Zymeworks Hosts R&D Day Highlighting Continued Clinical Progress in Oncology Programs and Expansion into Autoimmune and Inflammatory Diseases

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- *Company on track to deliver five Investigational New Drug (IND) applications as part of '5 by 5' solid tumor strategy 18 months ahead of original target*
- *Nomination of ZW209, a novel trispecific T cell engager, as fifth development candidate in the Company's solid tumor portfolio*
- *Expansion into autoimmune and inflammatory diseases (AIID) and hematology oncology leverages the Company's clinically validated Azymetric™ technology platform and expertise in multispecific therapeutics*
- *ZW1528, the Company's first development candidate in AIID, demonstrates dual blockade of two complementary pathways of respiratory inflammation and offers potential benefit in mixed-type chronic obstructive pulmonary disease (COPD)*
- *In-person and virtual R&D Day featuring Zymeworks research leadership and key opinion leaders to be held today at 8:30 am Eastern Standard Time (EST)*

VANCOUVER, British Columbia, Dec. 12, 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 highlights from its R&D Day reviewing the Company's development progress on its wholly-owned pipeline assets and expansion into new therapeutic areas in hematological cancers and autoimmune and inflammatory diseases (AIID).

"We are pleased to provide an update on our continued clinical progress with our solid tumor product portfolio, including the nomination of our fifth development candidate, ZW209, a novel, potential best-in-class, trispecific T cell engager that targets DLL3-expressing tumor cells. Importantly, the acceleration of our goal to build the initial '5 by 5' solid tumor portfolio in five years – 18 months ahead of our initial target – highlights the strength of Azymetric™, our clinically validated, proprietary technology platform, and our ability to efficiently advance innovative therapies, with a productive R&D organization," said Paul Moore, PhD, Chief Scientific Officer of Zymeworks. "This milestone demonstrates our team's significant drug discovery capabilities and unwavering commitment to bringing transformative therapies to patients who urgently need new treatment options. The Company's strong financial position provides the basis to properly support investment in an active and broad, wholly-owned R&D portfolio with strict criteria for continued investment based on results of early-clinical studies. A deep and diversified R&D portfolio in selected therapeutic categories in solid tumors, hematological cancers, and AIID provides significant optionality over future partnership and collaboration arrangements and our strategy to retain significant product rights in our R&D portfolio."

"We are excited about the potential of our growing R&D pipeline of novel, differentiated, and multifunctional antibody-based therapeutics as we work to address difficult-to-treat diseases with traditionally poor outcomes and look forward to being able to share initial clinical data from our solid tumor product portfolio, starting potentially during 2025."

Along with highlights from the Company's pipeline, the event will feature three key opinion leaders who will discuss the clinical landscape and unmet medical needs for patients with gynecological, thoracic, and digestive system cancers:

- Jaffer A. Ajani, MD, Professor of Medicine, MD Anderson Cancer Center
- Susana Banerjee, MBBS MA PhD FRCP, Professor and Medical Oncologist, The Royal Marsden NHS Foundation Trust
- Hatim Husain, MD, Medical Oncologist and Associate Professor in the Department of Medicine, UC San Diego Health

Solid Tumor R&D Portfolio

Zymeworks is on track to advance five drug candidates into clinical trials in solid tumors including gynecological, thoracic, and digestive system cancers by the first half of 2026. This is approximately 18 months ahead of the Company's original stated schedule of five IND applications by the end of 2027.

ZW209: Novel trispecific T cell engager targeting DLL3
ZW209, the Company's fifth development candidate, is a novel trispecific T cell engager (TriTCE) targeting DLL3-expressing tumor cells with an optimized design using the clinically validated Azymetric™ and EFECT™ platforms. By leveraging obligate cis-T cell binding and conditional CD28 engagement, this first-in-class molecule has been designed to prevent unintended T cell activation, while enabling tumor-targeted cytotoxicity. The innovative design has demonstrated differentiated long-term cytotoxicity in vitro at low E:T ratios, with enhanced T cell proliferation and survival, offering significant potential to increase durability of responses in DLL3-expressing cancers. The Company expects to submit an IND and

non-U.S. applications to commence Phase 1 clinical studies for ZW209 in 1H-2026.

ZW171: Mesothelin x CD3 targeted 2+1 format bispecific antibody
ZW171, a T cell-engaging bispecific antibody for the treatment of mesothelin (MSLN)-expressing solid tumors, was built using the Azymetric™ platform. ZW171's unique geometry, with two single-chain fragment variable (scFv) arms targeting MSLN and one Fab arm targeting the cluster of differentiation 3 protein (CD3) component of the T cell receptor, redirects the body's natural immune system to fight cancer cells.

A Phase 1 trial (NCT06523803) evaluating the safety and tolerability of ZW171 in advanced or metastatic ovarian cancer, non-small cell lung cancer (NSCLC), and other MSLN-expressing cancers was initiated in 2H-2024.

ZW191: Folate receptor-alpha (FRα) targeted topoisomerase I antibody-drug conjugate (ADC)
ZW191, a drug to antibody ratio (DAR) 8 ADC that targets FRα-expressing tumors including ovarian cancer, other gynecological cancers, and NSCLC, was built using the Company's drug conjugate platforms, including its novel topoisomerase I inhibitor (TOPO1i) based payload technology, ZD06519. The FRα monoclonal antibody incorporated in ZW191 was generated in-house and selected based on enhanced internalization characteristics to enable targeting of high, mid, and low levels of FRα expression. ZW191 is associated with greater anti-tumor activity compared to benchmark in FRα-expressing tumor models and is well-tolerated in cynomolgus monkeys up to 60 mg/kg[1].

