Zymeworks Outlines Strategic Priorities and Outlook for 2024 and 2025

January 4, 2024

- *Company well-positioned for further progress and broadening of R&D pipeline*
- *Cash resources of approximately $455 million as of December 31, 2023 (unaudited)*
- *Expected cash runway, including proceeds from recent private placement, into 2H 2027*
- *Top-line data readout from the Phase 3 trial evaluating zanidatamab in HER2-positive gastroesophageal adenocarcinoma (GEA), HERIZON-GEA-01, expected in 2024*
- *Expected regulatory reviews ongoing during 2024 for zanidatamab in second-line biliary tract cancers (BTC) in the United States and China with our partners Jazz Pharmaceuticals and BeiGene*
- *Expected Investigational New Drug (IND) applications and first-in-human (FIH) studies for ZW171 and ZW191 candidates in 2024 and ZW220 and ZW251 in 2025*
- *Progression on '5 by 5' portfolio and ADVANCE with R&D Day scheduled for Q4-24*
- *Additional leadership appointments announced separately today*
- *Company presentation on Thursday, January 11, 2024 at 08:15 a.m. Pacific Time (PT) at the J.P. Morgan 42nd Annual Healthcare Conference*

VANCOUVER, British Columbia, Jan. 04, 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 provided an update on key strategic priorities for 2024 and 2025.

"We begin 2024 in an exciting position, having met key objectives set for our programs in 2022 and 2023, including generating data supporting the clinical development of zanidatamab, identifying strong new preclinical product candidates and ensuring that we continue to have the financial resources and leadership necessary to support the Company's strategic objectives," said Kenneth Galbraith, Chair and Chief Executive Officer of Zymeworks. "We're looking forward to 2024 as we approach a pivotal Phase 3 data readout this year with our partners Jazz Pharmaceuticals and BeiGene from the HERIZON-GEA-01 clinical trial for our lead candidate, zanidatamab, in first-line gastroesophageal andenocarcinoma. These data, coupled with the potential for initial regulatory approvals for zanidatamab in second-line biliary tract cancers in 2025 or earlier, are expected to be significant events in our progress to make a meaningful difference in the lives of cancer patients. Beyond zanidatamab, our growing global presence helps position us to achieve efficiency in clinical development, with a continued focus on advancing nominated product candidates from our '5 by 5' portfolio and our ADVANCE R&D strategy. We will continue to evaluate opportunities to broaden or accelerate our development efforts through the formation of strategic partnerships and collaborations."

"Our most important current R&D priority is to progress our differentiated portfolio of antibody-drug conjugates (ADCs) into clinical studies during 2024 and 2025, especially our potential best-in-class folate receptor-alpha-targeted ADC, ZW191, expected to enter FIH studies during 2024. Beyond ZW191, we are planning additional IND filings and FIH studies for ZW220 (NaPi2b) and ZW251 (GPC3) to commence in 2025. All three ADCs were designed with our moderate-potency, proprietary topoisomerase 1 inhibitor, ZD06519. Beyond ADCs, we look to make progress in our differentiated approach to next-generation multi-specific antibodies, starting with our planned IND filing and FIH studies in 2024 for ZW171, our 2+1 mesothelin-directed T-cell engager."

"We were also able to strengthen our board of directors with the additions of Carlos Campoy, Dr. Nancy Davidson and Derek Miller in 2023," said Mr. Galbraith. "These appointments, together with the separate announcement today of the broadening of the Zymeworks leadership team, underscore our commitment to having the expertise and experience in place at all levels to achieve our business objectives in 2024 and 2025."

Key 2023 Accomplishments:

- Our partner, Jazz Pharmaceuticals, presented positive pivotal Phase 2b trial data (NCT04466891) evaluating zanidatamab in HER2-amplified BTC at the American Society of Clinical Oncology annual meeting and initiated rolling Biologics License Application (BLA) submission for accelerated approval in second-line BTC with completion expected in the first half of 2024;
- Our partner, Jazz Pharmaceuticals, gained alignment with FDA on the confirmatory trial evaluating zanidatamab in first-line metastatic BTC patients;
- Continued patient enrollment in the HERIZON-GEA-01 (NCT05152147) pivotal clinical study for zanidatamab in first-line HER2-positive GEA remains on track to announce top-line data during 2024;
- Nominated two new preclinical product candidates (ZW220 and ZW251) that leverage Zymeworks' novel ADC technology platforms, with planned IND applications for both candidates in 2025;
- Through a series of publications and presentations, outlined additional preclinical data supporting the potential therapeutic benefit of IND candidates in our '5 by 5' program (ZW171, ZW191, ZW220, and ZW251);

