Zanidatamab Data Highlight Durable Antitumor Activity in HER2-Expressing Biliary Tract and Gastroesophageal Cancers at ASCO Gastrointestinal Cancers Symposium

January 15, 2021

- *Durable Responses Observed in Refractory Biliary Tract Cancer (BTC) and Gastroesophageal (GEA) Cancers*
- *Enrollment Continues for Zanidatamab Global Pivotal Trial in BTC; Global Pivotal Trial in First-Line GEA Slated to Open in Mid-2021*

VANCOUVER, British Columbia--(BUSINESS WIRE)-- Zymeworks Inc. (NYSE: ZYME), a clinical-stage biopharmaceutical company developing multifunctional biotherapeutics, today announced new and updated clinical data for the HER2-targeted bispecific antibody zanidatamab, in both HER2-expressing biliary tract cancer (BTC) and gastroesophageal adenocarcinoma (GEA). The data are being presented today at the American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium, taking place virtually January 15 – 17, 2021.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20210115005163/en/

“Data presented today at ASCO GI continue to demonstrate the potential of zanidatamab in advanced HER2-expressing cancers with high unmet need. The response rates and median duration of response in refractory BTC and GEA compare favorably to current standard of care and emerging treatments,” said Diana Hausman, M.D., Chief Medical Officer at Zymeworks. “The BTC data were the basis of the recent Breakthrough Therapy designation granted by the FDA, a key step in helping zanidatamab become the first potential HER2-targeted therapy approved in this indication. Furthermore, the activity in GEA supports our goal of establishing zanidatamab as the foundational HER2-targeted therapy for GEA and other HER2-positive cancers, not only in later stage disease, but also in earlier lines of treatment.”

The following presentations are available to conference registrants on the ASCO conference website as well as to the general public at ir.zymeworks.com/events-and-presentations/.

Zanidatamab Monotherapy and Chemotherapy Combinations in HER2-Expressing Gastroesophageal Cancer – Clinical Results – Abstract #164

Zanidatamab (ZW25) in HER2-expressing gastroesophageal adenocarcinoma (GEA): Results from a Phase 1 study (Presenter: Funda Meric-Bernstam, MD, UT MD Anderson Cancer Center, TX; Rapid Abstract oral presentation on Friday, January 15, 11:30 am-12:15 pm ET)

HER2 is overexpressed in approximately 20% of GEA patients. For these patients, trastuzumab in combination with chemotherapy is the only approved HER2-targeted therapy. Treatment options are currently limited if disease progression occurs after trastuzumab in combination with chemotherapy.

Findings from an ongoing Phase 1 study of zanidatamab in HER2-positive GEA were last presented in July 2020. New and updated results are being presented in a Rapid Abstract oral presentation today, January 15th, at 11:30 am ET at the ASCO Gastrointestinal Cancers Symposium followed by a webcast at 5:00 pm ET to discuss the data, led by zanidatamab study investigator Dr. Funda Meric-Bernstam, MD.

The data being reported are from HER2-expressing GEA patients who received zanidatamab either as monotherapy (n=35) or in combination with chemotherapies (n=28). The groups had a median of two to three (range 0-7) prior therapies, with a high percentage (88-91%) having received prior HER2-targeted therapies. The data continue to demonstrate that zanidatamab is well tolerated with the majority of treatment-related AEs considered mild to moderate in severity (Grade 1 or 2) and manageable in the outpatient setting.

In 33 response-evaluable patients who received zanidatamab as monotherapy (10 mg/kg weekly or 20 mg/kg every two weeks), the objective response rate (ORR) was 39% (13/33), 11 (33%) of which were confirmed by a subsequent scan. The disease control rate (DCR) was 61% (20/33) and median duration of response (DOR) was six months.

In 10 response-evaluable patients who received zanidatamab (20 mg/kg every two weeks) plus paclitaxel, the ORR was 60% (6/10), five (50%) of which were confirmed by a subsequent scan including one patient who experienced a complete response. The DCR was 90% (9/10) for this group. In 14 response-evaluable patients who received zanidatamab (20 mg/kg every two weeks or 30 mg/kg every three weeks) plus capecitabine, the confirmed ORR was 57% (8/14) and the DCR was 71% (10/14). Overall the median DOR for zanidatamab plus chemotherapy was 8.9 months and the median progression-free survival (PFS) was 5.6 months with eight (29%) patients still on study at the time of data cut-off.

