

**VYLOY™ (zolbetuximab) Plus Chemotherapy
Associated with Enhanced Survival Outcomes when
Common Adverse Events are Effectively Managed,
According to New Ad Hoc Analyses**

- *Exploratory ad hoc analyses from SPOTLIGHT and GLOW trials report quantitative differences in median progression-free survival (mPFS) and median overall survival (mOS) for patients treated with VYLOY plus chemotherapy when data from patients who discontinued early due to common adverse events were censored*
- *Effective management of adverse events remains an important component of supportive care for patients receiving treatment for advanced gastric or GEJ cancer*

NORTHBROOK, IL, January 8, 2026 – Astellas Pharma U.S., Inc. (Head of US Commercial: Mike Petroutsas, "Astellas") today announced the publication of exploratory ad hoc analyses from the combined Phase 3 SPOTLIGHT (NCT03504397) and GLOW (NCT03653507) studies in patients with HER2-negative, CLDN18.2-positive advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma in ESMO Open, characterizing the management of adverse events on treatment adherence and efficacy of VYLOY (zolbetuximab) plus chemotherapy and evaluating strategies for managing these side effects.

The exploratory analyses, which included 1,072 patients, reported higher mPFS and mOS estimates for patients treated with zolbetuximab plus chemotherapy after censoring data from patients who discontinued early or had inadequate treatment exposure due to nausea and/or vomiting.¹

Pooled data from the analyses show that mPFS with zolbetuximab plus chemotherapy was 10.4 months (95% confidence interval [CI]: 8.8-12.2), and 8.2 months (95% CI: 7.7-8.4) with placebo plus chemotherapy. The hazard ratio [HR] versus placebo was 0.65 (95% CI: 0.56-0.76).¹

Similarly, mOS with zolbetuximab plus chemotherapy was 17.9 months (95% CI: 16.4-19.5) and 13.7 months (95% CI: 12.4-15.3) with placebo plus chemotherapy with a HR versus placebo of 0.69 (95% CI: 0.60-0.80).¹

Sam Klempner, MD, Gastrointestinal Medical Oncologist, Massachusetts General Hospital, Boston:

“Nausea and vomiting are important symptoms that can affect patient comfort and treatment continuity for advanced gastric or GEJ cancer, particularly during early cycles when these symptoms are most common. Supportive care measures are therefore an important part of managing patients receiving cancer therapy.”

Zolbetuximab (VYLOY) is an FDA approved monoclonal antibody for patients with HER2-negative, CLDN18.2-positive advanced gastric or GEJ cancer. In combination with chemotherapy, zolbetuximab demonstrated statistically significant improvements in PFS and OS compared with placebo plus chemotherapy in the SPOTLIGHT and GLOW Phase 3 clinical trials.^{2,3} In SPOTLIGHT and GLOW, the incidence of serious treatment emergent adverse events (TEAEs) was similar in the zolbetuximab treatment groups compared with placebo plus chemotherapy. The most common all-grade TEAEs reported in the zolbetuximab treatment groups were nausea, vomiting and decreased appetite.^{2,3}

The ad-hoc analyses in these studies showed an association between nausea and vomiting and higher treatment discontinuation rates compared with placebo.

Timothy Forrest, RN, BSN, Massachusetts General Hospital, Boston:

“Early cycles are a critical window for supporting patients starting treatment for advanced gastric or GEJ cancer. Since we know nausea and vomiting are common in this setting, preparing patients, monitoring closely, and using guideline-aligned supportive care can make a meaningful difference to their comfort and ability to continue treatment as planned.”

Within the published exploratory analyses, the effect of guideline-aligned supportive care on early nausea and vomiting associated with zolbetuximab plus chemotherapy was assessed.¹ Data indicate that use of a guideline-recommended three-drug antiemetic regimen was associated with a higher proportion of patients who did not experience nausea or vomiting at cycle 1 dose 1 (C1D1; 60.8% and 75.3%, respectively).¹

Additionally, across the SPOTLIGHT and GLOW trials, 57.9% of patients who received steroids at C1D1 did not experience nausea (versus 49.7% without steroids) and 63.7% did not experience vomiting at C1D1 (versus 62.6% with no steroids).¹

Finally, results from the combined analysis suggest that a faster initial infusion may have contributed to adverse events such as nausea and vomiting observed during the first infusion. The authors noted that infusion-rate modifications may help mitigate these symptoms.¹

Exploratory ad hoc analyses are hypothesis generating, and further work investigating the clinical validity of these results would be of value.

