Clinical Data Demonstrating Promising Antitumor Activity with Zanidatamab in 1L Setting of HER2-Positive Breast and Gastroesophageal Cancers to be Presented at ASCO 2022

May 26, 2022

- *Study of zanidatamab in combination with docetaxel results in 90.5% confirmed objective response rate (cORR) in first-line treatment of advanced HER2-positive breast cancer*
- *Zanidatamab in combination with chemotherapy and tislelizumab shows 75.8% cORR and 100% disease control rate (DCR) in first-line treatment of advanced HER2-positive gastric/gastroesophageal junction adenocarcinoma*
- *Zymeworks to host Analyst & Investor Call Monday, June 6th at 4:30 pm Eastern Time (ET)*

VANCOUVER, British Columbia & SEATTLE--(BUSINESS WIRE)--May 26, 2022-- Zymeworks Inc. (NYSE: ZYME), a clinical-stage biopharmaceutical company developing next-generation multifunctional biotherapeutics, today announced new clinical data for the HER2-targeted bispecific antibody zanidatamab in both HER2-positive breast cancer and gastric/gastroesophageal junction adenocarcinoma. The data are being presented in two separate poster sessions at the American Society of Clinical Oncology (ASCO) Annual Meeting June 3-7, 2022 in Chicago, IL.

"These encouraging new data sets presented at ASCO provide further validation of zanidatamab's potential in the treatment of advanced HER2-positive cancers and follow the release of other promising data in gastroesophageal and breast cancer in 2021," said Neil Josephson, M.D., Chief Medical Officer at Zymeworks. "These new data continue to demonstrate the potential for zanidatamab to be an important advancement in the treatment of a wide range of HER2-expressing cancers, including in first-line treatment regimens."

The presentations detailed below are available to conference registrants on the ASCO conference website as well as to the general public at www.zymeworks.com/publications.

Poster Session: Zanidatamab in Combination with Chemotherapy and Tislelizumab in HER2-Positive Gastric/Gastroesophageal Junction Cancer – Clinical Results – Saturday, June 4, 08:00-11:00 am CDT

Zanidatamab, a HER2-targeted bispecific antibody, in combination with chemotherapy and tislelizumab as first-line therapy for patients with advanced HER2-positive gastric/gastroesophageal junction adenocarcinoma (G/GJEC): Preliminary results from a Phase 1b/2 study

Presenter: Keun Wook Lee, Department of Internal Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea

Over one million patients are diagnosed with gastric cancer every year worldwide, and it is the fourth most common cause of cancer-related deaths[1]. Human epidermal growth factor receptor 2 (HER2)-positive disease accounts for 15–25% of gastric cancers[2]. For these patients, trastuzumab in combination with chemotherapy is the global standard of care treatment but with an expected overall survival of less than 18 months, there remains a significant unmet need.

In 33 response-evaluable patients with advanced HER2-positive gastric/gastroesophageal junction adenocarcinoma treated with zanidatamab and tislelizumab in combination with the CAPOX chemotherapy regimen the cORR was 75.8% (25/33). The DCR was 100% (33/33) and duration of response (DOR) ranged from 2.1+ to 18.2+ months. Twenty patients (61%) remain on study at the time of data cut-off.

In addition, the data demonstrate that zanidatamab and tislelizumab in combination with the CAPOX chemotherapy is generally well tolerated, with the majority of treatment-related adverse events (TRAEs) considered mild to moderate in severity (Grade 1 or 2). The most common grade ≥ 3 TRAE was diarrhea, which was manageable in the outpatient setting; introduction of prophylactic loperamide reduced the incidence from 33% to 21%. Immune mediated adverse events occurred in 27% of patients, including ≥ Grade 3 events in 21% of patients and resulted in discontinuation of tislelizumab in 3 patients (9%). This manageable safety profile compares favorably to the current standard of care as well as to emerging treatments and is consistent with previous reports.[3]

This new data set further supports the launch of Zymeworks' global Phase 3 study (HERIZON- GEA-01; NCT05152147), which is investigating zanidatamab in combination with chemotherapy with or without tislelizumab for first-line treatment of locally advanced, unresectable, or metastatic HER2-positive gastroesophageal adenocarcinoma. Zymeworks, along with its Asia-Pacific partner BeiGene, plan to enroll 714 patients at approximately 300 sites across 38 countries. Enrollment is expected to be completed by the end of 2023. The study design will be presented in a Trials in Progress poster (Poster ID: P-26) at the European Society of Medical Oncology (ESMO) World Congress on Gastrointestinal Cancer taking place in Barcelona, Spain from June 29-July 2, 2022. The presentation will be available to conference registrants on the conference website as well as to the general public at www.zymeworks.com/publications at the time of presentation at the conference.

