



zymeworks

Zymeworks Presents Safety and Anti-Tumor Activity Data from the Ongoing Phase 1 Study of ZW25 at the American Society of Clinical Oncology Annual Meeting (ASCO 2017)

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VANCOUVER, British Columbia--(BUSINESS WIRE)-- Zymeworks Inc. ("Zymeworks"), a clinical-stage biopharmaceutical company dedicated to the discovery, development and commercialization of next-generation multifunctional biotherapeutics, today announced results from the dose escalation portion of the first-in-human study of ZW25, a novel Azymetric™ bispecific antibody targeting two distinct domains of the HER2 receptor.

ZW25 was well-tolerated at all dose levels evaluated with single agent anti-tumor activity in patients with advanced HER2-expressing cancers that had progressed after multiple lines of therapy, including HER2-targeted agents. These results provide the framework for further advancement of ZW25 across multiple cancer indications.

A total of 16 patients were enrolled in the study, including 8 with breast cancer, 6 with gastric, gastroesophageal junction, or esophageal (GE) cancer, and 2 with other HER2-expressing cancers. All patients were heavily pretreated having received a median of 4 prior systemic regimens for metastatic disease, which included trastuzumab. Breast cancer patients were also treated with T-DM1 (n=8); pertuzumab (n=6), and lapatinib (n=6) and had a median of 6 prior HER2-targeted regimens for metastatic disease.

"Despite the benefits provided by currently-available HER2-targeted therapies, significant medical need remains," said Dr. Diana Hausman, Chief Medical Officer of Zymeworks. "We are very encouraged by the safety profile and single agent anti-tumor activity of ZW25 in patients with advanced breast or GE cancer that has progressed after prior HER2-targeted therapies. These results will guide further development in the expansion cohort portion of this study."

Patients were treated with weekly ZW25 at 5 mg/kg (n=3), 10 mg/kg (n=6), or 15 mg/kg (n=7) in cycles of 4 weeks each. ZW25 was well-tolerated at all dose levels, with no dose-limiting toxicities. The majority of adverse events (AEs) were Grade 1 or 2, with no treatment-related serious AEs and no changes in cardiac function. The most common AEs were diarrhea and infusion reactions, reported in 7/16 patients each. Treatment-related Grade 3 AEs occurred in a single patient and included hypophosphatemia, fatigue, and arthralgia. Eight patients had anti-drug antibodies (ADA) prior to initiating treatment with ZW25; there was no evidence of increases from baseline levels and no patients developed new ADA.

Durable single-agent anti-tumor activity was seen with patients having received up to 8 cycles of treatment at the time of data cut-off. In 14 response-evaluable patients (defined as undergoing at least one tumor restaging), best overall response (BOR) was 2 partial response (PR), 4 stable disease (SD), and 8 progressive disease (PD). The majority of patients with measurable disease had a decrease in the size of target lesions. BOR in 8 breast cancer patients was 2 PR, 3 SD (> 6 months in one patient), and 3 PD, for an overall disease control rate (CR, PR, or SD) of 63%. Three of the breast cancer patients developed PD due to brain metastases but maintained systemic disease control at the time of progression. BOR in 4 response-evaluable patients with GE cancers included SD > 4 cycles in 1 patient, and 3 PD. Four patients remain active on study.

"We will continue to rapidly advance development across multiple cancer indications, with the goal of establishing ZW25 as the HER2-targeted therapy of choice for physicians and their patients," said Dr. Ali Tehrani, President and CEO of Zymeworks. "These results also highlight the value of Zymeworks' Azymetric bispecific platform and support the accelerated development of additional multifunctional therapeutics in our candidate pipeline."

ZW25 Phase 1 Clinical Trial Details

The dose escalation portion of the study enrolled patients with HER2-expressing cancers (either HER2 IHC 1+, 2+ or 3+, or FISH-positive) whose cancer had progressed after treatment with all therapies known to confer clinical benefit. HER2 status was assessed in archived or fresh biopsies locally and at a central laboratory. Patients with HER2-high breast cancer (HER2 IHC 3+ or IHC2+ and FISH-positive) had to have received previous treatment with trastuzumab, pertuzumab, and T-DM1. Patients with HER2-high gastric or gastroesophageal cancers had to have been previously treated with trastuzumab. Patients could have measurable or non-measurable tumor lesions per RECIST 1.1. Patients with known active brain metastases were excluded from the study. Patients were assessed during treatment for safety, including changes in cardiac function, tumor response per RECIST 1.1 every 8 weeks, ZW25 drug levels, and potential development of anti-drug antibodies.

About ZW25

ZW25 is Zymeworks' lead product candidate currently being evaluated in a Phase 1 clinical trial in the United States, based on Zymeworks' Azymetric™ platform. It is a bispecific antibody that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding, resulting in dual HER2 signal blockade, increased binding and removal of HER2 protein from the cell surface, and potent effector function. These combined mechanisms of action have led to significant anti-tumor activity in preclinical models of HER2-expressing cancer. Zymeworks is developing ZW25 as a best-in-class HER2-targeting antibody intended as a treatment option for patients with any solid tumor that expresses HER2.

About Zymeworks Inc.

Zymeworks is a clinical-stage biopharmaceutical company dedicated to the discovery, development and commercialization of next-generation multifunctional biotherapeutics, initially focused on the treatment of cancer. Zymeworks' suite of complementary therapeutic platforms and its fully-integrated drug development engine provide the flexibility and compatibility to precisely engineer and develop highly-differentiated product candidates. Zymeworks' lead product candidate, ZW25, is a novel bispecific antibody currently being evaluated in a Phase 1 clinical trial. Zymeworks is also advancing a deep pipeline of preclinical product candidates and discovery-stage programs in immuno-oncology and other therapeutic areas. In addition to Zymeworks' wholly-owned pipeline, its therapeutic platforms have been further leveraged through multiple strategic partnerships with global biopharmaceutical companies.

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 include statements that relate to Zymeworks' Phase 1 clinical trial, ASCO presentation and other information that is not historical information. 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 our current expectations and various assumptions. We believe there is a reasonable basis for our expectations and beliefs, but they are inherently uncertain. We may not realize our expectations, and our 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 our registration statement on Form F-1 and in our supplemented PREP prospectus dated April 27, 2017 filed in connection with our initial public offering on May 3, 2017 (copies of which filings may be obtained at www.sec.gov and www.sedar.com). Consequently, forward-looking statements should be regarded solely as our current plans, estimates and beliefs. You should not place undue reliance on forward-looking statements. We cannot guarantee future results, events, levels of activity, performance or achievements. We do not undertake and specifically decline 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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Zymeworks Inc.
Investor Inquiries:
David Matousek, 604-678-1388
Senior Manager, Investor Relations & Corporate Communications
[\[email protected\]](#)

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