Zymeworks Provides Corporate Update and Reports Third Quarter 2024 Financial Results

October 31, 2024

- *First patient dosed in Phase 1 clinical trial evaluating ZW171 in advanced mesothelin (MSLN)-expressing cancers*
- *Preclinical data presented on ZW220 and ZW251 at EORTC-NCI-AACR conference*
- *Our partner Jazz Pharmaceuticals presented new and updated clinical data at ESMO 2024 on zanidatamab highlighting its potential for the treatment of multiple HER2-positive (HER+) indications*
- *Zymeworks to host in-person and virtual R&D day in New York City on December 12, 2024*
- *The Company has completed the initial $30 million of its Share Repurchase Program for 2,545,402 shares at an average price per share of $11.79 as of October 31, 2024*
- *Reported $374.9 million in cash resources as of September 30, 2024, which when combined with certain anticipated regulatory milestone payments provides a projected cash runway into 2H 2027*
- *Will host conference call with management today at 4:30 p.m. Eastern Time (ET)*

VANCOUVER, British Columbia, Oct. 31, 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 reported financial results for the three and nine months ended September 30, 2024 and provided a summary of recent business highlights.

“2024 has been a pivotal year for us so far, marking several significant firsts across our pipeline. Our partner Jazz Pharmaceuticals has submitted a New Drug Application for zanidatamab, the late-stage HER2-targeting bispecific antibody to the FDA and we eagerly anticipate the potential for its first United States approval in second-line biliary tract cancer, with an assigned action date of November 29. This would be an important achievement not only for us and our partners Jazz and BeiGene, but for BTC patients with limited treatment options,” said Kenneth Galbraith, Chair and Chief Executive Officer of Zymeworks. “In parallel, we’ve dosed the first patient in our global Phase 1 study for our first bispecific T cell engager, ZW171.”

Mr. Galbraith continued, “We believe that the novel design for our nominated candidates represents the next wave of innovation in oncology. As we continue to advance these early-stage assets into the clinic, we are also strategically expanding our focus on new modalities and therapeutic areas within our next generation of R&D candidates, broadly in solid tumors, hematologic cancers and autoimmune and inflammatory diseases. Later this year, we look forward to sharing more about these next-generation of antibody-drug conjugates and multi-specific antibodies which leverage our technology platforms to target multiple disease pathways. We believe this approach will be key to continue driving the long-term growth of our R&D pipeline and delivering transformative therapies to patients worldwide.”

Recent Highlights and Current Developments

- The Company will host an in-person and virtual R&D day in New York, NY on December 12, 2024. A live webcast of the event will be available via the Investor section of our company website and will begin at 8:30 am Eastern Time. As part of the event, we will feature in-depth presentations including:
    - Updates on our portfolio of solid tumor targeting antibody-drug conjugates (ADCs) and T-cell engager (TCE) molecules, featuring key opinion leaders from these therapeutic areas who will join the Company’s management team to discuss ongoing R&D and clinical activities;
    - Candidate nomination from our Trispecific TCE platform as the last product candidate selected in our '5 by 5' R&D strategy; and
    - Strategy and rationale for expansion into new therapeutic areas in hematological cancers and autoimmune and inflammatory diseases and preclinical development progress on potential investigational new drug (IND) applications for multiple new product candidates in 2026 and beyond.

Progression of Wholly-Owned Research & Development Programs

- In October 2024, we 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, non-small cell lung cancer (NSCLC), and other MSLN-expressing cancers. 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 (PFS), duration of response (DoR) rates, and overall survival. The Company expects to conduct the Phase 1 study at investigator sites in North America, Europe, and the Asia-Pacific region.

