UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): December 19, 2022

Zymeworks Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-41535**	**88-3099146**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

108 Patriot Drive, Suite A **Middletown, Delaware** **(Address of principal executive offices)**	**19709** **(Zip Code)**

(302) 274-8744
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.00001 per share	ZYME	The Nasdaq Stock Market LLC
Preferred Stock Purchase Rights	N/A	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On December 19, 2022, Zymeworks Inc. (the "Company") issued a press release announcing positive topline results from the Company's pivotal Phase 2b HERIZON-BTC-01 open-label, single-arm clinical trial investigating zanidatamab, a HER2-targeted bispecific antibody, as monotherapy in patients with previously treated HER2-amplified and expressing biliary tract cancers. A copy of this press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated December 19, 2022.
104	Cover Page Interactive Data File (embedded as Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ZYMEWORKS INC.
(Registrant)

Date: December 19, 2022

By: */s/ Neil Klompas*
Name: Neil Klompas
Title: President and Chief Operating Officer

Zymeworks Announces Positive Topline Data in the Pivotal HERIZON-BTC-01 Trial of Zanidatamab

- Zanidatamab as monotherapy produced a confirmed objective response rate (cORR) of 41.3% and median duration of response of 12.9 months in patients with previously treated HER2-amplified and expressing biliary tract cancers (BTC)
- Pending receipt of regulatory approvals, zanidatamab has the potential to be the first HER2-targeted therapy for patients with BTC
- Zymeworks to host conference call today at 8:00 am Eastern Time (ET)

Vancouver, British Columbia (December 19, 2022) – Zymeworks Inc. (NASDAQ: ZYME), a clinical-stage biotechnology company developing multifunctional biotherapeutics, today announced positive topline results from the pivotal Phase 2b HERIZON-BTC-01 open-label, single-arm clinical trial investigating zanidatamab, a HER2-targeted bispecific antibody, as monotherapy in patients with previously treated HER2-amplified and expressing BTC.

The positive topline results showed that 41.3% (95% CI: 30.4, 52.8) of enrolled patients with HER2-amplified and expressing (IHC2+ and 3+) disease achieved an objective response as assessed by independent central review. The median duration of response was 12.9 months (95% CI: 5.95 to not reached). The safety profile of zanidatamab in this trial was consistent with that observed in previously reported monotherapy studies, with no new safety signals identified. Full results from the pivotal trial are expected to be presented at a medical meeting in 2023.

Biliary tract cancers, including gallbladder cancer and cholangiocarcinoma, are diagnosed in more than 210,000 people every year[1], with most patients presenting with inoperable disease[2]. Disease control with front-line therapy is modest and patients need treatment options after progression[3,4]. The human epidermal growth factor receptor 2 (HER2) is a promising target in approximately 5%-10% of cholangiocarcinomas and up to 20% of gallbladder cancers[5]. Currently no HER2-targeted therapy has been approved for the treatment of BTC.

“Through our work with the BTC patient community, we see first-hand the challenge these patients face in not only getting a diagnosis, but in the limited treatment options available,” said Stacie Lindsey, Founder & CEO of the Cholangiocarcinoma Foundation. “Each investigative trial begins to close the gap on this high unmet medical need by helping to bring more treatment options to BTC patients and we’re looking forward to watching zanidatamab’s progression through the global regulatory review process.”

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1 Siegel RLet al., Cancer statistics, 2020. CA Cancer J Clin. 2020;70:7-30

2 Schroff RT et al., Adjuvant Therapy for Resected Biliary Tract Cancer: ASCO Clinical Practice Guideline. Clin. Oncol.2019;37:1015-1027

3 Khankhel ZS et al., Second-line treatments in advanced biliary tract cancer: systematic literature review of efficacy, effectiveness and safety Future Oncol. 2022;18:18, 2321–2338

4 Lamarca A, et al., Second-line chemotherapy in advanced biliary cancer: a systematic review. Ann. Oncol. 2014;25:12, 2328–2338