ZW191 potentially offers a unique and differentiated profile compared to other FRα-targeted ADCs currently in development with potential activity in breadth of FRα-expressing tumors.

A Phase 1 trial (NCT06555744) evaluating the safety and tolerability of ZW191 in advanced FRα-expressing solid tumors including ovarian cancer, endometrial cancer, and NSCLC was initiated in 2H-2024.

ZW220: NaPi2b targeted topoisomerase I ADC
ZW220, a DAR4 ADC that targets sodium-dependent phosphate transporter 2b (NaPi2b)-expressing ovarian cancer and NSCLC, was built using the Company's proprietary TOPO1i-based payload technology, ZD06519. The NaPi2b-targeting monospecific antibody incorporated in ZW220 was generated in-house and selected based on a favorable binding profile and enhanced internalization properties to enable targeting of both high- and low-expressing NaPi2b-expressing tumors. ZW220 potentially offers a differentiated safety profile compared to other NaPi2b-targeted ADCs currently in development, demonstrating high tolerability in animal studies, suggesting potential for high doses in humans. The Company expects to submit an IND and non-U.S. applications to commence Phase 1 clinical studies for ZW220 in 1H-2025.

ZW251: Glypican-3 targeted topoisomerase I ADC
ZW251, a potential first-in-class DAR4 ADC designed for the treatment of glypican 3 (GPC3)-expressing hepatocellular carcinoma (HCC), incorporates the Company's proprietary TOPO1i-based payload technology, ZD06519. In preclinical studies, anti-tumor activity for ZW251 was observed in multiple patient-derived xenograft models of HCC reflecting a range of GPC3 over-expression. In animal studies, ZW251 displayed significant tolerability at doses up to 120 mg/kg. The Company expects to submit an IND and non-U.S. applications to commence Phase 1 clinical studies for ZW251 in 2H-2025.

The Company continues to develop and advance additional solid tumor product candidates beyond the 5 x 5 portfolio, with a specific focus on GI tract cancers, supporting further potential IND applications in 2027 and beyond.

Expansion into AIID & Hematology Oncology

Zymeworks' strategic expansion into AIID and hematology oncology is driven by a targeted approach leveraging multispecific antibody therapeutics. By focusing on clinically validated targets with complex biology, the Company aims to address serious diseases affecting large patient populations who currently have restricted access to advanced therapeutics. The Company's platform technologies offer a high-efficacy, convenient, and cost-effective solution, applying learnings from existing programs. Through innovative fragment crystallizable (Fc) modifications and a deep understanding of disease mechanisms, Zymeworks is advancing therapies designed to deliver meaningful improvements for these patient populations.

ZW1528: IL-4Rα x IL-33 bispecific antibody
ZW1528, the Company's first program in AIID, is a novel IL-4R α x IL-33 bispecific molecule designed to address respiratory inflammation such as mixed-type chronic obstructive pulmonary disease (COPD), by inhibiting multiple pathways. By targeting three cytokines in a single biologic, ZW1528 offers a unique approach that leverages clinically validated targets. The bispecific antibody is designed to provide complete, prolonged IL-4Rα blockade with simultaneous blockade of IL-33. Based on non-clinical studies, with native IgG-like geometry, ZW1528 demonstrates high manufacturability and incorporates half-life extending Fc modifications. The Company expects to file an IND and non-U.S. applications to commence Phase 1 clinical studies for ZW1528 in 2H-2026.

The Company continues to develop and advance additional product candidates beyond ZW1528 in multiple different product formats in selected therapeutic indications in AIID and hematological cancers, with further potential IND applications planned from 2027 and beyond.

"Our expansion into AIID and hematology oncology, along with continued efforts in solid tumors, represents a carefully considered R&D strategy to create meaningful value for our stockholders, driven by the exceptional creativity and scientific rigor of our R&D organization. By strategically expanding our research to additional selected therapeutic indications that align with our technological strengths in multifunctional therapeutics, our goal is to continue delivering meaningful breakthroughs for patients building on our experience in the discovery and development of zanidatamab," said Kenneth Galbraith, Chair and Chief Executive Officer of Zymeworks. "By maintaining disciplined pipeline progression, and embracing selective, strategic partnerships, we are seeking to build transformative solutions that have the potential to redefine treatment paradigms, while preserving our focus and capital efficiency. I am deeply encouraged by our progress since our previous R&D Day in 2022 and excited about the groundbreaking work ahead and the potential impact we may deliver for patients."

R&D Day Webcast Information
A live webcast of the Company's R&D Day event will be available on the Investors section of Zymeworks' website. A replay of the webcast will be available following the presentation.

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. 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+) biliary tract cancer (BTC). Ziihera® is the first and only dual HER2-targeted bispecific antibody approved for HER2-positive BTC in the U.S. A BLA has also been accepted for review by the Center for Drug Evaluation (CDE) of the National Medical Products Administration (NMPA) in 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 with investigational new drug applications for ZW220 and ZW251 planned for 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 anticipated regulatory submissions and the timing thereof; expectations regarding future regulatory filings and approvals and the timing thereof; the timing of and results of interactions with regulators; the timing and status of ongoing and future studies and the related data; Zymeworks' clinical development of its product candidates and enrollment in its clinical trials; anticipated preclinical and clinical data presentations; the potential addressable market of zanidatamab and Zymeworks' other product candidates; potential safety profile and therapeutic effects of zanidatamab and Zymeworks' other product candidates; the commercial potential of technology platforms and product candidates; Zymeworks' early-stage pipeline; Zymeworks' ability to execute new collaborations and partnerships 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; zanidatamab and any of Zymeworks' other product candidates may not be successfully commercialized; 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 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.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

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[1] Lawn S., et al. Presented at AACR 2024 (abst #1862)

Source: Zymeworks Inc.