Zymeworks Advances HER2 Bispecific Antibody-Drug Conjugate, ZW49, into Expansion Cohort Stage of Clinical Development

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- *Active drug with multiple confirmed responses and stable disease observed in several tumor types*
- *Differentiated safety profile with the majority of adverse events being grade 1 or 2*
- *Expansion cohorts open and enrolling patients at 2.5 mg/kg once every three weeks*
- *Maximum tolerated dose not established, dose escalation continues in parallel*

VANCOUVER, British Columbia--(BUSINESS WIRE)-- Zymeworks Inc. (NYSE: ZYME), a clinical-stage biopharmaceutical company developing multifunctional biotherapeutics, announced today that the Company has begun enrolling patients into the expansion cohort portion of the ongoing Phase 1 clinical trial for ZW49, its novel HER2-targeted antibody-drug conjugate (ADC). Supporting data from the Phase 1 dose escalation portion were highlighted today via a webcast and conference call and are summarized below.

Phase 1 Dose Escalation Study Design

The dose escalation portion of the study employed a standard 3 + 3 design to evaluate escalating doses within different dosing regimens including once every two week (Q2W) and once every three week (Q3W) schedules with the objective of selecting a dose and schedule to advance into the expansion cohorts.

To date patients from sites across the US and Canada with a variety of heavily pretreated HER2-positive cancer types have been enrolled, including breast cancer, gastroesophageal adenocarcinoma, gynecologic cancers, non-small cell lung cancer, anal cancer, and colorectal cancer.

ZW49 Safety and Tolerability

In the 35 patients who have received ZW49 across all dosing regimens, there have been no dose limiting toxicities, no treatment-related hematologic toxicities including neutropenia or thrombocytopenia, no treatment-related pulmonary toxicity including interstitial lung disease or pneumonitis, and no treatment-related liver toxicity. There have been no treatment-related deaths.

Over 90% of treatment-related adverse events have been mild or moderate (Grade 1 or 2) in severity, with the most common being keratitis, fatigue, and diarrhea, which have been reversible and manageable in an outpatient setting. There have been no discontinuations due to treatment-related adverse events, and the maximum-tolerated dose has not yet been established.

ZW49 Interim Antitumor Activity

ZW49 has demonstrated antitumor activity across all regimens and dose levels evaluated to date, including at the starting dose of 1 mg/kg Q2W. Partial responses and stable disease per RECIST 1.1 have been observed in both Q2W and Q3W dosing regimens, with the Q3W regimen starting to demonstrate a dose-response relationship. Beginning at the initial dose of 2.0 mg/kg Q3W, several patients experienced stable disease including some with disease control greater than four months. At the highest doses tested in the Q3W of 2.5 or 3.0 mg/kg there were six response-evaluable patients with centrally confirmed HER2-positive disease spanning several different tumor types. The antitumor activity in these six patients consisted of two patients with confirmed partial responses and two patients with stable disease, three of which are still active on study. This regimen is currently enrolling patients at the 3 mg/kg dose with the potential to add new escalation cohorts.

“We are encouraged by the antitumor activity we are seeing so far with ZW49 and look forward to accelerating development by expanding our dataset in disease-specific cohorts,” said Diana Hausman, M.D., Chief Medical Officer of Zymeworks. “In addition, the differentiated safety profile allows us to continue in dose escalation, with the opportunity to fully realize the therapeutic potential for ZW49.”

Expansion Cohort Phase

Based on the antitumor activity demonstrated by ZW49, three indication-specific expansion cohorts utilizing the 2.5 mg/kg Q3W regimen are open and enrolling patients. These include HER2-positive breast cancer, HER2-positive gastroesophageal adenocarcinoma, and a basket cohort of other HER2-positive cancers. The expansion cohorts are actively enrolling at sites in U.S. and Canada, and are expected to open soon at additional sites in South Korea and Australia in collaboration with our partner, BeiGene.

“I believe ZW49 is on track for becoming the HER2 ADC that delivers efficacy without compromising safety,” said Ali Tehrani, Ph.D., President and CEO of Zymeworks. “These data highlight that ZW49 can potentially provide physicians and their patients with a differentiated alternative to currently-approved HER2 ADCs. We look forward to presenting additional data at a medical conference later this year.”

About ZW49

ZW49, Zymeworks’ second product candidate, is a novel bispecific HER2-targeted ADC developed using Zymeworks’ proprietary Azymetric™ and ZymeLink™ platforms. ZW49 combines the unique design of zanidatamab with a proprietary cytotoxin and cleavable linker resulting in enhanced internalization and tumor cell killing. ZW49 is currently in a Phase 1 clinical trial and is being developed for several indications characterized by HER2 expression, especially for patients whose tumors have progressed or are refractory to HER2-targeted agents and those that express lower levels of HER2 and are ineligible for treatment with existing HER2-targeted therapies.

About ZymeLink™ Antibody-Drug Conjugates

The ZymeLink ADC platform is a modular suite of proprietary cytotoxins (cell-killing drugs), customizable linkers, and conjugation technologies designed for targeted delivery of cytotoxins to diseased cells with optimal safety and efficacy. The ZymeLink platform can be combined with a diverse array of targeted therapies, including traditional antibodies and Azymetric™ bispecific antibodies, to deliver cell-killing compounds to diseased target cells. These modular technologies are designed to develop next-generation ADCs with broad therapeutic windows.

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, zanidatamab (ZW25), is a novel Azymetric™ bispecific antibody which has been granted Breakthrough Therapy designation by the FDA and is currently enrolling in a pivotal clinical trial for refractory HER2-amplified biliary tract cancer (HERIZON-BTC-01) as well as several Phase 2 clinical trials for HER2-expressing gastroesophageal and breast cancers. Zymeworks' second clinical candidate, ZW49, is a novel bispecific HER2-targeting antibody-drug conjugate currently in Phase 1 clinical development and combines the unique design and antibody framework of zanidatamab with Zymeworks' proprietary ZymeLink™ linker and cytotoxin. Zymeworks is also advancing a deep preclinical pipeline in oncology (including immuno-oncology agents) and other therapeutic areas. In addition, its therapeutic platforms are being leveraged through strategic partnerships with nine biopharmaceutical companies. For additional information about Zymeworks, visit www.zymeworks.com and follow @ZymeworksInc on Twitter.

Zymeworks 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 Zymeworks' expectations regarding the enrollment of patients into the expansion cohort portion of the ongoing Phase 1 clinical trial for ZW49, dose escalation of ZW49, the therapeutic potential of ZW49, and other information that is not historical information. When used herein, words and phrases such as "continue", "believe", "starting to", "look forward to", "expected to", "potential to", 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, including assumptions regarding anticipated reporting of additional clinical and preclinical data, the efficacy of zanidatamab, ZW49, and Zymeworks' therapeutic platforms, and Zymeworks' ability to maintain its partnership arrangements. 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, 2020 (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
ir@zymeworks.com

Tiffany Tolmie
(604) 678-1388
ir@zymeworks.com

Media Inquiries:
Mary Klem
(604) 678-1388
media@zymeworks.com

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