Zymeworks Announces Presentations Highlighting Breadth of Oncology Portfolio at Upcoming Medical Conferences

May 22, 2025

- *Partner presentations reinforce ability of proprietary Azymetric™ platform to develop clinically validated therapeutic antibodies*
- *Long-term outcomes and survival data for Ziihera® (zanidatamab-hrii), which was developed using Azymetric™, to be presented at ASCO and highlight its potential to transform the treatment landscape for first-line HER2-positive gastroesophageal cancer*
- *ZW171 Trial-in-Progress (TiP) poster at ASCO, ZW191 TiP poster at ESMO Gynaecological Cancers Congress; trial enrollment remains on track*

VANCOUVER, British Columbia, May 22, 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 multiple presentations related to its oncology programs at upcoming medical conferences, including the American Society of Clinical Oncology (ASCO) Annual Meeting, and the European Society of Medical Oncology (ESMO) Gynaecological Cancers Congress.

“We are pleased to see multiple presentations at ASCO from our partners, including Jazz Pharmaceuticals, Johnson & Johnson, and Daiichi Sankyo, which further validate our expertise in multispecific and bispecific antibodies, and reinforce our shared commitment to tackling difficult-to-treat cancers,” said Kenneth Galbraith, Chair and Chief Executive Officer at Zymeworks. “In particular, we are looking forward to the outcomes and survival data presentations for zanidatamab in various tumor types, including HER2-positive gastroesophageal cancer, which underscore the potential of our Azymetric™ platform to develop novel therapies for diseases of high unmet medical need.”

ASCO Annual Meeting

Zymeworks and its partners will present multiple abstracts at the American Society of Clinical Oncology (ASCO) Annual Meeting, taking place May 31 – June 4, 2025 in Chicago, IL.

Ziihera

Title	Authors	Presentation Details
Long-term outcomes and overall survival for zanidatamab + chemotherapy in HER2-positive advanced or metastatic gastroesophageal adenocarcinoma: 4-year follow-up of a phase 2 trial	Elena Elimova, Jaffer Ajani, Howard Burris, Crystal S. Denlinger, Syma Iqbal, Yoon-Koo Kang, Jwa Hoon Kim, Keun-Wook Lee, Bruce Lin, Rutika Mehta, Do-Youn Oh, Sun Young Rha, Chengzhi Xie, Diana Shpektor, Phillip M. Garfin, Geoffrey Ku	Type: Rapid Oral Abstract Session: Gastrointestinal Cancer —Gastroesophageal, Pancreatic, and Hepatobiliary Date: Monday, June 2, 11:30 am-1:00 pm Central Daylight Time (CDT) Number: 4013
Concordance analysis between tumor tissue HER2 status by immunohistochemistry (IHC) and in situ hybridization (ISH) and a translational analysis of plasma ctDNA in patients (pts) with biliary tract cancer (BTC): An exploratory analysis from phase 2 HERIZON-BTC-01	James J. Harding , Jin Won Kim, Do-Youn Oh, Heung-Moon Chang, Emerson Y. Chen, Dong Uk Kim, Eric Chen, Joon Oh Park, Mohamedtaki A. Tejani, Jean-Phillippe Metges, John A. Bridgewater, Teresa Macarulla, Xiaotian Wu, Yi Zhao, Diana Shpektor, Phillip M. Garfin, Shubham Pant	Type: Poster Session: Gastrointestinal Cancer —Gastroesophageal, Pancreatic, and Hepatobiliary Date: Saturday, May 31, 9:00 am-12:00 pm CDT Number: 4102

Survival outcomes for zanidatamab-hrii compared to chemotherapy in previously treated HER2-positive (IHC3+) biliary tract cancer (BTC): HERIZON-BTC-01 vs a real-world (RW) external control arm (ECA)	Richard Kim , Xiaozhou Fan, Javier Sabater, Wayne Su, Kathleen Hurwitz, Kayla Hendrickson, Kara Bennett, Catherine Wiener, Phillip M. Garfin, Joan Zape, Mark A. Ozog, John A. Bridgewater, Juan W. Valle, Farshid Dayyani	Type: Poster Session: Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary Date: Saturday, May 31, 9:00 am-12:00 pm CDT Number: 4101

