

# Zymeworks Presents Results of the Completed Dose Escalation Portion of the Ongoing Phase 1 Study of ZW25 at the San Antonio Breast Cancer Symposium



## Continued Clinical Benefit of Single Agent ZW25 in Heavily Pretreated HER2-High Patients

**Vancouver, Canada (December 5, 2017)** – Zymeworks Inc. (NYSE/TSX: ZYME), a clinical-stage biopharmaceutical company dedicated to the development of next-generation multifunctional biotherapeutics, today presented the completed 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 cancers.

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 where patients received ZW25 either weekly at 5 mg/kg (n=3), 10 mg/kg (n=6), or 15 mg/kg (n=7) or bi-weekly (once every two weeks) at 20 mg/kg (n=6) in cycles of four weeks each.

### Study Highlights:

- Six Partial Responses (PR) were observed across all dosing groups including two new PRs from the 20 mg/kg bi-weekly cohort.
- Clinical benefit (Confirmed PR or stable disease (SD)  $\geq$  6 months) of single agent ZW25 observed in heavily pretreated HER2-high breast and GE cancer patients.
- Breast cancer patients received a median of six prior HER2-targeted regimens for metastatic disease; partial response in 56% (5/9) of breast cancer patients with measurable disease, with 89% (8/9) experiencing a decrease in target lesions.
- Three HER2-high GE cancer patients with measurable disease showed tumor shrinkage, including one Confirmed PR (71% decrease in target lesions) and one SD for > 6 months.
- ZW25 was well-tolerated at all doses and schedules, with the most common adverse events being diarrhea, infusion reactions, or nausea, all Grade 1 or 2 in severity.

- The dose escalation portion of the Phase 1 trial is complete and enrollment in the expansion cohorts is underway.
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Seventy-nine percent of breast and GE cancer patients with measurable disease (11/14) had a decrease in target lesions per RECIST criteria. The best overall response (BOR) in 17 response-evaluable (defined as undergoing at least one tumor restaging) breast and GE cancer patients was six PR (35%), three SD (18%) and eight progressive disease (PD; 47%).

“The expanding dataset continue to show responses and durable disease control with both weekly and every other week dosing and demonstrate the potential of ZW25 to address unmet need across multiple indications,” said Dr. Diana Hausman, Chief Medical Officer of Zymeworks. “We are seeing meaningful clinical benefit with single agent treatment in breast and gastric cancer patients who have progressive disease after numerous standard of care regimens. These early results, while impressive in their own right, are also distinct from other investigational agents being evaluated in refractory HER2-expressing cancer patients and support the continued evaluation of ZW25 both as a single agent and in combination with other cancer therapeutics.”

Of the eleven breast cancer patients, all were HER2-high and had received a median of six prior HER2-targeted regimens for metastatic disease including trastuzumab (n=11), T-DM1 (n=11), pertuzumab (n=9), and lapatinib (n=7) as well as other investigational agents. The BOR in these heavily pretreated patients was five PR (45%), two SD (18%), and three PD (27%), for an overall disease control rate (Complete Response, PR, or SD) of 64%. At least one PR was observed in every dosing group.

Of the eight GE patients, six were evaluable for response, and had received a median of four prior systemic regimens, including trastuzumab in all patients. Three of five patients with measurable disease had a decrease in tumor size, including one patient continuing on treatment with a Confirmed PR and 71% decrease in target lesions, as well as a second patient with SD for over 6 months.

“There is an ongoing need for novel treatments for patients who have exhausted available options for their HER2-expressing cancers,” said Dr. Erika Hamilton, Director of the Breast Cancer and Gynecologic Cancer Research Program at Sarah Cannon Research Institute in Nashville, Tennessee. “The preliminary anti-tumor activity and tolerability we have seen with single agent ZW25 has been encouraging. We are excited to be enrolling patients in the expansion cohort portion of this study.”

Enrollment is underway for the second part of the study utilizing ZW25 every other week at 20 mg/kg in four expansion cohorts spanning HER2-high breast, HER2-high gastric, HER2-intermediate breast and other HER2-gene amplified cancers.

“The dose escalation portion of the Phase 1 trial has been a success, demonstrating the tolerability and single agent anti-tumor activity of ZW25,” said Dr. Ali Tehrani, President and CEO of Zymeworks. “These data bring us one step closer to initiating a single agent registrational trial with the goal of submitting an initial Biologics License Application (BLA) for ZW25 in 2021. We plan to provide an update on the expansion cohort portion of the trial at the American Society of Clinical Oncology Annual Meeting in 2018.”

The poster will be formally presented on Friday December 8<sup>th</sup> from 5:00-7:00pm CT at the San Antonio Breast Cancer Symposium and is available through their website or through the Investor page of Zymeworks’ website at <http://ir.zymeworks.com/events-and-presentations>.

## **ZW25 Phase 1 Clinical Trial Details**

The dose escalation portion of the study enrolled 22 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. No dose-limiting toxicities were seen at any dose level or schedule. The most common adverse events were diarrhea, infusion reactions, or 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.

## **About ZW25**

ZW25 is Zymeworks' lead product candidate currently being evaluated in a Phase 1 clinical trial in the United States. It is a bispecific antibody, based on Zymeworks' Azymetric™ platform, that can simultaneously bind two non-overlapping epitopes of 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 and has led to significant anti-tumor activity in preclinical models of HER2-expressing cancer. Zymeworks is developing ZW25 as a best-in-class HER2-targeted 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. 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 an adaptive 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.

## **Cautionary Note Regarding 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 Zymeworks' Phase 1 clinical trial, its San Antonio Breast Cancer Symposium presentation, the potential of ZW25, Zymeworks' estimated timeframe for submitting an initial BLA for ZW25 to the U.S. FDA, and other information that is not historical information. When used herein, words such as "believe", "may", "plan", "will", "estimate", "continue", "anticipate", "intend", "expect" 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’ registration statement on Form F-1 and in its supplemented PREP prospectus dated April 27, 2017 filed in connection with Zymeworks’ initial public offering on May 3, 2017 (copies of which filings may be obtained at [www.sec.gov](http://www.sec.gov) and [www.sedar.com](http://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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