Zanidatamab Data Presented at the San Antonio Breast Cancer Symposium (SABCS) Demonstrate Encouraging Antitumor Activity in Heavily Pretreated Patients with HER2-Positive Breast Cancer

December 8, 2021

- *Overall confirmed objective response rate (cORR) of 36.4% and disease control rate (DCR) of 86.4%*
- *Median progression-free survival (mPFS) of 7.3 months overall*
- *Data support further investigation of zanidatamab plus chemotherapy as a novel therapeutic option for patients with HER2-positive metastatic breast cancer after three or more lines of prior therapy*

VANCOUVER, British Columbia--(BUSINESS WIRE)--Dec. 8, 2021-- Zymeworks Inc. (NYSE: ZYME), a clinical-stage biopharmaceutical company developing multifunctional biotherapeutics, today announced new clinical data for the HER2-targeted bispecific antibody, zanidatamab, in heavily pretreated HER2-positive breast cancer. The data are being presented at the San Antonio Breast Cancer Symposium (SABCS) taking place in San Antonio, Texas and virtually, December 7-10, 2021. In addition, Zymeworks will present a Trial in Progress poster detailing the ongoing clinical trial evaluating zanidatamab in combination with the CD47-blocker, evorpacept (ALX148).

Summary of Clinical Trial Results

The data presented at SABCS are from a clinical study of 24 patients with heavily pretreated HER2-positive metastatic breast cancer who received zanidatamab in combination with either vinorelbine (n=12), capecitabine (n=8), or paclitaxel (n=4). Patients received multiple prior regimens containing HER2-targeted agents including trastuzumab (96%), pertuzumab (96%), and T-DM1 (96%), and many also received a tyrosine kinase inhibitor.

In 22 efficacy-evaluable patients, treatment with zanidatamab and chemotherapy resulted in a cORR of 36.4% and DCR of 86.4%, and the majority of patients experienced a decrease in their tumor size. The mPFS is 7.3 months across all treatment regimens with 42% of patients still on study at the time of data cutoff. Zanidatamab in combination with single agent chemotherapy is well tolerated, with the majority of treatment-related adverse events considered mild to moderate in severity (Grade 1 or 2).

“Zanidatamab together with chemotherapy shows encouraging antitumor activity and a manageable safety profile in patients with HER2 -positive breast cancer that has progressed after treatment with multiple HER2-targeted agents,” said Neil Josephson, M.D., Chief Medical Officer at Zymeworks. “We were impressed by the activity and durability of disease control with zanidatamab, with over half of patients experiencing a confirmed response or stable disease lasting over 6 months. These results, together with data presented earlier this year in both HER2-expressing biliary tract cancer and gastroesophageal adenocarcinoma, build on our belief that zanidatamab has the potential to be a foundational therapy across multiple HER2-expressing solid tumor indications. We look forward to sharing additional data with zanidatamab in HER2-positive breast cancer from our other ongoing trials in the first half of 2022, including in combination with Ibrance and fulvestrant in late-line hormone receptor positive disease as well as in combination with docetaxel in the first-line setting.”

“Zanidatamab continues to generate clinical data that differentiate it from existing and emerging HER2-targeted standards of care,” said James Priour, Chief Commercial Officer at Zymeworks. “Expanding on our commitment to complete ongoing pivotal trials in biliary tract and gastric cancers, we see breast cancer as the next indication to pursue a potential label. As we await additional data in early lines of breast cancer, these data in late-line present an additional registrational opportunity. With the majority of HER2-positive breast cancer patients benefitting from new therapies and surviving longer than ever before, there is a significant commercial opportunity in the third- and fourth-line setting. We believe the data presented today demonstrate that zanidatamab and chemotherapy could be a new option for these patients.”

SABCS Presentations

The following presentations are available to conference registrants on the SABCS conference website as well as to the general public at https://www.zymeworks.com/publications.