Azymetric™ Platform Partners

Title	Authors	Presentation Details
Phase 1 study results of JNJ-78278343 (pasritamig) in metastatic castration-resistant prostate cancer (mCRPC)	Capucine Baldini , Armelle Vinceneux, Debbie G. Robbrecht, Bernard D. Doger de Spéville, Karen A. Autio, Michael T. Schweizer, Emiliano Calvo, Laura Medina Rodriguez, Marloes V. Dongen. Jean-Laurent Deville, Alice Bernard-Tessier, Debopriya Ghosh, Kristin M. Shotts, Pharavee Jaiprasart, Leanne Cartee, Daria Gaut, Josh D. Lauring, Sherry C. Wang, Victor M. Villalobos, Mark N. Stein	Type: Rapid Oral Abstract Session: Genitourinary Cancer—Prostate, Testicular, and Penile Date: Sunday, June 1, 4:30-6:00 pm CDT Number: 5017
A Phase 1, first-in-human study of D5-2243, an HLA-A*02/NY-ESO-directed bispecific T-cell engager, in patients with advanced solid tumors	Sandra P. D'Angelo , Vivek Subbiah, Jean-Yves Blay, Michael J Wagner, Neeltje Steeghs, Jeonghwan Youk, Hideki Mizusako, Yoshihiro Ohue, Jin Jin, Abdul Waheed Rajper, Nicole Tesar, Patrick Schöffski	Type: Poster Session: Developmental Therapeutics—Immunotherapy Date: Monday, June 2, 1:30-4:30 pm CDT Number: TPS2668

ZW171

Title	Authors	Presentation Details
Design of a first-in-human multicenter open-label study of ZW171, a mesothelin x CD3 targeting bispecific T-cell engager, in participants with advanced solid tumors: ZWI-ZW171-101	Melissa L. Johnson , John T. Hamm, Fiona Thistlethwaite, Myung-Ju Ahn, Erin L. Schenk, Jason J. Luke, Diana L. Hanna, Anna R. Minchom, Byoung Chul Cho, Dong-Wan Kim. Rebecca Kristeleit, Dmitriy Zamarin, Catherine Davidson, Joseph Woolery, Pranshul Chauhan, Martin Wermke	Type: Poster Session: Developmental Therapeutics—Molecularly Targeted Agents and Tumor Biology Date: Monday, June 2, 1:30 pm-4:30 pm CDT Number: TPS3160

ESMO Gynaecological Cancers Congress

Zymeworks will present a TiP poster at the ESMO Gynaecological Cancers Congress, which is taking place June 19-21, 2025 in Vienna, Austria.

Title	Authors	Presentation Details
Design of a First-in-Human Multicenter Open-Label Study of ZW191, a Folate Receptor α–Targeting Antibody-Drug Conjugate Utilizing a Novel TOPO1i Payload, in Participants With Advanced Solid Tumors: ZWI-ZW191-101	David Sommerhalder , Alexander I. Spira, Tarek Meniawy, Kosei Hasegawa, David Shao Peng Tan, Daniel SW Tan, Byoung-Gie Kim, Pranshul Chauhan, Akira Kojima, Syed Raza, Noboru Yamamoto	Type: Poster Date: Friday, June 20, 12:40 pm-1:30 pm Central European Summer Time (CEST) Number: 444

“We are pleased to share TiP posters at ASCO and ESMO-Gyn, for ZW171 and ZW191 respectively, which will discuss additional details of our ongoing Phase 1 clinical trials evaluating our novel therapeutic candidates in multiple solid tumors,” said Sabeen Mekan, M.D., Senior Vice President, Clinical Development at Zymeworks. “We are making good progress with global enrollment across diverse patient populations for both trials. This broad enrollment will enable us to develop robust and meaningful analyses, and we look forward to presenting initial data at a future medical meeting.”