- Regained full development rights for zanidatamab zovodotin (ZW49) with plans to conduct a Phase 2 study in NSCLC in 2024;
- Strengthened board of directors through the addition of three new members, Carlos Campoy, Dr. Nancy Davidson, and Derek Miller;
- Expanded the global footprint of our Early-Stage Development team into Dublin, California, and Singapore while retaining key talent and establishing fit-for-purpose facilities;
- Inclusion of common stock in Russell 3000 Index and Nasdaq Biotechnology Index (NBI) as a result of redomicile to Delaware and switch from NYSE to Nasdaq completed in 2022; and
- Completed $50 million private placement to EcoR1 Capital, with proceeds expected to help extend cash runway into H2 2027.

“2023 was an important year for Zymeworks and for our shareholders,” said Mr. Galbraith. “With the significant accomplishments of last year, we believe we have the resources and expertise in place to continue to make substantial progress in 2024 and 2025, to advance our fully unencumbered development programs, and execute on our mission to improve the standard of care for difficult-to-treat diseases.”

Updated Financial Guidance

Zymeworks provided an update on its unaudited cash resources, which consist of cash, cash equivalents, and marketable securities. As of December 31, 2023, Zymeworks had cash resources on hand of approximately $455 million (unaudited).

“Based on current operating plans and including the recent private placement with EcoR1 Capital, we expect to have cash resources to fund our R&D programs and business operations into the second half of 2027,” said Chris Astle, Ph.D., Senior Vice President and Chief Financial Officer at Zymeworks. “Our strong financial position allows us to be opportunistic in evaluating additional R&D opportunities and pursuing potential strategic partnerships and collaborations. We are committed to ensuring that future spending remains prioritized and allocated to development programs that we believe are differentiated and most likely to drive future increases in enterprise value. We will continue to assess clinical data emerging from our development programs and the rapidly evolving competitive environment to ensure efficient allocation of our cash and human resources.”

Key 2024 and 2025 Priorities

Zanidatamab Development Collaborations

Our collaboration agreements with Jazz Pharmaceuticals (“Jazz”) and BeiGene, Ltd (“BeiGene”) represent important components of the commercialization strategy for zanidatamab and our strategy to continue to expand our future product pipeline.

Under our amended agreement with Jazz, we have received an aggregate of $375 million in proceeds to date, and remain eligible to receive up to $525 million upon the achievement of certain regulatory milestones and up to $862.5 million in potential commercial milestone payments, and tiered royalties between 10% and 20% on future zanidatamab sales, pending regulatory approval of zanidatamab. Our collaboration agreement with BeiGene in certain Asia Pacific (APAC) regions (excluding Japan but including the People’s Republic of China, South Korea and other countries, Australia, and New Zealand) remains important given the high prevalence of BTC and GEA in the APAC region. Through our collaboration with BeiGene on zanidatamab, we remain eligible to receive up to $195 million in additional development and commercial milestones together with tiered royalties ranging from the high single digit percentages up to 19.5% on net sales of zanidatamab, pending regulatory approval.

During 2024, we look forward to providing further updates on our collaboration agreements and our progress towards regulatory filings and potential approvals, new clinical studies, and future data releases, including the anticipated announcement of top-line clinical data from the ongoing pivotal study, HERIZON-GEA-01, in first-line HER2-positive GEA.

Research and Early-Stage Development Programs

Our scientific strategy supports our goal to build a broad and differentiated product pipeline of ADCs and multispecific antibody therapeutics (MSATs) to be developed from our technology platforms, targeting five new INDs by 2026 (‘5 by 5’ program). We expect to submit INDs for ZW171 and ZW191 in 2024, and INDs for ZW220 and ZW251 in 2025. During 2024, we expect to nominate the final ‘5 by 5’ product candidate for preclinical development with an expected IND filing in 2026.

Zanidatamab zovodotin represents a unique and differentiated product candidate among the HER2 ADCs currently under active development. Based on our development efforts to date, we believe that zanidatamab zovodotin has the potential to become a novel treatment option for advanced HER2+ cancers, supporting further but limited clinical development. It will be evaluated in a planned Phase 2 study in HER2 over-expressing NSCLC patients in combination with a checkpoint inhibitor. We anticipate the results of this clinical study may provide the rationale for one or more registrational studies, which we would expect to undertake with a future collaboration partner.

We plan to continue to be active in presenting and publishing data from our preclinical and clinical programs in 2024 as well as evaluate opportunities beyond our ‘5 by 5’ program by leveraging our proprietary technologies to target additional therapeutic applications such as autoimmune and inflammatory diseases, bispecific biparatopic ADCs, dual-payload ADCs, multi-specific immune cell engagers and immune-oncology pursuant to our ADVANCE R&D strategy. An R&D Day to highlight our progress and future R&D strategy will be held in the fourth quarter of 2024.

