Ziihera® (zanidatamab-hrii) Combinations Achieve Unprecedented Results in First-Line HER2+ Locally Advanced or Metastatic GEA including more than Two Years Median Overall Survival Benefit

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- *Positive results from Phase 3 HERIZON-GEA-01 results support Ziihera as the HER2-targeted agent-of-choice in HER2+ first-line metastatic GEA and Ziihera plus chemotherapy to replace trastuzumab as the new standard of care, with or without tislelizumab regardless of PD-L1 status*
- *Late-breaking results to be presented at the 2026 ASCO Gastrointestinal Cancers Symposium (ASCO GI) on January 8, 2026*
- *Ziihera engineered and initially developed by Zymeworks using our proprietary Azymetric™ technology platform*
- *Zymeworks is eligible to receive up to $440.0 million in milestone payments to be earned related to regulatory approvals of Ziihera in GEA in the United States, Europe, Japan, and China*

VANCOUVER, British Columbia, Jan. 06, 2026 (GLOBE NEWSWIRE) -- Zymeworks Inc. (Nasdaq: ZYME), a biotechnology company managing a portfolio of licensed healthcare assets, while developing a diverse pipeline of novel, multifunctional biotherapeutics, today announced positive efficacy and safety results from the Phase 3 HERIZON-GEA-01 trial evaluating Ziihera® (zanidatamab-hrii) in combination with chemotherapy, with or without the PD-1 inhibitor Tevimbra® (tislelizumab), as first-line treatment for adults with HER2-positive (HER2+) locally advanced or metastatic gastroesophageal adenocarcinoma (GEA), including cancers of the stomach, gastroesophageal junction and esophagus.

The data will be presented as a late-breaking oral presentation at the 2026 ASCO Gastrointestinal Cancers Symposium (ASCO-GI) in San Francisco on January 8, 2026 from 8:57- 9:07 am PST (abstract number: LBA285).

“These results underscore the promise of zanidatamab to meaningfully advance care for patients with HER2-positive disease. They also reflect the power of our Azymetric™ platform to generate highly differentiated, multifunctional biologics and validate our partnership-driven approach with Jazz and BeOne to efficiently deliver innovative therapies on a global scale,” said Kenneth Galbraith, Chair and Chief Executive Officer of Zymeworks. “Importantly, the HERIZON-GEA-01 data further establish *Ziihera* as the new HER2-targeted agent-of-choice in first-line locally advanced or metastatic HER2-positive GEA with the potential to redefine first-line treatment for patients in this setting. Alongside continued progress across Jazz and BeOne’s broader development efforts, these data reinforce our belief in *Ziihera*’s potential across a range of HER2-expressing solid tumors. We look forward to Jazz and BeOne moving rapidly towards global regulatory submissions based on the HERIZON-GEA-01 data.”

The study found:

- Both investigational arms, *Ziihera* plus tislelizumab and chemotherapy and *Ziihera* plus chemotherapy, led to a statistically significant and clinically meaningful prolongation of progression-free survival (PFS) with approximately 35% reduction in the risk of disease progression or death versus trastuzumab plus chemotherapy. This resulted in a median PFS of more than one year, representing a greater than four month improvement compared to the control arm.
- *Ziihera* plus tislelizumab and chemotherapy demonstrated a statistically significant and clinically meaningful overall survival (OS) benefit with a median OS of more than two years (26.4 months), the longest reported in a Phase 3 trial in GEA, representing a greater than seven-month improvement in median OS and a 28% reduction in the risk of death versus trastuzumab plus chemotherapy.
- At this first interim analysis, *Ziihera* plus chemotherapy showed a median OS of more than two years, with a strong trend toward statistical significance, favoring *Ziihera* plus chemotherapy versus trastuzumab plus chemotherapy. An additional planned OS interim analysis for *Ziihera* plus chemotherapy is currently expected in mid-2026.
- The OS and PFS benefits were generally consistent across major prespecified subgroups including geographic region and PD-L1 status for both investigational arms.

