, Chair and Chief Executive Officer of Zymeworks. “As part of Zymeworks’ disciplined approach to the management of our broad product portfolio, we are committed to careful and consistent evaluation of clinical progress for each product candidate to ensure our resources are directed towards those product candidates with the greatest potential impact for patients. We continue to advance our broader product pipeline, including the ongoing Phase 1 trial of ZW191 and the initiation of a Phase 1 study for ZW251 expected in 2025. We are also preparing an IND filing for ZW209, our DLL3-directed trispecific T cell engager, planned in the first half of 2026.”

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’ expectations regarding implementation of its strategic priorities; statements that relate to potential therapeutic effects and commercial potential of zanidatamab and Zymeworks’ other product candidates; Zymeworks’ plans for clinical development of its product candidates and enrollment in its clinical trials, including any cessation or suspension thereof; the timing and status of ongoing and future studies and the related data; potential safety profile and therapeutic effects of zanidatamab and Zymeworks’ other product candidates; expected financial performance and future financial position; the timing and status of ongoing and future studies and the release of data; and other information that is not historical information. When used herein, words such as “plan”, “believe”, “expect”, “may”, “continue”, “anticipate”, “potential”, “will”, “on track”, “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; zanidatamab may not be successfully commercialized; Zymeworks' evolution of its business strategy related to anticipated and potential future milestones and royalty streams and existing and potential new partnerships may not be successfully implemented; 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.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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