About the Azymetric Platform

Azymetric™ is a heterodimeric antibody technology that gives the ability to engineer, screen, and effectively choose the optimal geometry and valency for our targeted treatments. These customized therapeutic antibodies are engineered to simultaneously bind to multiple distinct locations on a target or to multiple targets, resulting in unique mechanisms of action not accessible through typical monospecific antibodies. Azymetric antibodies can block multiple signaling pathways, recruit immune cells to tumors, enhance receptor clustering and internalization, and increase tumor-specific targeting. Zymeworks’ other technologies can combine with Azymetric to engineer the antibody backbone of a bispecific antibody-drug conjugate or the base of

a multispecific therapeutic, to potentially overcome known therapeutic barriers and help design potential best-in-class bispecifics and trispecifics.

Clinical validation of the Azymetric platform is demonstrated by the accelerated approval our partner Jazz Pharmaceuticals received from the U.S. Food and Drug Administration in 2024 for Ziihera® (zanidatamab-hrii), a treatment for advanced HER2-positive biliary tract cancer in adults who have received prior therapy.

About ZW171

ZW171 is a bispecific antibody designed to enable T cell-mediated tumor cell killing through simultaneous binding to the extracellular domain of mesothelin (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 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.

About ZW191

ZW191 is an antibody-drug conjugate (ADC) that is engineered to target a protein called folate receptor-α (FRα) that is found on the surface of a variety of tumors such as on ovarian, endometrial, and lung cancers. ZW191's differentiated design is built using our novel, bystander active, TOPO1i payload technology, ZD06519; its FRα-targeting monoclonal antibody was selected based on compelling internalization characteristics to enable targeting of high, mid, and low levels of FRα expression. A drug-antibody-ratio (DAR) of eight was selected due to the restricted expression profile of FRα in normal tissues and to enhance our ability to deliver payload to tumors with lower levels of FRα. FRα is a clinically validated target, found in approximately 75% of high-grade serous ovarian carcinomas, 50% of endometrial cancers, and in 70% of non-small cell lung cancer. Preclinical data demonstrate strong ZW191 activity across a range of FRα-expressing patient-derived xenografts, including models with low levels of FRα. The ability to target lower levels of FRα is in part due to the DAR-eight format and the observed superior internalization, payload delivery, and tissue penetration derived from the ZW191 monoclonal antibody compared to other FRα monoclonal antibodies used in ADCs currently or previously in development. In a good laboratory practices toxicology study, ZW191 achieved a highest non-severely toxic dose in non-human primates of 60 mg/kg, which presents a compelling profile and enables the expectation of potentially achieving an efficacious dose level in the Phase 1 clinical trial.

About Ziihera

Ziihera (zanidatamab-hrii) is a bispecific HER2-directed antibody that binds to two extracellular sites on HER2. Binding of zanidatamab-hrii with HER2 results in internalization leading to a reduction in HER2 expression of the receptor on the tumor cell surface. Zanidatamab-hrii induces complement-dependent cytotoxicity (CDC), antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP). These mechanisms result in tumor growth inhibition and cell death in vitro and in vivo[5]. In the United States, Ziihera is indicated for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) biliary tract cancer (BTC), as detected by an FDA-approved test[5]. The U.S. Food and Drug Administration (FDA) granted accelerated approval for this indication based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)[5].

Zanidatamab is not yet approved outside of the United States.

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 FDA granted Breakthrough Therapy designation for zanidatamab development in patients with previously treated HER2 gene-amplified 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 1L 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.

More information about *Ziihera*, the Full Prescribing Information, including Boxed Warning and Patient Information, is available here.

Important Safety Information for ZIIHERA

WARNING: EMBRYO-FETAL TOXICITY
Exposure to ZIIHERA during pregnancy can cause embryo-fetal harm. Advise patients of the risk and need for effective contraception.

