Zymeworks Announces FDA Clearance of Investigational New Drug Application for ZW171, a novel 2+1 T-cell Targeting Bispecific Antibody for Mesothelin-expressing Cancers

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VANCOUVER, British Columbia, June 17, 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 United States Food and Drug Administration (FDA) has cleared the investigational new drug (IND) application for ZW171, a novel 2+1 T-cell targeting bispecific antibody for mesothelin (MSLN)-expressing cancers.

"We are excited to reach this R&D milestone with ZW171, reflecting our commitment to advancing innovative therapies for cancer treatment," said Paul Moore, Chief Scientific Officer of Zymeworks. "ZW171's unique design is intended to address the limitations of current bispecific T-cell engagers by enhancing tumor selectivity and improving safety. With promising preclinical results, ZW171 has the potential to provide a more effective and tolerable treatment option for patients with MSLN-expressing cancers, including ovarian cancer, non-small cell lung cancer, mesothelioma, and other cancers[1]. We look forward to initiating clinical development of ZW171 during 2024 and continuing to advance additional product candidates in our '5 by 5' strategy over the next 24 months."

The Company expects to file applications seeking regulatory permission to commence clinical studies for ZW171 in other non-US jurisdictions in the second half of 2024.

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[1]. 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[2]. 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[3]. 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 and optimized using our Azymetric™ and EFECT™[4] 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.

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

2. Hassan R, et al. Nat Med. 2023;29:2099-2109

3. 1. Wang L, et al., Cancer Immunol Res. 2019; 7(12): 2013–2024

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

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 deep pipeline of product candidates based on its experience and capabilities in both antibody-drug conjugates and multispecific antibody therapeutics across multiple novel targets in indications that represent areas of significant unmet medical need. In addition to Zymeworks' wholly owned 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 potential addressable market of Zymeworks' preclinical candidates; Zymeworks' development of its preclinical candidates; the timing and status of ongoing and future studies and the related data; expectations and timing regarding future regulatory filings and approvals; the timing of and results of interactions with regulators; potential safety profile and therapeutic effects of zanidatamab and Zymeworks' other product candidates; the commercial potential of technology platforms and product candidates and other information that is not historical information. When used herein, words such as "plan", "believe", "expect", "may", "continue", "anticipate", "potential", "will", "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; 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.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.

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