



zymeworks

Zymeworks Presents Additional Safety and Anti-Tumor Activity Data from the Ongoing Phase 1 Study of ZW25 at the European Society for Medical Oncology 2017 Congress (“ESMO”)

September 11, 2017

VANCOUVER, British Columbia--(BUSINESS WIRE)-- Zymeworks Inc. (“Zymeworks”), (NYSE: ZYME; TSX: ZYME) a clinical-stage biopharmaceutical company dedicated to the discovery, development and commercialization of next-generation multifunctional biotherapeutics, today provided additional data from the dose escalation portion of its Phase 1 study of ZW25, a novel Azymetric™ bispecific antibody targeting two distinct domains of the HER2 receptor. The HER2-mediated signaling pathway is believed to contribute to tumor growth in a number of different cancers.

Key Takeaways:

- The expanded dataset includes an additional three-month follow-up for on-study patients following the American Society of Clinical Oncology (“ASCO”) conference in June 2017, as well as safety data on six new patients.
- The best overall response in HER2-high, heavily pretreated breast cancer patients improved from two to four partial responses, resulting in a disease control rate of 63%. This included a partial response at each weekly dosing cohort.
- ZW25 continues to be well-tolerated at all doses and schedules, with the most common adverse events being Grade 1 or 2 diarrhea, infusion reactions or nausea.
- The dose escalation portion of the Phase 1 trial is complete and the new expansion cohorts have begun enrolling.

ZW25 was well-tolerated at all dose levels evaluated. Single agent anti-tumor activity was present in patients with advanced HER2-expressing cancers that had progressed after multiple lines of therapy, including HER2-targeted agents. The safety and anti-tumor activity profile of ZW25 across multiple dose levels suggests the potential for a wide therapeutic window. These results have provided the framework for the initiation and enrollment of patients into the cohort expansion portion of the Phase 1 trial for ZW25 across multiple discrete cancer indications.

A total of 22 patients have been enrolled in the study, including 11 with breast cancer, eight with gastric, gastroesophageal junction, or esophageal (“GE”) cancer, and three with other HER2-expressing cancers. Part one of the multi-part study was a standard dose escalation of ZW25 where patients received ZW25 either weekly at 5 mg/kg (n=3), 10 mg/kg (n=6), or 15 mg/kg (n=7) to identify a dose and schedule to take forward for further evaluation as well as the exploration of an alternative bi-weekly (once every two weeks) schedule at 20 mg/kg (n=6) in cycles of four weeks each. Data presented at ESMO included safety and anti-tumor activity for all patients treated in weekly dosing cohorts, and available safety data for patients from the bi-weekly cohort. All patients had received multiple prior regimens of systemic therapy for metastatic disease (range 1-10), representing a heavily pretreated population.

“The patients enrolled in this study are representative of the ongoing unmet need in HER2-expressing cancers, including HER2-high breast cancer,” said Dr. Diana Hausman, Chief Medical Officer of Zymeworks. “We are very encouraged by the safety profile of ZW25, as well as by the single agent anti-tumor activity that has been observed, particularly in patients who have progressive disease after multiple prior HER2-targeted regimens. We believe these data provide strong support for the further development of ZW25.”

No dose-limiting toxicities were seen at any dose level or schedule. The most common adverse events were diarrhea, infusion reactions, and nausea, all Grade 1 or 2 in severity. There were no treatment-related serious adverse events, cardiac events or decreases in left ventricular ejection fraction.

Durable single-agent anti-tumor activity was seen with patients having received up to 11 cycles of treatment at the time of data cut-off. The majority of patients with measurable disease had a decrease in target lesions per RECIST 1.1. The best overall response (“BOR”) in 12 response-evaluable (defined as undergoing at least one tumor restaging) breast and GE patients, was four partial response (“PR”; 33%), two stable disease (“SD”; 17%) and six progressive disease (“PD”; 50%).

Of the eight breast cancer patients in the weekly dosing cohorts, all were HER2-high and had received a median of six prior HER2-targeted regimens for metastatic disease including trastuzumab (n=8), T-DM1 (n=8), pertuzumab (n=6), and lapatinib (n=6). BOR was four PR (50%), one SD for > 10 months (13%), and three PD (38%), for an overall disease control rate (CR, PR, or SD) of 63%.

Of the six patients with GE cancer that were treated in the weekly dosing cohorts, three were HER2-high and three were HER2-low. Four patients were response-evaluable, with a BOR of one SD (>7 months in HER2-high esophageal cancer), and three PD.

“We are pleased to update the preliminary clinical data that we released at ASCO in June, highlighted by two of the patients with prior best response of stable disease improving to partial responses, bringing the total to four,” said Dr. Ali Tehrani, President and CEO of Zymeworks. “ZW25 has not only

shown impressive single agent anti-tumor activity, but also prolonged disease control with several patients on study that have continued to improve. Our aim is to provide another update on the progress of ZW25 at the upcoming San Antonio Breast Cancer Symposium in December of this year."

September 11th Webcast and Conference Call

Zymeworks will host a webcast and conference call on September 11, at 4:30 p.m. ET (1:30 p.m. PT) to review the data presented at ESMO, and provide a general clinical update. Also on the call will be Dr. Funda Meric-Bernstam, the Chair of the Department of Investigational Cancer Therapeutics, Medical Director of the Institute for Personalized Cancer Therapy ("IPCT"), and a Professor in the Divisions of Cancer Medicine and Surgery at The University of Texas MD Anderson Cancer Center.

The webcast can be accessed through: <http://services.choruscall.ca/links/zyme20170911.html>.

The live call may be accessed by dialing 1-800-319-4610 for North American callers, or 1-604-638-5340 for international callers. Callers should dial in five to ten minutes prior to the scheduled start time, and ask to join the "Zymeworks call".

A telephone replay of the conference call will be available by dialing 1-800-319-6413 or 1-604-638-9010 and entering access code 1653. The replay will be available after the conclusion of the conference call until September 25, 2017.

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, ESMO presentation and other information that is not historical information. In addition, any statements or information that refer to expectations, beliefs, plans, our aim, 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.



View source version on businesswire.com: <http://www.businesswire.com/news/home/20170911005261/en/>

Investor Inquiries:

David Matousek, 604-678-1388

Senior Manager, Investor Relations & Corporate Communications

[\[email protected\]](#)

Source: Zymeworks Inc.