

**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): November 9, 2021

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

British Columbia, Canada
(State or other jurisdiction
of incorporation)

001-38068
(Commission
File Number)

98-1398788
(IRS Employer
Identification No.)

Suite 540, 1385 West 8th Avenue, Vancouver, British Columbia, Canada
(Address of principal executive offices)

V6H 3V9
(Zip Code)

(604) 678-1388
(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 Shares, no par value per share	ZYME	New York Stock Exchange

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 7.01 REGULATION FD DISCLOSURE

On November 9, 2021, Zymeworks Inc. (“Zymeworks”) issued a press release announcing, together with its partner BeiGene, the launch of HERIZON-GEA-01. This is a randomized, global Phase 3 study evaluating Zymeworks’ investigational HER2-targeted bispecific antibody, zanidatamab, plus chemotherapy, with or without BeiGene’s anti-PD-1-targeted antibody tislelizumab, versus standard of care (trastuzumab plus chemotherapy), for the first-line treatment of metastatic HER2-positive gastroesophageal adenocarcinoma.

On November 9, 2021, Zymeworks issued a further press release announcing that Neil Josephson, M.D., who has been serving as Zymeworks’ interim Chief Medical Officer (CMO) since May of this year, will transition to the permanent CMO position, effective November 15.

On November 9, 2021, Zymeworks filed these two press releases with the Canadian securities regulatory authorities on the System for Electronic Document Analysis and Retrieval (“SEDAR”) at www.sedar.com. Copies of these press releases are attached as Exhibit 99.1 and Exhibit 99.2 hereto.

The information provided under this Item (including Exhibit 99.1 and Exhibit 99.2, attached hereto) shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934 (the “Exchange Act”) or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

ITEM 9.01 FINANCIAL STATEMENTS AND EXHIBITS

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	Press Release dated November 9, 2021.
99.2	Press Release dated November 9, 2021.
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: November 9, 2021

By: /s/ Neil A. Klompas

Name: Neil A. Klompas

Title: Executive Vice President, Business
Operations and Chief Financial Officer



**Zymeworks Launches Global Phase 3 Zanidatamab Trial in First-Line
HER2-Positive Gastroesophageal Adenocarcinoma (GEA)**

- *HERIZON-GEA-01 study is now open and enrolling patients to evaluate zanidatamab and chemotherapy with or without tislelizumab, versus standard of care*
- *Phase 2 data demonstrate potential benefit of zanidatamab in first-line GEA, with response rates and durability that compare favorably to both current standard of care and emerging treatments*
- *Study design enables a potential supplemental biologics license application (BLA) for zanidatamab in first-line HER2-positive GEA as early as 2024*
- *Zymeworks will host a conference call and webcast at 4:15pm ET today to discuss the HERIZON-GEA-01 Phase 3 trial design as well as the commercial strategy in HER2-positive gastrointestinal cancers*

Vancouver, British Columbia (November 9, 2021) – Zymeworks Inc. (NYSE: ZYME), a clinical-stage biopharmaceutical company developing multifunctional biotherapeutics, today announced, together with its partner BeiGene, the launch of HERIZON-GEA-01. This is a randomized, global Phase 3 study evaluating Zymeworks’ investigational HER2-targeted bispecific antibody, zanidatamab, plus chemotherapy, with or without BeiGene’s anti-PD-1-targeted antibody tislelizumab, versus standard of care (trastuzumab plus chemotherapy), for the first-line treatment of metastatic HER2-positive GEA.

“We are incredibly excited to launch our second pivotal, and first Phase 3 clinical trial for zanidatamab, HERIZON-GEA-01,” said Ali Tehrani, Ph.D., Zymeworks’ President & CEO. “Gastrointestinal cancers have significant unmet patient need and we have the opportunity to help a large and growing patient population. With two potential Biologics License Applications over the next 3 years, we believe zanidatamab has the potential to achieve blockbuster status and position Zymeworks as the leader in the treatment of HER2-positive GI cancers.”

The primary objective of the HERIZON-GEA-01 study is to evaluate the efficacy and safety of zanidatamab in combination with physician’s choice chemotherapy [CAPOX (capecitabine/oxaliplatin) or FP (5FU/cisplatin)] with or without tislelizumab compared to trastuzumab plus physician’s choice chemotherapy in subjects with advanced or metastatic HER2-positive GEA. Primary endpoints are progression-free survival by RECIST 1.1, assessed by blinded independent central review, and overall survival.

The HERIZON-GEA-01 study seeks to enroll approximately 700 patients at approximately 300 sites across 38 countries. BeiGene will oversee trial sites in Asia (excluding Japan), Australia and New Zealand, and Zymeworks will oversee trial sites in the rest of the world, including North and South America, Japan, Europe, Middle East, and Africa.

“We are pleased the HERIZON-GEA-01 study has begun enrollment and our aim is to establish zanidatamab as the foundational agent of a new standard of care with tislelizumab for the first-line treatment of HER2-positive GEA,” said Neil Josephson, M.D., Zymeworks’ Interim Chief Medical Officer. “Based on the study design, we expect to have progression-free survival data as soon as 2024, which could enable submission of a supplemental Biologics License Application that same year.”

GEA is the fifth most common cancer worldwide and approximately 20 percent of patients diagnosed with this form of cancer are HER2-positive. HER2-positive GEA has high morbidity and mortality and patients are urgently in need of new treatment options.

“The encouraging zanidatamab Phase 2 data support its further investigation with tislelizumab in this Phase 3 HERIZON-GEA-01 trial in first-line HER2-positive gastroesophageal adenocarcinomas,” said Yong (Ben) Ben, M.D., Chief Medical Officer, Solid Tumors, at BeiGene. “We are excited to continue our collaboration with Zymeworks as we strive to address the unmet medical needs in this patient population by accelerating the development of zanidatamab.”