Zanidatamab in Combination with Chemotherapy in Late-Line HER2-Postive Breast Cancer – Clinical Results Presented Today

Title: *Zanidatamab (ZW25), a HER2-targeted bispecific antibody, in combination with chemotherapy (chemo) for HER2-positive breast cancer (BC): Results from a phase 1 study*.
Lead Author: Philippe L. Bedard, M.D., Princess Margaret Cancer Center, Toronto, ON Canada.
Abstract: #93
Program Number: P2-13-07

Zanidatamab in Combination with Evorpacept (ALX148) – Trial in Progress Poster Presented Today

Title: *Zanidatamab (ZW25) in Combination with Evorpacept (ALX148) in Advanced Human Epidermal Growth Factor Receptor 2 (HER2)-expressing Cancers, Including Breast Cancer: a Phase 1b/2, Multicenter, Open-Label, Dose-Finding and Cohort-Expansion Study (ZWI-ZW25-204)*
Lead Author: Sara A. Hurvitz, M.D., University of California, Los Angeles; Jonsson Comprehensive Cancer Center, Los Angeles, CA, US
Abstract: #182
Program Number: OT1-14-01

Zymeworks is presenting a trial in progress poster at the SABCS for a Phase 1b/2 multi-center clinical study in HER2-expressing cancers, including

breast cancer. This study is evaluating the novel combination of zanidatamab, a HER2-targeted bispecific antibody, and evorpacept, a CD47-blocker, for the treatment of advanced and/or metastatic HER2-positive and HER2-low breast cancer and other HER2-expressing cancers. Treatment with zanidatamab in combination with evorpacept has the potential to augment immune clearance of HER2-expressing cancer cells, by blocking the CD47 signal that inhibits phagocytosis of these cells.

The study is currently open for enrollment. For further information (including updates to active sites), visit www.clinicaltrials.gov [NCT05027139]

About Zanidatamab

Zanidatamab is a bispecific antibody, based on Zymeworks' Azymetric™ platform, that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. Zanidatamab's unique binding properties result in multiple mechanisms of action including HER2-receptor clustering, internalization, and downregulation; inhibition of growth factor-dependent and -independent tumor cell proliferation; antibody-dependent cellular cytotoxicity and phagocytosis; and complement-dependent cytotoxicity. Zanidatamab is currently being evaluated in two pivotal clinical trials, one for the first-line treatment of advanced or metastatic HER2-positive gastroesophageal adenocarcinoma (HERIZON-GEA-01) and one for previously treated HER2-amplified biliary tract cancer (HERIZON-BTC-01). Zanidatamab is also being evaluated in several Phase 2 clinical trials for HER2 expressing gastroesophageal, colorectal, and breast cancers. The FDA has granted zanidatamab with Breakthrough Therapy designation for patients with previously treated HER2 gene-amplified biliary tract cancer, as well as two Fast Track designations, one as monotherapy for refractory biliary tract cancer and one in combination with standard of care chemotherapy for first-line gastroesophageal adenocarcinoma. These designations mean zanidatamab is eligible for Accelerated Approval, Priority Review and Rolling Review, as well as intensive FDA guidance on an efficient drug development program. Zanidatamab has also received Orphan Drug designations from the FDA as well as the European Medicines Agency for the treatment of biliary tract and gastric cancers.

About Evorpacept

Evorpacept is a next-generation CD47 blocking therapeutic that combines a high-affinity CD47 binding domain with an inactivated, proprietary Fc domain. Evorpacept is designed to avoid the limitations caused by hematologic toxicities inherent in other CD47 blocking approaches, and to leverage the immune activation of broadly used anti-cancer agents through combination strategies. ALX Oncology is developing evorpacept in multiple Phase 1 and Phase 2 clinical trials globally across a range of hematologic and solid malignancies in combination with a number of leading anti-cancer agents. The FDA has granted two Fast Track designations to evorpacept, one for the first-line treatment of patients with head and neck squamous cell carcinoma, and one for the second-line treatment of patients with HER2-positive gastric or gastroesophageal junction carcinoma. The FDA's Fast Track designation provides the opportunity for more frequent meetings with the FDA over the course of drug development and allows for eligibility for Accelerated Approval and Priority Review if relevant criteria are met, as well as for Rolling Review.

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, is a novel Azymetric™ HER2-targeted bispecific antibody currently being evaluated in multiple Phase 1, Phase 2, and pivotal clinical trials globally as a targeted treatment option for patients with solid tumors that express HER2. Zymeworks' second clinical candidate, ZW49, is a novel bispecific HER2 -targeted 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.

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, but are not limited to, statements that relate to Zymeworks' clinical development of its product candidates, related clinical trials, potential therapeutic effects of zanidatamab, Zymeworks' preclinical pipeline, and other information that is not historical information. When used herein, words such as "will", "developing", "potential", "look forward to", "continue", "believe", "could be", "is eligible for", 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, the factors described under "Risk Factors" in Zymeworks' Quarterly Report on Form 10-Q for its quarter ended September 30, 2021 (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. Investors 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

Jack Spinks
(604) 678-1388

ir@zymeworks.com

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

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