- The Company is actively recruiting patients in the global Phase 1, open-label, multicenter study of ZW191 (NCT06555744). The study aims to enroll 145 participants with advanced solid tumors across North America, Europe, and the Asia-Pacific region. The study is designed to evaluate the safety, tolerability, pharmacokinetics, and preliminary anti-tumor activity of ascending doses of ZW191.
- In October 2024, Zymeworks presented preclinical data at the European Organisation for Research and Treatment of Cancer-National Cancer Institute-American Association for Cancer Research (ENA) Conference on two ADC product candidates, ZW220 and ZW251, both of which are scheduled for IND applications in 2025. Presentations included:
    - An oral presentation titled *"ZW220, a NaPi2b-directed topoisomerase I inhibitor Antibody-Drug Conjugate, demonstrates compelling preclinical activity in NSCLC, ovarian and uterine cancer models, with a favorable toxicology profile in non-human primates"*
    - A poster presentation titled *"ZW251, a novel glypican-3-targeting antibody-drug conjugate bearing a topoisomerase I inhibitor payload, demonstrates compelling preclinical activity in hepatocellular carcinoma models"*

"We're thrilled to have presented promising preclinical data at several key scientific conferences this year, including the ENA conference in October, and these presentations continue to underscore the breadth, diversity and strength of our platform," stated Paul Moore, Ph.D., Chief Scientific Officer at Zymeworks. "Specifically, preclinical data on our NaPi2b- and glypican-3-targeting antibody-drug conjugates have demonstrated both potent and selective anti-tumor activity in multiple cancer models, with favorable toxicology profiles and robust tumor growth inhibition, highlighting the transformative potential of our approach utilizing our proprietary payload and antibody. We anticipate submitting INDs and non-U.S. applications in the first half of 2025 for ZW220, and in the second half of 2025 for ZW251."

Zanidatamab Continues to Progress with Promising Developments

- In September 2024, our partner Jazz announced new and updated presentations at the European Society of Medical Oncology (ESMO) Annual Congress 2024 on zanidatamab highlighting its potential for the treatment of multiple HER2+ indications, including HER2+ metastatic gastroesophageal adenocarcinoma (mGEA) and advanced/metastatic colorectal cancer (mCRC). The presentations included:
    - Efficacy and tolerability findings from an ongoing, open-label Phase 2 study (NCT03929666) evaluating zanidatamab in combination with chemotherapy as first-line treatment for patients with HER2-expressing metastatic GEA, which comprises gastric, esophageal and gastroesophageal junction adenocarcinomas. Data from 41 patients with HER2-positive metastatic GEA who were treated with zanidatamab in combination with physician's choice of chemotherapy treatment demonstrated a median progression-free survival (mPFS) of 15.2 [95% CI: 9.5, 33.4] months. After a median duration of follow-up of 41.5 (range, 23.0-52.7) months, the median overall survival was not mature, a Kaplan-Meier-estimated 24-month overall survival was 65% [95% CI: 48.0, 78.0] and the 30-month overall survival was 59% [95% CI: 41.0, 73.0].
    - A mini-oral presentation from another arm of the Phase 2, open-label trial (NCT03929666) that includes a cohort of patients with metastatic colorectal cancer treated with first-line zanidatamab plus chemotherapy ± bevacizumab (bev). In 11 response-evaluable patients, there were 10 confirmed partial responses and one patient with stable disease as a best response. The cORR was 91% (95% CI: 58.7, 99.8) and median DoR was not reached (2.9+,16.7+ months). All patients experienced treatment related adverse events (TRAEs) – Grade 3-4 TRAEs occurred in five (38%) patients, three (23%) of whom experienced diarrhea. No patients discontinued zanidatamab due to a TRAE and there were no treatment-related deaths. Zanidatamab plus chemotherapy ± bev demonstrated encouraging anti-tumor activity with a generally manageable safety profile as first-line treatment for patients with HER2-positive metastatic colorectal cancer.
    - A poster presentation on the trial design for the ongoing, global, Phase 3, randomized, open-label trial (NCT06282575) investigating the efficacy and safety of zanidatamab with cisplatin and gemcitabine (CisGem) versus CisGem alone ± a programmed cell death protein-1/ligand 1 (PD-1/L1) inhibitor (pembrolizumab or durvalumab at physician's discretion if locally approved) as first-line treatment for patients with advanced HER2-positive BTC. The primary endpoint is PFS in patients with immunohistochemistry (IHC) 3+ tumors. Secondary/exploratory endpoints include: overall survival (IHC 3+ subgroup; overall population), PFS (overall population), cORR, incidence and severity of adverse events and patient-reported outcomes. The study is currently recruiting patients.