Phase 2 Study Results

In September, Zymeworks presented data at the European Society for Medical Oncology Annual Meeting from a Phase 2 clinical study of 36 patients with HER2-expressing GEA who received zanidatamab in combination with either CAPOX (n=14), FP (n=2), or mFOLFOX6 (5FU/leucovorin/oxaliplatin; n=20). None of the patients had received prior HER2-targeted therapies.

In 28 response-evaluable patients with metastatic HER2-positive GEA, zanidatamab plus chemotherapy resulted in a confirmed objective response rate (cORR) of 75% and disease control rate (DCR) of 89% overall, with a cORR of 93% and DCR of 100% in the proposed Phase 3 regimen of zanidatamab and CAPOX/FP. All patients except one experienced a decrease in their tumor size. Across all treatment regimens, the median duration of response is 16.4 months and the median progression-free survival is 12.0 months, with 61% of patients still on study at the time of data cutoff.

In addition, the data demonstrate that zanidatamab plus 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 in cycle 1 from 44% to 18%. No severe (grade 3) infusion-related reactions or cardiac events were observed.

Conference Call and Webcast

The company will host a conference call and webcast to discuss the HERIZON-GEA-01 Phase 3 trial design as well as the commercial strategy in HER2-positive gastrointestinal cancers. The event will be led by Ali Tehrani, Ph.D., Zymeworks' President and CEO, Neil Josephson, M.D., Zymeworks' Interim Chief Medical Officer, and James Priour, MBA, Zymeworks' Chief Commercial Officer. The speakers will be available to answer questions at the conclusion of the call.

Date: Tuesday, November 9th

Time: 4:15 pm ET (1:15 pm PT)

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. 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. 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 monotherapy 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 from the FDA as well as the European Medicines Agency for the treatment of biliary tract and gastric cancers.

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 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, is a novel Azymetric™ HER2-targeted bispecific antibody which is currently enrolling in two pivotal clinical trials, one for HER2-positive gastroesophageal adenocarcinoma (HERIZON-GEA-01) and one for refractory HER2-amplified biliary tract cancer (HERIZON-BTC-01) for which it has been granted Breakthrough Therapy designation by the FDA. Zanidatamab is also being evaluated in several Phase 2 clinical trials for HER2-expressing gastroesophageal, colorectal, and breast cancers. Zymeworks' second clinical candidate, ZW49, is a novel bispecific HER2-targeting 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 nine biopharmaceutical companies. For additional information about Zymeworks, visit www.zymeworks.com and follow [@ZymeworksInc](https://twitter.com/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 Zymeworks’ clinical development of its product candidates, related clinical trials, anticipated timelines and interactions with regulators, potential therapeutic effects of zanidatamab, the commercial potential of zanidatamab, including its potential to achieve blockbuster status, Zymeworks’ preclinical pipeline, and other information that is not historical information. When used herein, words such as “plan”, “expect”, “may”, “potential”, “will”, “aim”, “believe”, 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. These risks and uncertainties, many of which are beyond our control, include, but are not limited to: the impact of the COVID-19 pandemic on our business, research and clinical development plans and timelines and results of operations, including impact on our clinical trial sites, collaborators, and contractors who act for or on our behalf, may be more severe and more prolonged than currently anticipated; clinical trials may not demonstrate safety and efficacy of any of our or our collaborators’ product candidates; our ongoing discovery and preclinical efforts may not yield additional product candidates; any of our or our collaborators’ 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; even if approved, the commercial success of our product candidates may fail to meet our expectations due to factors outside of our control, including the impact of competition; we may not achieve additional milestones in our proprietary or partnered programs; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; regulatory agencies may be delayed in reviewing, commenting on or approving any of our or our collaborators’ clinical development plans as a result of the COVID-19 pandemic, which could further delay development timelines; the impact of competition; the impact of expanded product development and clinical activities on operating expenses; impact of new or changing laws and regulations; adverse conditions in the general domestic and global economic markets; as well as the other risks identified under “Risk Factors” in Zymeworks’ Quarterly Report on Form 10-Q for its quarter ended September 30, 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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Zymeworks Names Neil Josephson, M.D., Chief Medical Officer

Vancouver, British Columbia (November 9, 2021) – Zymeworks Inc. (NYSE: ZYME), a clinical-stage biopharmaceutical company developing multifunctional biotherapeutics, today announced that Neil Josephson, M.D., who has been serving as the company’s interim Chief Medical Officer (CMO) since May of this year, will transition to the permanent CMO position, effective November 15.

“Over the past six months, Neil has done an exemplary job of leading Zymeworks’ Medical organization and the advancement of our clinical pipeline,” said Ali Tehrani, Ph.D., Zymeworks’ President and CEO. “I am very pleased that Neil will be at the helm as we enroll our second pivotal trial for zanidatamab in HER2-positive gastroesophageal adenocarcinomas and continue to expand the development of zanidatamab and ZW49 in additional indications, including breast cancer.”

Dr. Josephson joined Zymeworks in 2019 as Vice President, Clinical Research and was promoted to Senior Vice President, Clinical Research last year, before his May appointment to interim CMO. Prior to joining Zymeworks, Dr. Josephson spent nearly six years at Seagen Inc., most recently as Vice President of Clinical Development, where he worked on multiple early and late-stage programs, including leading the approval of ADCETRIS® for the 1st line treatment of advanced Hodgkin’s lymphoma. Before joining Seagen, he was an Associate Professor of Medicine in the Division of Hematology at the University of Washington. He received an M.D. degree from Columbia University and an A.B. from Dartmouth College.

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