In 2019, Zymeworks initiated a global, multicenter Phase 2 clinical trial (NCT03929666) evaluating zanidatamab in combination with standard of care chemotherapy for the first-line treatment of HER2-positive metastatic GEA. Taken together, data from the Phase 1 and Phase 2 studies further support

the company's plans to initiate, with partner BeiGene, a pivotal study for zanidatamab plus chemotherapy +/- tislelizumab (anti-PD1), as first-line treatment for advanced HER2-positive GEA in mid-2021.

Zanidatamab Monotherapy in HER2-Amplified Biliary Tract Cancer – Clinical Results – Abstract #299

Zanidatamab (ZW25) in HER2-positive biliary tract cancers (BTCs): Results from a Phase 1 study (Presenter: Funda Meric-Bernstam, MD, UT MD Anderson Cancer Center, TX)

Globally, more than 210,000 people are diagnosed with BTC every year and as many as one-fifth of these patients have tumors that express HER2. Currently no HER2-targeted therapy has been approved for the treatment of BTC.

Findings from the ongoing Phase 1 study of zanidatamab in HER2-amplified BTC were last shared in July 2020. The updated and new results are being presented today in a poster session at the ASCO Gastrointestinal Cancers Symposium.

Data were reported on 21 patients diagnosed with HER2-amplified BTC who received zanidatamab at the recommended dose of 20 mg/kg every two weeks. Patients received a median of two (range 1-8) prior therapies and five (24%) of the patients were previously treated with the HER2-targeted therapy trastuzumab.

Zanidatamab was well tolerated and demonstrated durable antitumor activity in these patients. All zanidatamab-related adverse events (AEs) were mild or moderate in severity (Grade 1 or 2). The confirmed objective response rate (ORR) in trastuzumab-naïve patients was 47% (7/15) and overall ORR was 40% (8/20). The overall disease control rate (DCR) was 65% (13/20), and median duration of response (DOR) was 7.4 months with several patients still on study at the time of data cut-off.

Based on these results, in July 2020 Zymeworks initiated a global pivotal Phase 2b trial (HERIZON-BTC-01; ZW25-203) [NCT04466891] of zanidatamab monotherapy in patients with HER2-amplified BTC that has been previously treated with at least one gemcitabine-containing systemic chemotherapy regimen. The US Food and Drug Administration (FDA) recently granted Breakthrough Therapy designation for zanidatamab in patients with previously treated HER2 gene-amplified BTC, based on evaluation of the Phase 1 data. This global pivotal Phase 2 study of zanidatamab in BTC may enable the submission of a Biologics License Application by Zymeworks in the United States as early as 2022.

Zanidatamab HERIZON-BTC-01 Trial in Progress Poster Presented Today – Abstract TPS352

A Phase 2b, Open-label, Single-arm Study of Zanidatamab (ZW25) Monotherapy in Patients with Advanced or Metastatic HER2-amplified Biliary Tract Cancers (BTC): HERIZON-BTC-01 Study (Lead Author: Shubham Pant, MD, UT MD Anderson Cancer Center, TX)

Zymeworks is presenting a trial in progress poster at ASCO GI for a global pivotal Phase 2 trial in HER2-amplified BTC (HERIZON-BTC-01; ZW25-03). Multiple clinical sites are now open to enrollment in the U.S., South Korea, Italy and Spain, with additional sites planned in Canada, Chile, China, France and the UK [Phase 2:NCT04466891]. This study is designed to support accelerated approval based on a primary endpoint of objective response rate, and key secondary endpoints of duration of response and safety.

About the Zanidatamab Phase 1 Clinical Trial

Zymeworks' Phase 1 zanidatamab study has three parts. From part one of the study (the dose-escalation phase), 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 zanidatamab's single-agent tolerability and antitumor activity against a variety of cancer types in different settings. The third part of the study (the combination phase) is underway and evaluating zanidatamab in combination with selected chemotherapy agents in gastroesophageal and breast cancer patients with HER2 high or lower HER2 expression levels.

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 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 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 bispecific antibody-drug conjugate currently in Phase 1 clinical development and combines the unique design and antibody framework of zanidatamab with Zymeworks' proprietary ZymeLink™ linker-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 the potential of zanidatamab in advanced HER2-expressing cancers with high unmet need, Zymeworks' global pivotal trial for zanidatamab in BTC (including the potential submission of a BLA), Zymeworks' plans to launch a second pivotal trial with BeiGene, and other information that is not historical information. When used herein, words such as "may", "plan", "continue", 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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