Zymeworks Presents Preclinical Data on ZW1528 at the American Thoracic Society International Conference

May 19, 2025

- *Company's first development candidate in autoimmune and inflammatory disease (AIID) demonstrates potent blockade of IL-4, IL-13, and IL-33 signaling pathways critical in respiratory inflammation*
- *Novel bispecific design shows promising potential manufacturability and stability to support high dosing concentration and subcutaneous administration*
- *Regulatory filing to support Phase 1 studies expected in 2H-2026*

VANCOUVER, British Columbia, May 19, 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 the presentation of new preclinical data for ZW1528, a novel IL-4Rα x IL-33 bispecific molecule designed to address respiratory inflammation, at the American Thoracic Society (ATS) International Conference being held May 18-21, 2025 in San Francisco, CA.

"Our expansion into autoimmune and inflammatory diseases represents a carefully considered R&D strategy to leverage our expertise in multispecific antibodies to deliver meaningful impact for patients with difficult-to-treat respiratory disorders," said Paul Moore, Ph.D., Chief Scientific Officer of Zymeworks. "The preclinical data presented at ATS demonstrate that ZW1528 binds with high affinity to both IL-4Rα and IL-33, driving potent blockade of two distinct signaling axes implicated in inflammatory disease, including chronic obstructive pulmonary disease (COPD). With its unique dual mechanism of action, ZW1528, which was created using our proprietary AzymetricÔ technology, may translate to better control of COPD in a broader patient population compared to existing therapies."

Key findings for ZW1528 include:

- High-affinity binding to both IL-33 and IL-4Rα and effective blockade of IL-4, IL-13, and IL-33 signaling at levels comparable to clinical benchmark monoclonal antibody controls.
- Suppression of both Type 2 and non-Type 2 responses in primary human immune cells of COPD patients *in vitro*.
- Efficacy in vivo in acute and chronic murine models of lung inflammation driven by house dust mites.
- Extended pharmacokinetics in rodent and non-human primate models, with incorporation of Fc extending half-life optimization.
- Biophysical stability at high concentration (150 mg/mL), supporting potential for subcutaneous administration.

Poster Presentation Details:

Title: ZW1528, a Bispecific Antibody Targeting IL-4Rα and IL-33, Potently Inhibits Key Mediators of Airway Inflammation
Abstract Number: 2982
Session Category: B33 – WHEEZING THROUGH THE MECHANISMS: UNPACKING ASTHMA'S SECRETS
Session Title: Thematic Poster Session
Poster Board: P1567
Date and Time: May 19, 2025 at 11:30 am – 1:15 pm Pacific Time

Beyond ZW1528, Zymeworks is also developing ZW1572, a bispecific inhibitor of IL-4Rα and IL-31 for atopic dermatitis, as part of its growing IL-4Rα program portfolio. The Company continues to advance additional product candidates in multiple formats across selected therapeutic indications in AIID and hematological cancers, with further Investigational New Drug and equivalent non-U.S. application submissions planned for 2028 and beyond.

Additional information can be found on the ATS website, and a copy of the poster is available on the Publications page of Zymeworks' website.

About ZW1528

ZW1528 is a novel IL-4Rα x IL-33 bispecific molecule designed to address respiratory inflammation such as mixed-type chronic obstructive pulmonary

disease (COPD) by inhibiting multiple pathways. By blocking three cytokines (IL-4, IL-13 and IL-33) in a single biologic, ZW1528 offers a unique approach to inhibit clinically validated pathways. The bispecific antibody is designed to provide complete, prolonged IL-4Rα blockade with simultaneous blockade of IL-33. Based on non-clinical in vitro studies, the bispecific can independently suppress IL-13, IL-4, and IL-33 driven cell signaling equivalent to that achieved with anti-IL-4Rα monoclonal antibody (mAb) or anti-IL-33 clinical benchmarks mAbs. Furthermore, in preclinical studies, ZW1528-mediated blockade of cytokine-driven activation of human epithelial cells was superior to that achieved with mAbs targeting either IL-4Rα or IL-33, indicating potential benefits of dual blockade. Additionally, preclinical studies with human peripheral blood mononuclear cells demonstrate ZW1528 provides blockade of IL-33 mediated effects beyond that achievable with an anti-IL33 benchmark mAb. With native Immunoglobulin G-like geometry, ZW1528 demonstrates the potential for high manufacturability and incorporates half-life extending Fc modifications.

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 BeiGene, Ltd. (BeiGene) and Jazz Pharmaceuticals Ireland Limited (Jazz Pharmaceuticals), granting each exclusive rights to develop and commercialize zanidatamab in different territories. The U.S. FDA granted accelerated approval of Ziihera® (zanidatamab-hrii) 50mg/mL for injection for intravenous use for the treatment of adults with previously-treated, unresectable or metastatic HER2-positive (IHC 3+) second-line biliary tract cancer (BTC). Ziihera® is the first and only dual HER2-targeted bispecific antibody approved for HER2-positive BTC in the U.S. Zanidatamab is currently under regulatory review in the EU and China for second-line BTC and is 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. Phase 1 studies for ZW171 and ZW191 are now actively recruiting with an investigational new drug application for ZW251 planned for mid-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' preclinical 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; anticipated IND submissions and the timing thereof; 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", "on track", "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 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.

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