Business Updates

- As of September 30, 2024, Zymeworks has repurchased 1,818,530 shares of the Company's common stock for a cost of $20.6 million, under the Repurchase Program announced in August 2024. As of October 31, 2024, the Company has completed the initial $30 million of the Repurchase Program for 2,545,402 shares at an average price per share of $11.79.
- On October 15, 2024, Hollings C. Renton submitted his resignation from Zymeworks' board of directors, including as chair

and member of the board of directors' compensation committee, effective December 10, 2024 (the date of the Company's 2024 Annual General Meeting of Stockholders). Mr. Renton's resignation was not the result of any disagreement with the Company on any matter relating to the Company's operations, policies or practices.

Financial Results for the Nine Months Ended September 30, 2024

Revenue was $45.3 million for the nine months ended September 30, 2024 compared to $59.1 million for the same period in 2023. Revenue for the nine months ended September 30, 2024 included $32.8 million for development support and drug supply revenue from Jazz, $8.0 million of milestone revenue from BeiGene in relation to the acceptance by the CDE of the NMPA in China of the BLA for zanidatamab for 2L treatment of HER2-positive BTC, $2.5 million of milestone revenue from GSK in relation to the sequence pair nomination under the 2016 licensing agreement and $2.0 million from BeiGene and other partners for research support payments. Revenue for the same period in 2023 included $56.3 million for development support and drug supply revenue from Jazz and $2.8 million from BeiGene and our other partners for research support and other payments. The decrease in revenue from Jazz reflects the transfer of responsibility for certain clinical trials regarding zanidatamab to Jazz, with such future costs to be borne by Jazz instead of being incurred by us and reimbursed by Jazz.

Research and development expense was $97.6 million for the nine months ended September 30, 2024 compared to $118.1 million for the same period in 2023. The decrease in research and development expense was primarily due to a decrease in expenses for zanidatamab, as a result of transfer of responsibility for this program to Jazz, and a decrease in expenses for ZW171 and ZW191. This decrease, compared to the same period in 2023, was partially offset by an increase in expenses for ZW220 and ZW251 and other preclinical and research activities. Stock-based compensation expense increased primarily due to a lower expense in 2023 as a result of the cancellation and modification of awards in respect of employees transferred to Jazz.

General and administrative expense was $45.3 million for the nine months ended September 30, 2024 compared to $55.6 million for the same period in 2023. The decrease in general and administrative expense was primarily due to a decrease in external consulting expenses for information technology, legal fees, and other expenses for advisory services, insurance and depreciation and amortization expenses compared to the same period in 2023. This was partially offset by costs incurred due to the termination of our long-term facility lease in Seattle in 2024 and an increase in stock-based compensation expense over 2023, primarily due to reversal of compensation expense for options cancellations and modifications in 2023.

During the nine months ended September 30, 2024, we recorded a non-cash impairment charge of $17.3 million as a result of our decision to discontinue the zanidatamab zovodotin clinical development program which utilized the technology represented by acquired in-process research and development assets.

Other income, net was $16.1 million for the nine months ended September 30, 2024 compared to $14.6 million for the same period in 2023. The increase was primarily driven by an increase in the average interest yields of these investments during the period.

Income tax expense decreased by $3.8 million for the nine months ended September 30, 2024 compared to the same period in 2023, primarily due to a reduction in U.S. taxes under the global intangible low-taxed income rules and Subpart F income rules for the nine months ended September 30, 2024.

Net loss for the nine months ended September 30, 2024 was $99.2 million compared to $104.2 million loss for the same period in 2023. The decrease in net loss was primarily due to lower research and development and general and administrative expenses, as well as a decrease in income tax expense, which was partially offset by a decrease in revenue and an impairment charge recognized in 2024, related to zanidatamab zovodotin.