Astellas is committed to supporting patients and the oncology care community by continuing to generate insights that enhance the patient and healthcare professional experience and better understand supportive care needs and treatment experiences.

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About the SPOTLIGHT Phase 3 Clinical Trial

SPOTLIGHT is a Phase 3, global, multi-center, double-blind, randomized study assessing the efficacy and safety of zolbetuximab plus mFOLFOX6 (a combination chemotherapy regimen that includes oxaliplatin, leucovorin, and fluorouracil) compared to placebo plus mFOLFOX6 as a first-line treatment in patients with locally advanced, unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma whose tumors were CLDN18.2 positive. The study enrolled 565 patients at 215 study locations in the

U.S., Canada, United Kingdom, Australia, Europe, South America, and Asia. The primary endpoint was progression-free survival (PFS) of participants treated with the combination of zolbetuximab plus mFOLFOX6 compared to those treated with placebo plus mFOLFOX6. Secondary endpoints included overall survival (OS), objective response rate (ORR), duration of response (DOR), safety and tolerability, and quality-of-life parameters.

Data from the SPOTLIGHT clinical trial were presented during the 2023 American Society of Clinical Oncology (ASCO) Gastrointestinal (GI) Cancers Symposium in an oral presentation on January 19, 2023, and were subsequently published in [The Lancet](#) on April 14, 2023. The final analyses of SPOTLIGHT and GLOW, including additional supporting data in the appendix, were later published as a Letter to the Editor in the [New England Journal of Medicine](#) in 2024.

For more information, please visit clinicaltrials.gov under [Identifier NCT03504397](#).

About the GLOW Phase 3 Clinical Trial

GLOW is a Phase 3, global, multi-center, double-blind, randomized study assessing the efficacy and safety of zolbetuximab plus CAPOX (a combination chemotherapy regimen that includes capecitabine and oxaliplatin) compared to placebo plus CAPOX as a first-line treatment in patients with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma whose tumors were CLDN18.2 positive. The study enrolled 507 patients at 166 study locations in the U.S., Canada, United Kingdom, Europe, South America, and Asia, including Japan. The primary endpoint was PFS in participants treated with the combination of zolbetuximab plus CAPOX compared to those treated with placebo plus CAPOX. Secondary endpoints included OS, ORR, DOR, safety and tolerability, and quality-of-life parameters.

Data from the GLOW study were initially presented at the March 2023 ASCO Plenary Series with an updated oral presentation at the 2023 ASCO Annual Meeting on June 3, 2023, and were subsequently published in [Nature Medicine](#) on July 31, 2023.

For more information, please visit clinicaltrials.gov under [Identifier NCT03653507](#).

About VYLOY

VYLOY (zolbetuximab) is a monoclonal antibody (mAb) specifically designed to target tumor cells that express claudin 18.2 (CLDN18.2), a transmembrane protein. By binding to CLDN18.2, zolbetuximab induces cancer cell death and inhibits tumor growth by activating two distinct immune system pathways - antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC), as demonstrated in preclinical studies.

In both the SPOTLIGHT and GLOW Phase 3 clinical trials, approximately 38% of patients screened had tumors that were CLDN18.2 positive, defined as $\geq 75\%$ of tumor cells demonstrating moderate to strong membranous CLDN18.2 immunohistochemical staining.

Astellas collaborated with Roche on the Ventana™ CLDN18 (43-14a) RXDX assay which, where approved, can be used by pathologists or laboratories to identify patients eligible for targeted treatment with zolbetuximab.

About Astellas

Astellas is a global life sciences company committed to turning innovative science into value for patients. We provide transformative therapies in disease areas that include oncology, ophthalmology, urology, immunology and women's health. Through our research and development programs, we are pioneering new healthcare solutions for diseases with high unmet medical need. Learn more at www.astellas.com.

