Zymeworks Reports Last Patient Enrolled in Pivotal Study of Zanidatamab in Treatment of HER2-Expressing Late-Line Biliary Tract Cancer

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VANCOUVER, British Columbia & SEATTLE--(BUSINESS WIRE)--Apr. 28, 2022-- Zymeworks Inc. (NYSE: ZYME), a clinical-stage biopharmaceutical company developing next-generation multifunctional biotherapeutics, today announced that it has completed enrollment in its global HERIZON-BTC-01 pivotal clinical trial evaluating the antitumor activity of zanidatamab monotherapy in patients with previously treated advanced or metastatic HER2-amplified biliary tract cancers (BTC), including gallbladder cancer and cholangiocarcinoma (bile duct cancer). Efficacy and safety results from HERIZON-BTC-01 are expected to be announced by early 2023.

“Completing enrollment in our first pivotal trial is a tremendous accomplishment for Zymeworks. I’m extremely proud of our team and our collaborators at BeiGene for their hard work in reaching this milestone ahead of expectations,” said Neil Josephson, M.D., Chief Medical Officer. “Currently there are limited options for patients with advanced HER2-amplified biliary tract cancer who experience disease progression after front-line therapy. Zanidatamab has the potential to meet the urgent global clinical need for a safe and effective therapy for patients with this difficult to treat cancer.”

Biliary tract cancers, including gallbladder cancer and cholangiocarcinoma, account for approximately 3% of all adult cancers and is often associated with a poor prognosis[1]. Globally, more than 210,000 people are diagnosed with BTC every year[2] and most patients (> 65%) with BTC are diagnosed with tumors that cannot be removed surgically. The human epidermal growth factor receptor 2 (HER2) is a well-described target for anti-cancer therapy. About 5% to 19% of patients with BTC have tumors that express HER2[3], suggesting that these patients may have the potential to benefit from HER2-targeted therapy. Currently no HER2-targeted therapy has been approved for the treatment of BTC.

HERIZON-BTC-01 is a global, multicenter, open-label, single-arm study (NCT04466891) with a primary endpoint of confirmed objective response rate (ORR) by independent central review (ICR) per the Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1). Secondary endpoints are duration of response (DOR), proportion of subjects with a DOR ≥16 weeks, disease control rate (DCR), progression-free survival (PFS), overall safety (OS) and safety. HER2 amplification, as determined by in situ hybridization (ISH) in tumor tissue, was an inclusion criterion for all subjects enrolled into the two study cohorts: Cohort 1, the primary efficacy cohort, with tumor tissue showing HER2 immunohistochemistry (IHC) 2+ or 3+ staining, and cohort 2 with tumor tissue showing HER2 IHC 0 or 1+ staining. The study was initiated in July 2020 and has active sites in North America, Asia Pacific, Europe and South America.

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 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 received Break Through Designation from the Center of Drug Evaluation (CDE) in China for treating patients with biliary tract cancer who have failed prior systemic therapies. 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.

Zymeworks has an existing intermediate-size Expanded Access Protocol (EAP) for use of zanidatamab in patients with HER2-positive advanced solid tumors who are not eligible for other zanidatamab clinical trials, and who in the opinion of the treating oncologist, would potentially benefit from treatment with zanidatamab. Additional information is available on our website at https://zymeworks.com/patients.

About the Zymeworks-BeiGene Collaboration

In November 2018, Zymeworks and BeiGene entered into license and collaboration agreements in which BeiGene was granted an exclusive license for the research, development, and commercialization of zanidatamab and ZW49 in Asia (excluding Japan), Australia, and New Zealand. The companies are collaborating on joint global development for selected indications, with the goal of developing zanidatamab and ZW49 worldwide across multiple HER2-expressing cancers and lines of therapy.

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 news release include, but are not limited to, statements that relate to the expected timing of the announcement of efficacy and safety results from HERIZON-BTC-01, the potential therapeutic effects of zanidatamab and Zymeworks' other product candidates, Zymeworks' clinical development of its product candidates, related clinical trials, the commercial potential of technology platforms and product candidates, Zymeworks' preclinical pipeline, and other information that is not historical information. When used herein, words such as "expect", "may", "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 Annual Report on Form 10-K for its year ended December 31, 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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[1] Valle JW, Lamarca A, Goyal L, Barriuso J, Zhu AX. New Horizons for precision medicine in biliary tract cancers. Cancer Discov. 2017;7(9):943-962.

[2] GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1789-1858.

[3] Galdy S, Lamarca A, McNamara MG, et al. HER2/HER3 pathway in biliary tract malignancies; systematic review and meta-analysis: a potential therapeutic target? Cancer Metastasis Rev. 2017;36(1):141-157.

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