Efficacy Summary from HERIZON-GEA-01

Primary Endpoints			

Endpoint	Trastuzumab plus chemotherapy (control arm)	*Ziihera* plus chemotherapy	*Ziihera* plus tislelizumab and chemotherapy
Median PFS (95% confidence interval [CI])	8.1 months (7.0–8.9)	12.4 months (9.8–14.5)	12.4 months (9.8–18.5)
PFS Hazard Ratio (HR) (95% CI)	—	0.65 (0.52–0.81) *P*<0.0001	0.63 (0.51–0.78) *P*<0.0001
Median OS (95% CI)	19.2 months (16.8–21.8)	24.4 months (20.4–30.0)	26.4 months (21.5–30.3)
OS HR (95% CI)	—	0.80 (0.64–1.01)* *P=0.0564*	0.72 (0.57–0.90) *P*=0.0043
Key Secondary Endpoints			
Endpoint	**Trastuzumab plus chemotherapy (control arm)**	***Ziihera* plus chemotherapy**	***Ziihera* plus tislelizumab and chemotherapy**
Objective Response Rate (ORR)	65.7%	69.6%	70.7%
Median Duration of Response (DoR)	8.3 months	14.3 months	20.7 months
18-Month PFS Rate	20.9%	38.0%	43.9%
30-Month OS Rate	30.0%	42.2%	43.8%
Subgroup Findings	—	Consistent PFS benefit across PD-L1 status, geographic region, and ECOG performance status	Consistent PFS and OS benefit across PD-L1 status, geographic region, and ECOG performance status

** Did not reach statistical significance at the first interim OS analysis.*

The safety profile of *Ziihera* in combination with chemotherapy, with or without tislelizumab, was consistent with the known effects of HER2-directed therapy and immunotherapy, and no new safety signals were identified. Duration of treatment was longest on the *Ziihera* plus tislelizumab and chemotherapy arm. Rates of Grade ≥3 treatment-related adverse events (TRAEs) were 71.8% with *Ziihera* plus tislelizumab and chemotherapy, 59.0% with *Ziihera* plus chemotherapy, and 59.6% with trastuzumab plus chemotherapy. Discontinuations due to *Ziihera*- or trastuzumab-related and treatment discontinuations due to adverse events were 11.9% with *Ziihera* plus tislelizumab and chemotherapy, 8.5% with *Ziihera* plus chemotherapy, and 2.3% in the trastuzumab plus chemotherapy arm. The most common Grade ≥3 TRAE was diarrhea (24.5% of patients with Ziihera plus tislelizumab and chemotherapy; 20.0% with *Ziihera* plus chemotherapy; and 12.9% of patients in the trastuzumab plus chemotherapy arm). Importantly, discontinuation of either *Ziihera* or trastuzumab due to treatment-related diarrhea was uncommon (4.1% of patients with *Ziihera* plus tislelizumab and chemotherapy, 1.3% with *Ziihera* plus chemotherapy, and 0% of patients in the trastuzumab plus chemotherapy arm). Treatment-emergent diarrhea generally occurred early in treatment and resolved within three weeks. The manageable safety profile supports the feasibility of these combinations in the first-line metastatic setting.

Under the Company's existing arrangements with Jazz and BeOne Medicines, Zymeworks is eligible to receive substantial near-term milestone payments related to future regulatory approvals in GEA totaling $440.0 million, as follows: United States - $250.0 million; Europe - $100.0 million; Japan - $75.0 million; China - $15.0 million. The Company also expects that royalty revenue from *Ziihera* sales will increase as potential regulatory approvals are obtained in global markets for GEA. In addition, Zymeworks could be eligible to receive future milestones and increased royalties from the development, regulatory approval, and commercialization of any additional indications for *Ziihera* by Jazz and BeOne, including breast cancer.

The full U.S. Prescribing Information for *Ziihera*, including BOXED Warning, is available at: https://pp.jazzpharma.com/pi/ziihera.en.USPI.pdf

About the HERIZON-GEA-01 Phase 3 Trial
HERIZON-GEA-01 (NCT05152147) is a global, randomized, open-label Phase 3 trial, conducted jointly by Jazz and BeOne Medicines, to evaluate and compare the efficacy and safety of Ziihera plus chemotherapy, with or without tislelizumab, to trastuzumab plus chemotherapy as first-line treatment for adult patients with advanced/metastatic HER2+ GEA. The trial randomized 914 patients from approximately 300 trial sites in more than 30 countries. Appropriate patients for this trial had unresectable locally advanced, recurrent or metastatic HER2+ GEA (adenocarcinomas of the stomach or esophagus, including the gastroesophageal junction), defined as 3+ HER2 expression by IHC or 2+ HER2 expression by IHC with ISH positivity per central assessment. Patients were randomized to the three trial arms: Ziihera in combination with chemotherapy and tislelizumab; Ziihera in combination with chemotherapy; and trastuzumab plus chemotherapy. The trial is evaluating dual primary endpoints, PFS per blinded independent central review (BICR) and OS.