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity
ZIIHERA can cause fetal harm when administered to a pregnant woman. In literature reports, use of a HER2-directed antibody during pregnancy resulted in cases of oligohydramnios and oligohydramnios sequence manifesting as pulmonary hypoplasia, skeletal abnormalities, and neonatal death.
Verify the pregnancy status of females of reproductive potential prior to the initiation of ZIIHERA. Advise pregnant women and females of reproductive potential that exposure to ZIIHERA during pregnancy or within 4 months prior to conception can result in fetal harm. Advise females of reproductive potential to use effective contraception during treatment with ZIIHERA and for 4 months following the last dose of ZIIHERA.

Left Ventricular Dysfunction
ZIIHERA can cause decreases in left ventricular ejection fraction (LVEF). LVEF declined by >10% and decreased to <50% in 4.3% of 233 patients. Left ventricular dysfunction (LVD) leading to permanent discontinuation of ZIIHERA was reported in 0.9% of patients. The median time to first occurrence of LVD was 5.6 months (range: 1.6 to 18.7). LVD resolved in 70% of patients.

Assess LVEF prior to initiation of ZIIHERA and at regular intervals during treatment. Withhold dose or permanently discontinue ZIIHERA based on severity of adverse reactions.

The safety of ZIIHERA has not been established in patients with a baseline ejection fraction that is below 50%.

Infusion-Related Reactions
ZIIHERA can cause infusion-related reactions (IRRs). An IRR was reported in 31% of 233 patients treated with ZIIHERA as a single agent in clinical studies, including Grade 3 (0.4%), and Grade 2 (25%). IRRs leading to permanent discontinuation of ZIIHERA were reported in 0.4% of patients. IRRs occurred on the first day of dosing in 28% of patients; 97% of IRRs resolved within one day.

Prior to each dose of ZIIHERA, administer premedications to prevent potential IRRs. Monitor patients for signs and symptoms of IRR during ZIIHERA administration and as clinically indicated after completion of infusion. Have medications and emergency equipment to treat IRRs available for immediate use.

If an IRR occurs, slow, or stop the infusion, and administer appropriate medical management. Monitor patients until complete resolution of signs and symptoms before resuming. Permanently discontinue ZIIHERA in patients with recurrent severe or life-threatening IRRs.

Diarrhea
ZIIHERA can cause severe diarrhea.
Diarrhea was reported in 48% of 233 patients treated in clinical studies, including Grade 3 (6%) and Grade 2 (17%). If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic tests as clinically indicated to exclude other causes of diarrhea. Withhold or permanently discontinue ZIIHERA based on severity.

ADVERSE REACTIONS
Serious adverse reactions occurred in 53% of 80 patients with unresectable or metastatic HER2-positive BTC who received ZIIHERA. Serious adverse reactions in >2% of patients included biliary obstruction (15%), biliary tract infection (8%), sepsis (8%), pneumonia (5%), diarrhea (3.8%), gastric obstruction (3.8%), and fatigue (2.5%). A fatal adverse reaction of hepatic failure occurred in one patient who received ZIIHERA.
The most common adverse reactions in 80 patients with unresectable or metastatic HER2-positive BTC who received ZIIHERA (≥20%) were diarrhea (50%), infusion-related reaction (35%), abdominal pain (29%), and fatigue (24%).

USE IN SPECIFIC POPULATIONS

Pediatric Use
Safety and efficacy of ZIIHERA have not been established in pediatric patients.

Geriatric Use
Of the 80 patients who received ZIIHERA for unresectable or metastatic HER2-positive BTC, there were 39 (49%) patients 65 years of age and older. Thirty-seven (46%) were aged 65-74 years old and 2 (3%) were aged 75 years or older.
No overall differences in safety or efficacy were observed between these patients and younger adult patients.

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

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[5] ZIIHERA (zanidatamab-hrii) Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.

Source: Zymeworks Inc.