5 Vogel A et al., on behalf of on behalf of the ESMO Guidelines Committee. Biliary tract cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up, 2022. Ann Oncol doi: https://doi.org/10.1016/j.annonc.2022.10.506

“We are thrilled to report these positive topline data from the HERIZON-BTC-01 clinical trial, which further support the potential of zanidatamab as a new chemotherapy-free therapeutic option for HER2-amplified and expressing BTC. These data demonstrate that zanidatamab, as a single agent, improves on the current standard of care for patients in a difficult-to-treat disease who currently have a poor prognosis based on the limited treatment options currently available,” said Neil Josephson, M.D., Chief Medical Officer at Zymeworks. “I want to thank all of the patients, their families and the investigators who participated in this important study.”

Conference Call for Investors and Analysts

Zymeworks management will host a conference call and webcast for investors and analysts on December 19, 2022 at 8:00 am ET. The event will be webcast live with dial-in details and webcast replays available on Zymeworks’ website at http://ir.zymeworks.com/events-and-presentations.

About HERIZON-BTC-01

HERIZON-BTC-01 is a global, multicenter, open-label, single-arm study (NCT04466891) with a primary endpoint of confirmed objective response rate (cORR) by independent central review (ICR) per the Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1). Secondary endpoints include duration of response (DOR), proportion of subjects with a DOR ≥16 weeks, disease control rate (DCR), progression-free survival (PFS), overall survival (OS) and safety. HER2 amplification, as determined centrally 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, and shares sites with the pivotal Phase 3 trial, HERIZON-GEA-01 (NCT05152147), in first-line gastroesophageal adenocarcinoma (GEA) patients.

About Zanidatamab

Zanidatamab is an investigational, 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. Zymeworks continues to enroll subjects in the Phase 3 randomized clinical trial, HERIZON-GEA-01, evaluating zanidatamab in combination with chemotherapy plus or minus tislelizumab for HER2-expressing GEA. Zymeworks has entered into separate agreements with each of BeiGene, Ltd. (BeiGene) and Jazz Pharmaceuticals Ireland Limited (Jazz), granting each of BeiGene and Jazz with exclusive rights to develop and commercialize zanidatamab throughout various countries around the world.

Zymeworks has an ongoing Expanded Access Program (EAP) for use of zanidatamab in patients with HER2-positive advanced solid tumors who are not eligible for zanidatamab clinical trials, meet the criteria for EAP, 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 Zymeworks Inc.

Zymeworks is a clinical-stage biotechnology company dedicated to the discovery, development and commercialization of novel, multifunctional biotherapeutics. Zymeworks' 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, zanidatamab zovodotin (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" or information within the meaning of the applicable securities legislation, including Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements in this press release include, but are not limited to, statements that relate to the potential of zanidatamab in advanced HER2-expressing cancers with high unmet need; the potential therapeutic effects of zanidatamab and Zymeworks' other product candidates; Zymeworks' clinical development of its product candidates and enrollment in its clinical trials; anticipated clinical data presentations, including the expected presentation of full results from HERIZON-BTC-01 in 2023; expectations regarding future regulatory filings and approvals and the timing thereof; the commercial potential of technology platforms and product candidates including zanidatamab; the potential addressable market of zanidatamab; and other information that is not historical information. When used herein, words such as "plan", "believe", "expect", "may", "anticipate", "potential", "pending", "will", "would", 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: future clinical trials may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; promising results from pre-clinical development activities or early clinical trial results may not be replicated in later clinical trials; any of Zymeworks' or its partners' product candidates, including zanidatamab, 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 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; 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 September 30, 2022 (a copy of which may be obtained at www.sec.gov and www.sedar.com).

Although Zymeworks believes that such forward-looking statements are reasonable, there can be no assurance they will prove to be correct. Investors should not place undue reliance on forward-looking statements. The above assumptions, risks and uncertainties are not exhaustive. Forward-looking statements are made as of the date hereof and, except as may be required by law, Zymeworks undertakes no 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.

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