Zymeworks Announces Updated Clinical Data for Novel Bispecific Antibody, ZW25, Presented at the EORTC-NCI-AACR Symposium

November 14, 2018

- *ZW25 Active and Well Tolerated Across Multiple HER2-expressing Tumor Types*
- *Durable Anti-Tumor Activity with Confirmed Partial Responses and Median Progression-Free Survival > Six Months*
- *82 Percent of Heavily Pretreated Patients Experienced Disease Control*

DUBLIN--(BUSINESS WIRE)-- Zymeworks Inc. (NYSE/TSX: ZYME), a clinical-stage biopharmaceutical company developing multifunctional therapeutics, announced today the plenary presentation of updated ZW25 clinical data by Murali Beeram, MD, a clinical investigator at the START Center for Cancer Care, San Antonio, Texas. Data from Zymeworks' ongoing multi-center Phase 1 study showed single agent ZW25, a bispecific antibody, induced anti-tumor activity and was well tolerated in heavily pretreated patients with a variety of HER2-expressing cancers.

"Today we report, for the first time, the durability of ZW25's anti-tumor activity," said Ali Tehrani, Ph.D., President and CEO of Zymeworks. "With a median of over six months of progression-free survival in these heavily pretreated patients, these data further support our previously-communicated clinical strategy which includes registration-enabling studies for single-agent ZW25 in gastrointestinal-related cancers where the unmet need is so great worldwide."

ZW25 Clinical Results Presented Today

The plenary presentation includes all 24 gastroesophageal and other cancer patients treated at the Phase 2 recommended dose, of which 17 were response-evaluable (defined as having measurable disease and at least one tumor restaging) at the time of data cut-off. Of these 17 patients, eight had gastroesophageal cancers, four had colorectal cancer and five had other HER2-expressing cancers including gall bladder, cholangiocarcinoma, cervical, fallopian tube and salivary gland. The participants in the study were heavily pretreated with a median of three prior cancer treatments.

The overall disease control rate (DCR), which includes patients with partial responses and stable disease was 82%. There were seven partial responses (41%), seven stable disease (41%) and three progressive disease (18%). The median progression-free survival (mPFS) in all 24 patients was 6.21 months (95% CI 1.94-9.33).

"To observe this level of activity across so many different tumor types is quite compelling," said Murali Beeram, MD. "These were heavily pretreated patients who had essentially run out of therapeutic options, so for them to respond so favorably is indeed encouraging."

In the eight gastroesophageal cancer patients, who had a median of four prior systemic treatments, the response rate was 50%. In the four colorectal and five other HER2-expressing cancer patients the response rate was 33%. Anti-tumor activity was assessed per RECIST every eight weeks.

In the study, ZW25 was well tolerated. All treatment-related adverse events were Grade 1 or 2 with the exception of one patient with Grade 3 fatigue, and no treatment-related serious adverse events were seen. There were no Grade 4 or 5 adverse events. The most common adverse events (25% or greater) were diarrhea, infusion reaction and nausea.

"The favorable tolerability we have seen with ZW25 supports its use as both a single agent and in combination with approved anti-cancer agents," said Diana Hausman, MD, Zymeworks' Chief Medical Officer. "We are excited to be advancing ZW25's development and have plans to explore its efficacy in a number of tumor types, including gastroesophageal and breast cancer."

Plenary Presentation Details

The presentation is part of the Symposium on Molecular Targets and Cancer Therapeutics sponsored by the European Organization for Research and Treatment of Cancer (EORTC), the National Cancer Institute (NCI) and the American Association for Cancer Research (AACR).

Title: "Single Agent Activity of ZW25, a HER2-Targeted Bispecific Antibody, in HER2-Expressing Gastroesophageal and Other Cancers"

Session: Proffered papers, Plenary Session 2, Abstract 6

*Time:*Wednesday November 14, 3:45 pm GMT

Location: Auditorium

About the Trial

Zymeworks' adaptive Phase 1 study has three parts. Enrollment in the first portion of the study (the dose-escalation phase) has been completed. 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 is evaluating ZW25 in combination with selected chemotherapy agents in gastroesophageal and breast cancer patients with HER2 high or lower HER2 expression levels.

About ZW25

ZW25 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 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 Orphan Drug Designation to ZW25 for the treatment of both gastric and ovarian cancers.

About the Azymetric™ Platform

The Azymetric platform enables the transformation of monospecific antibodies into bispecific antibodies, giving them the ability to simultaneously bind two different targets. Azymetric bispecific technology enables the development of multifunctional biotherapeutics that can block multiple signaling pathways, recruit immune cells to tumors, enhance receptor clustering and degradation, and increase tumor-specific targeting. These features are intended to enhance efficacy while reducing toxicities and the potential for drug-resistance. Azymetric bispecifics have been engineered to retain the desirable drug-like qualities of naturally occurring antibodies, including low immunogenicity, long half-life, and high stability. In addition, they are compatible with standard manufacturing processes with high yields and purity with the potential to significantly reduce drug development costs and timelines.

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. The company's second product candidate, ZW49, capitalizes on the unique design and antibody framework of ZW25 and is a bispecific antibody-drug conjugate, or ADC, armed with the company's proprietary ZymeLink™ cytotoxic payload. 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 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", "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' Quarterly Report on Form 10-Q for its fiscal quarter ended September 30, 2018 (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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