Zymeworks Receives FDA Breakthrough Therapy Designation for HER2-Targeted Bispecific Antibody Zanidatamab in Patients with Biliary Tract Cancer

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VANCOUVER, British Columbia--(BUSINESS WIRE)-- Zymeworks Inc. (NYSE: ZYME), a clinical-stage biopharmaceutical company developing multifunctional biotherapeutics, today announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation for zanidatamab in patients with previously-treated HER2 gene-amplified biliary tract cancer (BTC).

The FDA grants Breakthrough Therapy designation to new medicines that are intended to treat a serious condition and where clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint. Zanidatamab will now be eligible for Accelerated Approval, Priority Review and Rolling Review, as well as intensive FDA guidance on an efficient drug development program.

“This Breakthrough Therapy designation from the FDA, based on data generated in BTC patients treated in the initial Phase 1 trial, is recognition of the potential of zanidatamab to provide a new approach to cancer treatment,” said Diana Hausman, M.D., Chief Medical Officer at Zymeworks. “This milestone supports our strategy for accelerated approval and will help make zanidatamab available for patients as quickly as possible.”

“BTC is a rare and aggressive cancer,” said James Priour, Senior Vice President, Commercial, at Zymeworks. “Receiving this designation from the FDA is testament to the potential of zanidatamab to be the first HER2-targeting therapy approved for metastatic BTC patients.”

Earlier this year, Zymeworks initiated a global Phase 2b registration-enabling study of single agent zanidatamab in patients with previously treated HER2 gene-amplified BTC. This study, which is currently enrolling patients, is designed to support accelerated approval based on a primary endpoint of objective response rate, and secondary endpoints of duration of response and safety and may enable submission of a Biologics License Application (BLA) as early as 2022.

This Breakthrough Therapy designation was based on an ongoing clinical trial of zanidatamab in patients with locally advanced (unresectable) and/or metastatic HER2-expressing tumors including BTC. Updated clinical data for single agent zanidatamab patients with BTC has been accepted for presentation at the upcoming American Society of Clinical Oncology’s Virtual Gastrointestinal Cancers Symposium (ASCO GI) January 15-17, 2021.

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 registration-enabling clinical trials globally as a targeted treatment option for patients with solid tumors that express HER2. In addition to Breakthrough Therapy designation for zanidatamab in BTC, the U.S. FDA has granted 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). Zanidatamab has also received Orphan Drug designations for the treatment of biliary tract, gastric and ovarian cancers from the U.S. FDA, as well as Orphan Drug designation for the treatment of gastric cancer from the European Medicines Agency.

About Biliary Tract Cancer

Biliary tract cancer (BTC), including gallbladder cancer and cholangiocarcinoma (bile duct cancer), accounts for approximately 3% of all adult cancers and is associated with a poor prognosis. Globally, more than 210,000 people are diagnosed with BTC every year. Most patients (> 65%) with BTC are diagnosed with tumors that cannot be removed surgically, and even those patients who undergo potentially curative surgery have a high recurrence rate. Treatment options are limited for patients with advanced BTC who experience disease progression after front-line chemotherapy.

The human epidermal growth factor receptor 2 (HER2) is a well-described target for anti-cancer therapy. Tumor cells that produce a higher than normal level of HER2 tend to grow more quickly and spread to other parts of the body. About 5% to 19% of patients with BTC have tumors that express HER2, suggesting that these patients may potentially benefit from HER2-targeted therapy.Currently no HER2-targeted therapy has been approved for the treatment of BTC.

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 registration-enabling clinical trial for refractory HER2+ biliary tract cancer as well as several Phase 2 clinical trials for HER2+ 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 more information, visit www.zymeworks.com.

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, the potential submission of a Biologics License Application, Zymeworks' clinical and preclinical development of its product candidates, and other information that is not historical information. When used herein, words such as "will", "may", 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 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. 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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