Poster Session: Zanidatamab in Combination with Docetaxel in HER2-Positive Breast Cancer – Clinical Results – Monday, June 6, 08:00-11:00 am CDT

Zanidatamab, a HER2-targeted bispecific antibody, in combination with docetaxel as first-line therapy for patients with advanced HER2-positive breast cancer: Preliminary results from a Phase 1b/2 study

Presenter: Keun Seok Lee, National Cancer Center, Center for Breast Cancer, Goyang, Republic of Korea

Worldwide, breast cancer is the most commonly diagnosed cancer and the leading cause of cancer deaths in women, with over 650,000 deaths in 2020[1,4]. HER2-positive breast cancer accounts for approximately 20% of all breast cancers[5,6,7]. Though HER2-targeted agents have improved outcomes in HER2-positive breast cancer, most patients treated for advanced disease eventually relapse and develop resistant disease[8,9].

In 21 response-evaluable patients with advanced HER2-positive breast cancer treated with zanidatamab and docetaxel the cORR was 90.5%, with 15 patients (78.9%) having an ongoing response at the time of the data cut. The median follow-up was 7.0 months (range 1.1-17.4 months) and the six-month progression-free survival rate was 95.2%.

The combination of zanidatamab and docetaxel had a manageable safety profile with the incidence of TRAEs consistent with standard of care therapy. The most common TRAEs were neutrophil count decreased (13 patients; 54.2%), diarrhea (13 patients; 54.2%), and anemia (nine patients; 37.5%), and the most common ≥ Grade 3 TRAEs were neutrophil count decreased (12 patients; 50.0%), diarrhea (3 patients; 12.5%), and white blood cell count decreased (2 patients; 8.3%).

"We will continue to support ongoing R&D efforts to generate and report robust data highlighting and reinforcing the potential applications of our therapeutics and technology platforms in the treatment of a wide range of diseases," said Kenneth Galbraith, Chair and CEO of Zymeworks. "We remain focused on exploring potential research and collaboration opportunities that can lead to a broader portfolio of innovative therapies for patients in need around the world with difficult-to-treat cancers."

Conference Call and Webcast

Zymeworks will host a conference call and webcast on **Monday, June 6th at 4:30 pm ET** to discuss the clinical data presented at ASCO and provide an overview on the clinical development strategy for zanidatamab. The event will be led by Kenneth Galbraith, Zymeworks' Chair and CEO, and Neil Josephson, M.D., Zymeworks' Chief Medical Officer. Members of Zymeworks' executive team will be available to answer questions at the conclusion of the call.

Interested parties can access the live webcast via the Zymeworks' website at https://ir.zymeworks.com/events-and-presentations. A recorded replay will be accessible after the event through the Zymeworks website.

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. 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 leading to encouraging antitumor activity in patients. Zymeworks is developing zanidatamab in multiple Phase 1, Phase 2, and pivotal clinical trials globally as a targeted treatment option for patients with solid tumors that express HER2. The FDA has granted Breakthrough Therapy designation for zanidatamab in patients with previously treated HER2 gene-amplified biliary tract cancer (BTC), and two Fast Track designations to zanidatamab, one as a single agent for refractory BTC and one in combination with standard of care chemotherapy, for first-line gastroesophageal adenocarcinoma (GEA). 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 for the treatment of biliary tract, gastric and ovarian cancers, as well as Orphan Drug designation for the treatment of gastric cancer from the European Medicines Agency.

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 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 global biopharmaceutical companies. For more information on our ongoing clinical trials visit www.zymeworksclinicaltrials.com. 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 press release include, but are not limited to, statements that relate to the potential therapeutic effects of zanidatamab and Zymeworks' other product candidates, Zymeworks' clinical development of its product candidates, related clinical trials, anticipated clinical data presentations, the commercial potential of technology platforms and product candidates, Zymeworks' preclinical pipeline, the ability to advance product candidates into later stages of development, and other information that is not historical information. When used herein, words such as "will", "plans", "may", "expected", "continue", "potential", 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 impact of the COVID-19 pandemic on Zymeworks' business, research and clinical development plans and timelines and results of operations, including impact on its clinical trial sites, collaborators, and contractors who act for or on Zymeworks' behalf, may be more severe and more prolonged than currently anticipated; clinical trials may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; any of Zymeworks' or its partners' product candidates may fail in development, may not receive required regulatory approvals, or may be delayed to a point where they are not commercially viable; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of new or changing laws and regulations; market conditions; inability to maintain or enter into new partnerships or strategic collaborations and the factors described under "Risk Factors" in Zymeworks' quarterly and annual

reports filed with the Securities and Exchange Commission, including its Quarterly Report on Form 10-Q for its quarter ended March 31, 2022 (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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