About Gastroesophageal Adenocarcinoma
GEA, including cancers of the stomach, gastroesophageal junction, and esophagus, is the fifth most common cancer worldwide, and approximately 20% of patients have HER2+ disease.[1,2,3] HER2+ GEA has high morbidity and mortality, and patients are urgently in need of new treatment options. The overall prognosis for patients with GEA remains poor, with a global five-year survival rate of less than 30% for gastric cancer and about 19% for GEA.[4]

About Zymeworks Inc.
Zymeworks is a global biotechnology company managing a portfolio of licensed healthcare assets and developing a diverse pipeline of novel, multifunctional biotherapeutics to improve the standard of care for difficult-to-treat diseases, including cancer, inflammation, and autoimmune disease. The Company's asset and royalty aggregation strategy focuses on optimizing positive future cash flows from an emerging portfolio of licensed products such as Ziihera® (zanidatamab-hrii) and other licensed products and product candidates, such as pasritamig. In addition, Zymeworks is also building a portfolio of healthcare assets that can generate strong cash flows, while supporting the early-stage development of innovative medicines. Zymeworks engineered and developed *Ziihera*, a HER2-targeted bispecific antibody using the Company's proprietary Azymetric™ technology, and has entered into separate agreements with BeOne Medicines Ltd. (formerly BeiGene, Ltd.) and Jazz Pharmaceuticals Ireland Limited granting each exclusive rights to develop and commercialize zanidatamab in different territories. Zymeworks is rapidly advancing a robust pipeline of product candidates, leveraging its expertise in both antibody drug conjugates and multispecific antibody therapeutics targeting novel

pathways in areas of significant unmet medical need. The Company's complementary therapeutic platforms and fully integrated drug development engine provide the flexibility and compatibility to precisely engineer and develop highly differentiated antibody-based therapeutics. These capabilities have been further leveraged through strategic partnerships with global biopharmaceutical companies. For information about Zymeworks, visit www.zymeworks.com and follow @ZymeworksInc on X.

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 HER2-positive locally advanced or metastatic gastroesophageal adenocarcinoma with or without tislelizumab, including the potential for zanidatamab to be the HER2-targeted agent-of-choice and new standard of care in first-line HER2-positive locally advanced or metastatic gastroesophageal adenocarcinoma; the anticipated benefits of its collaboration agreements, including Zymeworks' ability to receive any future milestone payments and royalties thereunder; the potential addressable market of zanidatamab; the timing of and results of interactions with regulators; Zymeworks' clinical development of its product candidates and enrollment in its clinical trials; the timing and status of ongoing and future studies and the related data; the timing of anticipated regulatory submissions; anticipated preclinical and clinical data presentations; expectations regarding future regulatory filings and approvals and the timing thereof; potential safety profile and therapeutic effects of zanidatamab and Zymeworks' other product candidates; the commercial potential of technology platforms and product candidates; Zymeworks' ability to satisfy potential regulatory and commercial milestones with existing and future partners; anticipated continued receipt of revenue from existing and future partners; Zymeworks' expectations regarding implementation of its strategic priorities and the anticipated benefits thereof; implementation of its evolving asset aggregation strategy, including existing and potential future royalty streams and existing and potential new partnerships; Zymeworks' ability to execute new collaborations and partnerships and other information that is not historical information. When used herein, words such as "plan", "believe", "expect", "may", "continue", "anticipate", "potential", "will", "on track", "progress", 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: 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; Zymeworks may not achieve milestones or receive additional payments under its collaborations; regulatory agencies may impose additional requirements or delay the initiation of clinical trials; the impact of new or changing laws and regulations; market conditions, including the impact of tariffs; potential negative impacts of FDA regulatory delays and uncertainty around recent policy developments; changes in the leadership of federal agencies such as the FDA, staff layoffs, budget cuts to agency programs and research, and changes in drug pricing controls; the impact of pandemics and other health crises 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; zanidatamab may not be successfully commercialized; Zymeworks' evolution of its business strategy related to anticipated and potential future milestones and royalty streams and existing and potential new partnerships may not be successfully implemented; Zymeworks' business strategy may not deliver meaningful stockholder returns; Zymeworks may be unsuccessful in actively managing and/or aggregating revenue-generating assets alongside its active R&D operations; ongoing or future clinical trials may not demonstrate safety and efficacy of any of Zymeworks' or its collaborators' product candidates; data providing early validation of our ADC platform and next-generation pipeline programs may not be replicated in future studies; Zymeworks' assumptions and estimates regarding its financial condition, future financial performance and estimated cash runway may be incorrect; 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 (copies of which may be obtained at www.sec.gov and www.sedarplus.ca).

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.

Investor inquiries:
Shrinal Inamdar
Senior Director, Investor Relations
(604) 678-1388
ir@zymeworks.com

Media inquiries:
Diana Papove
Senior Director, Corporate Communications
(604) 678-1388
media@zymeworks.com

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Source: Zymeworks Inc.