Zymeworks Announces First Patient Dosed in Phase 1 Clinical Trial Evaluating ZW171 in Advanced Mesothelin-Expressing Cancers

October 21, 2024

- *Global Phase 1 clinical trial will evaluate the safety and tolerability of ZW171 in treatment of ovarian cancer, non-small cell lung cancer (NSCLC), and other mesothelin (MSLN) expressing cancers*

VANCOUVER, British Columbia, Oct. 21, 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 first patient has been dosed in the first-in-human Phase 1 trial (NCT06523803) to evaluate the safety and tolerability of the investigational therapy ZW171 in the treatment of advanced or metastatic ovarian cancer, NSCLC, and other MSLN-expressing cancers.

MSLN has strong expression in a broad number of tumor indications, including ovarian cancer (~84%[1]), with moderate to strong expression in NSCLC (~36%[1]), making it an appealing target for therapeutic development with our proprietary T cell engager technology. In preclinical studies, ZW171 has demonstrated in vivo potent preferential killing of MSLN-overexpressing target cells and stimulation MSLN-dependent T cell activation, mitigating the risk of on-target-off tumor toxicity and peripheral T cell activation and cytokine release syndrome.

Data presented at the American Association for Cancer Research Annual Meeting in 2023 demonstrated that ZW171 exhibits greater anti-tumor activity compared to benchmark in MSLN-expressing tumor models and is well tolerated in cynomolgus monkeys up to 30 mg/kg[2].

“We are very pleased to have initiated the clinical evaluation of ZW171 for the treatment of patients with ovarian cancer and NSCLC, where it has the potential to be a highly effective therapy with favorable tolerability based on our preclinical research results,” said Jeff Smith, M.D., FRCP, Executive Vice President and Chief Medical Officer at Zymeworks. “Initiation of this trial marks a significant step forward in our effort to bring a potential new treatment to people living with difficult to treat cancers and highlights our goal to advance two therapeutic candidates, ZW171 and ZW191, into clinical studies in 2024.”

The Phase 1 study is a two-part, open-label multi-center study that is expected to enroll approximately 160 adult patients with advanced MSLN-expressing cancers. Part 1 of the study will evaluate the safety and tolerability of ZW171 and involve dose escalation in patients with advanced ovarian and NSCLC, with secondary endpoints assessing pharmacokinetics and confirmed objective response rate. Part 2 of the study will involve dose expansion in three cohorts (ovarian cancer, NSCLC, and a basket cohort enrolling patients with any MSLN-expression) and will evaluate the anti-tumor activity of ZW171, with primary endpoints focused on safety and tolerability and secondary endpoints assessing progression-free survival, duration of response rates, and overall survival. The Company expects to conduct the Phase 1 study at investigator sites in the United States, Europe, and the Asia-Pacific region.

“We are also encouraged by the levels of interest in ZW171, which represents a promising and differentiated approach in the treatment of advanced mesothelin-expressing cancers,” Dr. Smith added, noting, “Our trial is designed to rapidly generate clinical data on our differentiated product profile relative to other mesothelin-expressing therapeutics in clinical development.”

About ZW171

ZW171 is a bispecific antibody designed to enable T cell-mediated tumor cell killing through simultaneous binding to the extracellular domain of MSLN protein on tumor cells and the engagement of CD3 on T cells. Moderate to high membranous MSLN expression is frequent in ovarian cancer, non-small cell lung cancer, mesothelioma and other cancers[3]. Preliminary evidence of anti-tumor activity with engineered T-cell therapy supports utility of T-cell targeted therapies in treatment of MSLN-expressing solid tumors[4]. ZW171’s unique 2+1 format and incorporation of a novel low-affinity anti-CD3 binder aims to improve the therapeutic window in patients by limiting on-target, off-tumor effects and cytokine release syndrome (CRS) while maintaining potent anti-tumor activity against MSLN-expressing cancers[5]. By selectively binding to tumors and sparing normal tissues, ZW171 is designed to improve both tolerability and anti-tumor activity against MSLN-expressing cancers. Engineered using our Azymetric™ and EFECT™ technologies, ZW171 demonstrates enhanced anti-tumor activity and safety in preclinical models, inducing potent, preferential killing of MSLN-overexpressing cells while mitigating the risk of on-target, off-tumor activity, peripheral T cell activation, and CRS.

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 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; anticipated regulatory submissions and the timing thereof; 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: future clinical trials may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; 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] Weidemann, S. et al. Biomedicines 2021, Apr 7;9(4):397

[2] Afacan N, et al. Presented at: AACR. 2023 (abstr #2942)

[3] Chang K, Pastan I, Proc Natl Acad Sci U S A. 1996;93(1):136-40

[4] Hassan R, et al. Nat Med. 2023;29:2099-2109

[5] Wang L, et al., Cancer Immunol Res. 2019; 7(12): 2013–2024

Source: Zymeworks Inc.