U.S. VYLOY (zolbetuximab-clzb) Indication and Important Safety Information

INDICATION

VYLOY, in combination with fluoropyrimidine- and platinum-containing chemotherapy, is indicated for the first-line treatment of adults with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors are claudin (CLDN) 18.2 positive as determined by an FDA-approved test.

Warnings and Precautions

Hypersensitivity reactions, including serious anaphylaxis reactions, and serious and fatal infusion-related reactions (IRR) have been reported in clinical studies when VYLOY has been administered. **Any grade hypersensitivity reactions**, including anaphylactic reactions, occurring with VYLOY in combination with mFOLFOX6 or CAPOX was 18%. **Severe (Grade 3 or 4) hypersensitivity reactions**, including anaphylactic reactions, occurred in 2% of patients. Seven patients (1.3%) permanently discontinued VYLOY for hypersensitivity reactions, including two patients (0.4%) who permanently discontinued VYLOY due to anaphylactic reactions. Seventeen (3.2%) patients required dose interruption, and three patients (0.6%) required infusion rate reduction due to hypersensitivity reactions. **All grade IRRs** occurred in 3.2% in patients administered VYLOY in combination with mFOLFOX6 or CAPOX. Severe (Grade 3) IRRs occurred in 2 (0.4%) patients who received VYLOY. An IRR led to permanent discontinuation of VYLOY in 2 (0.4%) patients and dose interruption in 7 (1.3%) patients. The infusion rate was reduced for VYLOY for 2 (0.4%) patients due to an IRR. Monitor patients during infusion with VYLOY and for 2 hours after completion of infusion or longer if clinically indicated, for hypersensitivity reactions with symptoms and signs that are highly suggestive of anaphylaxis (urticaria, repetitive cough, wheeze and throat tightness/change in voice). Monitor patients for signs and symptoms of IRRs including nausea, vomiting, abdominal pain, salivary hypersecretion, pyrexia, chest discomfort, chills, back pain, cough and hypertension. If a severe or life-threatening hypersensitivity or IRR reaction occurs, discontinue VYLOY permanently, treat symptoms according to standard medical care, and monitor until symptoms resolve. For any Grade 2 hypersensitivity or IRR, interrupt the VYLOY infusion until Grade ≤ 1 , then resume at a reduced infusion rate for the remaining infusion. Follow Grade 2 management for Grade 3 infusion-related nausea and vomiting. Premedicate the patient with antihistamines for the subsequent infusions, and closely monitor the patient for symptoms and signs of a hypersensitivity reaction. The infusion rate may be gradually increased as tolerated.

Severe Nausea and Vomiting. VYLOY is emetogenic. Nausea and vomiting occurred more often during the first cycle of treatment. **All grade nausea and vomiting** occurred in 82% and 67% respectively of patients treated with VYLOY in combination with mFOLFOX6 and 69% and 66% in combination with CAPOX, respectively. **Severe (Grade 3) nausea** occurred in 16% and 9% of patients treated with VYLOY in combination with mFOLFOX6 or CAPOX respectively. **Severe (Grade 3) vomiting** occurred in 16% and 12% of patients treated with VYLOY in combination with mFOLFOX6 or CAPOX. Nausea led to permanent discontinuation of VYLOY in combination with mFOLFOX6 or CAPOX in 18 (3.4%) patients and dose interruption in 147 (28%) patients. Vomiting led to permanent discontinuation of VYLOY in combination with mFOLFOX6 or CAPOX in 20 (3.8%) patients and dose interruption in 150 (28%) patients. Pretreat with antiemetics prior to each infusion of VYLOY. Manage patients during and after infusion with antiemetics or fluid replacement. Interrupt the infusion, or permanently discontinue VYLOY based on severity.

ADVERSE REACTIONS

Most common adverse reactions ($\geq 15\%$): Nausea, vomiting, fatigue, decreased appetite, diarrhea, peripheral sensory neuropathy, abdominal pain, constipation, decreased weight, hypersensitivity reactions, and pyrexia.

Most common laboratory abnormalities ($\geq 15\%$): Decreased neutrophil count, decreased leucocyte count, decreased albumin, increased creatinine, decreased hemoglobin, increased glucose, decreased lymphocyte count, increased aspartate aminotransferase, decreased platelets, increased alkaline phosphatase, increased alanine aminotransferase, decreased glucose, decreased sodium, decreased phosphate, decreased potassium, and decreased magnesium.