Legacy Partnerships and Future Collaborations

Zymeworks continues to have active licensing arrangements with seven key pharmaceutical and biotechnology partners, with two product candidates currently in clinical development. During 2024 and 2025, the Company remains eligible to earn additional milestone payments under our existing agreements as products continue to advance in development as well as potential payments for expansion or extension of existing agreements. The Company will also continue to evaluate the feasibility of monetization of all or a portion of our rights to receive future milestone payments and royalties under these legacy agreements.

We will also explore new opportunities for development collaborations in early-stage clinical programs, and plan to continue to evaluate the potential for additional multi-product collaborations and partnerships to broaden or accelerate our development plans.

J.P. Morgan Healthcare Conference Presentation and Webcast

Management will participate in the J.P. Morgan 42nd Annual Healthcare Conference taking place in San Francisco, California, from January 8-11, 2024, and present on January 11 at 8:15 am PT. The presentation and webcast will be available on Zymeworks' website .

About Zanidatamab

Zanidatamab is an investigational bispecific antibody that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. This unique design and increased binding results in multiple mechanisms of action, including dual HER2 signal blockade, removal of HER2 protein from the cell surface, and immune-mediated cytotoxicity leading to encouraging antitumor activity in patients. Zanidatamab is being developed in multiple clinical trials as a targeted treatment option for patients with solid tumors that express HER2. Zanidatamab is being developed by Jazz and BeiGene, Ltd. (BeiGene) under license agreements from Zymeworks, which first developed the molecule.

The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation for zanidatamab in patients with previously treated HER2 gene-amplified biliary tract cancers (BTC), and two Fast Track designations for zanidatamab: one as a single agent for refractory BTC and one in combination with standard of care chemotherapy for first-line gastroesophageal adenocarcinoma (GEA). Additionally, zanidatamab has received Orphan Drug designations from FDA for the treatment of BTC and GEA, as well as Orphan Drug designation from the European Medicines Agency for the treatment of BTC and gastric cancer. Zanidatamab was also granted Breakthrough Therapy designation from the Center for Drug Evaluation (CDE) in China.

About Zymeworks Inc.

Zymeworks is a global 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. 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 Zymeworks' expectations regarding implementation of its strategic priorities, including those with respect to its pipeline and R&D strategy; preliminary and unaudited estimates of its cash, cash equivalents, and marketable securities; Zymeworks' anticipated financial runway and funding of its current operations; Zymeworks' estimated reimbursements from collaboration partners; future financial position; timing of milestones with respect to zanidatamab, zanidatamab zovodotin and other potential product candidates; potential therapeutic effects and commercial potential of zanidatamab and Zymeworks' other product candidates; the anticipated benefits of the collaboration agreement with Jazz; the anticipated benefits of Zymeworks' agreements with BeiGene and its other collaborators; Zymeworks' ability to receive additional payments pursuant to its collaboration agreements, including any future milestone payments and royalties; the commercial potential of zanidatamab and Zymeworks' and its partners' ability to obtain regulatory approval of and successfully commercialize zanidatamab; the timing of and results of the interactions with regulators, including anticipated regulatory filings and the timing thereof; current and future partnerships and strategic collaborations; Zymeworks' development of its product candidates and enrollment in its clinical trials; the timing and status of ongoing and future clinical trials and studies and presentation of related data; the ability to advance product candidates into later stages of development; the timing of anticipated IND filings; and other information that is not historical information. When used herein, words such as "believe", "future", "anticipate", "approximately", "will", "plans", "may", "potential", "expect", "should", "continue", 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: Zymeworks' assumptions regarding its financial condition may be incorrect; 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 may be unable to maintain or enter into new partnerships or strategic collaborations; and the other risks described under "Risk Factors" in Zymeworks' Quarterly Report on Form 10-Q for its quarter ended September 30, 2023 (a copy of which may be obtained at www.sec.gov and www.sedar.com).

Furthermore, we are in the process of finalizing our financial results for the fourth quarter and fiscal year 2023, and therefore our finalized and audited results and final analysis of those results are not yet available. The preliminary expectations regarding year-end cash, cash equivalents, and marketable securities are the responsibility of management, are subject to management's review and actual results could differ from management's expectations. The actual results are also subject to audit by our independent registered public accounting firm and no assurance is given by our independent registered public accounting firm on such preliminary expectations. You should not draw any conclusions as to any other financial results

as of and for the year ended December 31, 2023, based on the foregoing estimates.

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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