



Zymeworks Announces Phase 1 Data for ZW25 in Combination with Chemotherapy in Advanced Gastroesophageal Adenocarcinoma at AACR-NCI-EORTC International Conference

October 28, 2019

- *ZW25 Plus Chemotherapy Shows Durable Activity in Patients with Heavily Pretreated Gastroesophageal Adenocarcinoma*
- *Data Continue to Support Ongoing Phase 2 Trial of ZW25 Plus Standard of Care Chemotherapy Therapy as First-Line Treatment*

BOSTON--(BUSINESS WIRE)-- Zymeworks Inc. (NYSE: ZYME), a clinical-stage biopharmaceutical company developing multifunctional therapeutics, today announces the first data from its Phase 1 study evaluating novel bispecific antibody ZW25 in combination with chemotherapy in HER2-expressing gastroesophageal adenocarcinoma (GEA) in a poster presentation at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, taking place October 26 - 30 in Boston.

"Today we report the promising anti-tumor activity of ZW25 in combination with chemotherapy for people with HER2-expressing GEA," said Diana Hausman, M.D., Chief Medical Officer at Zymeworks. "These results compare favorably with current standard of care treatments for patients who have progressed after first-line therapies, including trastuzumab and chemotherapy. The data further support the prioritization of our ongoing Phase 2 trial of ZW25 plus chemotherapy as a first-line treatment for GEA and our goal of establishing ZW25 as the new best-in-class therapy for people with HER2-expressing cancers."

The FDA has granted Fast Track designation to ZW25 for first-line HER2-positive GEA in combination with standard of care chemotherapy, and a Phase 2 trial evaluating combination treatment in this setting is actively enrolling patients ([NCT03929666](#)).

"The patients in this Phase 1 study have a difficult-to-treat, advanced stage of cancer, which has progressed despite multiple prior therapies," said Funda Meric-Bernstam, M.D., Professor and Chair of the Department of Investigational Cancer Therapeutics, Medical Director of the Institute for Personalized Cancer Therapy at The University of Texas MD Anderson Cancer Center. "The preliminary activity and tolerability of ZW25 combination treatment with paclitaxel or capecitabine brings hope to these patients and warrants further investigation in a first-line setting."

Clinical Data Presented Today

Safety and Efficacy of ZW25, a HER2-Targeted Bispecific Antibody in Combination with Chemotherapy in Patients with Locally Advanced and/or Metastatic HER2-Expressing Gastroesophageal Cancer (Abstract# B001, Poster Presentation on Monday, October 28 at 12:30 pm ET)

The results from part three of an ongoing Phase 1 study present the safety and efficacy of ZW25, at the recommended dose of 20 mg/kg every other week, in combination with paclitaxel or capecitabine as a treatment for 14 patients with heavily pretreated HER2-expressing GEA. Patients received a median of 2.5 prior systemic therapies, and 93% had progressed following trastuzumab treatment.

Nine of 14 patients were response-evaluable. Overall, the majority of patients experienced a decrease in their target lesions with a disease control rate of 78%, comprising five (56%) partial responses and two (22%) stable disease. These responses were observed in both low and high HER2-expressing GEA. At the time of the data cut-off, four of the five partial responses had been confirmed, and five (56%) response-evaluable patients were still on study.

The overall safety profile of ZW25 plus chemotherapy was similar to that seen with chemotherapy alone. The most common treatment-related adverse events (TRAE) occurring in two or more patients were primarily Grade 1 or 2 and manageable with symptomatic treatment. Of the TRAE occurring in two or more patients, Grade 3 or higher events attributed to ZW25 and/or chemotherapy were fatigue and neutropenia (2 patients each) and stomatitis, peripheral neuropathy, and hypokalaemia (1 patient each). Five patients had chemotherapy dose reductions due to TRAEs, but no patients needed ZW25 dose reductions due to adverse events.

About the Phase 1 Clinical Trial

Zymeworks' Phase 1 study has three parts. From part one of the study (the dose-escalation phase), the recommended single-agent dose was determined to be 20 mg/kg once every two weeks or 10 mg/kg weekly. In the second part of the study (the cohort expansion phase), additional patients are being enrolled to further assess ZW25's single-agent tolerability and anti-tumor activity against a variety of cancer types in different settings. The third part of the study (the combination phase) is underway and evaluating ZW25 in combination with selected chemotherapy agents in patients with HER2 high or lower HER2 expression levels.

About ZW25

ZW25 is being evaluated in Phase 1 and Phase 2 clinical trials across North America and South Korea. It is a bispecific antibody, based on Zymeworks' Azymetric™ platform, that can simultaneously bind two distinct locations on HER2, known as biparatopic binding. This unique design results in multiple mechanisms of action including dual HER2 signal blockade, increased binding and removal of HER2 protein from the cell surface, and potent effector function leading to encouraging anti-tumor activity in patients. Zymeworks is developing ZW25 as a HER2-targeted treatment option for patients with any solid tumor that expresses HER2. The FDA has granted Fast Track designation to ZW25 for first-line gastroesophageal adenocarcinoma in combination with standard of care chemotherapy and Orphan Drug designation to ZW25 for the treatment of both gastric and ovarian cancers.

About Zymeworks Inc.

Zymeworks is a clinical-stage biopharmaceutical company dedicated to the development of next-generation multifunctional biotherapeutics. Zymeworks' suite of therapeutic platforms and its fully integrated drug development engine enable precise engineering of highly differentiated product candidates. Zymeworks' lead clinical candidate, ZW25, is a novel Azymetric™ bispecific antibody currently in Phase 2 clinical development. Zymeworks' second clinical candidate, ZW49, is a bispecific antibody-drug conjugate currently in Phase 1 clinical development and combines the unique design and antibody framework of ZW25 with Zymeworks' proprietary ZymeLink™ cytotoxic payload. Zymeworks is also advancing a deep preclinical pipeline in immuno-oncology and other therapeutic areas. In addition, its therapeutic platforms are being leveraged through strategic partnerships with nine biopharmaceutical companies. For more information, visit www.zymeworks.com.

Cautionary Note Regarding Zymeworks' Forward Looking Statements

This press release includes "forward-looking statements" within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and "forward-looking information" within the meaning of Canadian securities laws, or collectively, forward-looking statements. Forward-looking statements in this news release include statements that relate to ZW25 and its potential as an anti-cancer treatment, Zymeworks' clinical plans and future results, Zymeworks' technology platform, and other information that is not historical information. When used herein, words such as "believe", "may", "plan", 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, market conditions and the factors described under "Risk Factors" in Zymeworks' Quarterly Report on Form 10-Q for the three month period ended June 30, 2019 (a copy of which may be obtained at www.sec.gov and www.sedar.com). Consequently, forward-looking statements should be regarded solely as Zymeworks' current plans, estimates and beliefs. You should not place undue reliance on forward-looking statements. Zymeworks cannot guarantee future results, events, levels of activity, performance, or achievements. Zymeworks does not undertake and specifically declines any 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, except as may be required by law.

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Investor Inquiries:
Ryan Dercho, Ph.D.
(604) 678-1388
[\[email protected\]](#)

Tiffany Tolmie
(604) 678-1388
[\[email protected\]](#)

Media Inquiries:
Kavita Shah, Ph.D.
(604) 678-1388
[\[email protected\]](#)

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