SPOTLIGHT Study: 279 patients with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma whose tumors were CLDN18.2 positive who received at least one dose of VYLOY in combination with mFOLFOX6

Serious adverse reactions occurred in 45% of patients treated with VYLOY in combination with mFOLFOX6; the **most common serious adverse reactions** ($\geq 2\%$) were vomiting (8%), nausea (7%), neutropenia (2.9%), febrile neutropenia (2.9%), diarrhea (2.9%), intestinal obstruction (3.2%), pyrexia (2.5%), pneumonia (2.5%), respiratory failure (2.2%), pulmonary embolism (2.2%), decreased appetite (2.1%) and sepsis (2.0%). **Fatal adverse reactions** occurred in 5% of patients who received VYLOY in combination with mFOLFOX6 including sepsis (1.4%), pneumonia (1.1%), respiratory failure (1.1%), intestinal obstruction (0.7%), acute hepatic failure (0.4%), acute myocardial infarction (0.4%), death (0.4%), disseminated intravascular coagulation (0.4%), encephalopathy (0.4%), and upper gastrointestinal hemorrhage (0.4%). Permanent discontinuation of VYLOY due to an adverse reaction occurred in 20% of patients; the **most common adverse reactions leading to discontinuation** ($\geq 2\%$) were nausea and vomiting. Dosage interruptions of VYLOY due to an adverse reaction occurred in 75% of patients; the **most common adverse reactions leading to dose interruption** ($\geq 5\%$) were nausea, vomiting, neutropenia, abdominal pain, fatigue, and hypertension.

GLOW Study: 254 patients with locally advanced unresectable or metastatic HER2-negative gastric or GEJ adenocarcinoma whose tumors were CLDN18.2 positive who received at least one dose of VYLOY in combination with CAPOX

Serious adverse reactions occurred in 47% of patients treated with VYLOY in combination with CAPOX; the **most common serious adverse reactions** ($\geq 2\%$) were vomiting (6%), nausea (4.3%), decreased appetite (3.9%), decreased platelet count (3.1%), upper gastrointestinal hemorrhage (2.8%), diarrhea (2.8%), pneumonia (2.4%), pulmonary embolism (2.3%), and pyrexia (2.0%). **Fatal adverse reactions** occurred in 8% of patients who received VYLOY in combination with CAPOX including sepsis (1.2%), pneumonia (0.4%), death (0.8%), upper gastrointestinal hemorrhage (0.8%), cerebral hemorrhage (0.8%), abdominal infection (0.4%), acute respiratory distress syndrome (0.4%), cardio-respiratory arrest (0.4%), decreased platelet count (0.4%), disseminated intravascular coagulation (0.4%), dyspnea (0.4%), gastric perforation (0.4%), hemorrhagic ascites (0.4%), procedural complication (0.4%), sudden death (0.4%), and syncope (0.4%). Permanent discontinuation of VYLOY due to an adverse reaction occurred in 19% of patients; the **most common adverse reaction leading to discontinuation** ($\geq 2\%$) was vomiting. Dosage interruption of VYLOY due to an adverse reaction occurred in 55% of patients; the **most common adverse reactions leading to dose interruption** ($\geq 2\%$) were nausea, vomiting, neutropenia, thrombocytopenia, anemia, fatigue, infusion-related reaction, and abdominal pain.

SPECIFIC POPULATIONS

Lactation Advise lactating women not to breastfeed during treatment with VYLOY and for 8 months after the last dose.

Full U.S. Prescribing Information

Cautionary Notes

In this press release, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market

existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas' intellectual property rights by third parties. Information about pharmaceutical products (including products currently in development) which is included in this press release is not intended to constitute an advertisement or medical advice.

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Contacts for inquiries or additional information:

Elysia Wood
US Commercial Communications
703-722-4656
Elysia.wood@astellas.com

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² Shitara K, Lordick F, Bang YJ, et al. Zolbetuximab plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastro-oesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double-blind, phase 3 trial. *Lancet* 2023;401(10389):1655-1668. Errata in: *Lancet* 2023;402(10398):290; *Lancet* 2024;403(10421):30.

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