As of September 30, 2024, we had $374.9 million of cash resources consisting of cash, cash equivalents and marketable securities, comprised of $122.4 million in cash and cash equivalents and $252.5 million in marketable securities. Based on current operating plans and assuming receipt of certain anticipated regulatory milestones, we expect our existing cash resources as of September 30, 2024, when combined with such anticipated milestone payments, will enable us to fund planned operations into the second half of 2027.

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. Phase 1 studies for ZW171 and ZW191 are now actively recruiting. 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 Zymeworks' expectations regarding implementation of its strategic priorities; the anticipated benefits of the collaboration agreements with Jazz and BeiGene, including Zymeworks' ability to receive any future milestone payments and royalties thereunder; the potential addressable market of zanidatamab; the timing of and results of interactions with regulators; Zymeworks' clinical development of its product candidates and enrollment in its clinical trials; the timing and status of ongoing and future studies and the related data; anticipated preclinical and clinical data presentations; expectations regarding future regulatory filings and approvals and the timing thereof; the timing of and results of interactions with regulators; potential safety profile and therapeutic effects of zanidatamab and Zymeworks' other product candidates; expected financial performance and future financial position; the commercial potential of technology platforms and product candidates; Zymeworks' ability to satisfy potential regulatory and commercial milestones with existing and future partners; the timing and status of ongoing and future studies and the release of data; anticipated continued receipt of revenue from existing and future partners; Zymeworks' early-stage pipeline; anticipated sufficiency of existing cash resources and certain anticipated regulatory milestone payments to fund Zymeworks' planned

operations into the second half of 2027; 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; 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.

ZYMEWORKS INC.
Condensed Interim Consolidated Statements of Loss and Comprehensive Loss
(Expressed in thousands of U.S. dollars except share and per share data) (unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2024	2023	2024	2023
Revenue				
Research and development collaborations	$ 16,000	$ 16,506	$ 45,273	$ 59,086
Operating expenses:				
Research and development	36,353	32,775	97,558	118,095
General and administrative	13,852	16,968	45,321	55,623
Impairment on acquired in-process research and development assets	—	—	17,287	—
Total operating expenses	50,205	49,743	160,166	173,718
Loss from operations	(34,205)	(33,237)	(114,893)	(114,632)
Other income, net	4,581	5,660	16,073	14,594
Loss before income taxes	(29,624)	(27,577)	(98,820)	(100,038)
Income tax expense	(226)	(1,110)	(369)	(4,154)
Net loss	$ (29,850)	$ (28,687)	$ (99,189)	$ (104,192)
Other comprehensive income (loss):				
Unrealized income (loss) on available for sale securities, net of tax of nil	1,905	(485)	604	(1,639)
Total other comprehensive income (loss)	1,905	(485)	604	(1,639)
Comprehensive loss	$ (27,945)	$ (29,172)	$ (98,585)	$ (105,831)
Net loss per common share:				
Basic	$ (0.39)	$ (0.41)	$ (1.30)	$ (1.53)
Diluted	$ (0.39)	$ (0.41)	$ (1.30)	$ (1.53)
Weighted-average common stock outstanding:				
Basic	76,128,531	70,575,773	76,244,893	68,212,756
Diluted	76,157,101	70,575,773	76,266,177	68,214,482

ZYMEWORKS INC.
Condensed Consolidated Balance Sheet
(Expressed in thousands of U.S. dollars) (unaudited)

	September 30, 2024	December 31, 2023
Assets		
Current assets:		
Cash, cash equivalents and short-term marketable securities	$ 297,200	$ 374,327
Accounts receivable	23,704	19,477
Other current assets	22,865	19,122
Long-term marketable securities	77,667	81,930
Other long-term assets	65,716	86,024
Total assets	$ 487,152	$ 580,880
Liabilities		

Current liabilities:		
Accounts payable and accrued expenses	$ 51,707	$ 45,992
Other current liabilities	32,202	9,771
Long-term liabilities	36,265	60,311
Total liabilities	120,174	116,074
Stockholders' equity	366,978	464,806
Total liabilities and stockholders' equity	$ 487,152	$ 580,880

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