27 July 2026

# Sonesitatug vedotin demonstrated a statistically significant and highly clinically meaningful improvement in overall survival in 2nd and later-line CLDN18.2-positive advanced gastric/GEJ cancers

***Results provide opportunity to expand CLDN18.2 positivity to ≥25% expression, representing approximately 60% of patients in this setting***

***CLARITY-Gastric01 is the first Phase III trial to show overall survival benefit with an anti-CLDN18.2 ADC in this setting***

***First pivotal readout from AstraZeneca's wholly owned ADC portfolio***

Positive high-level results from the CLARITY-Gastric01 global Phase III trial showed that sonesitatug vedotin (Sone-Ve) demonstrated a statistically significant and highly clinically meaningful improvement in overall survival (OS) in 2nd and later-line Claudin 18.2-positive advanced gastric cancers versus investigator's choice of therapy. The trial included patients with locally advanced or metastatic gastric cancer, gastroesophageal junction (GEJ) cancer, or oesophageal adenocarcinoma (EAC) with Claudin 18.2 (CLDN18.2) expression on at least 25% of tumour cells at any staining intensity.

The trial had dual primary endpoints of OS in 3rd and later-line treatment and progression-free survival (PFS) in the overall trial population. The trial met the dual primary endpoint of OS in 3rd and later-line treatment, and a key secondary endpoint of OS in the overall trial population of patients treated in the 2nd and later-line setting, demonstrating a statistically significant and highly clinically meaningful improvement.

For the other dual primary endpoint of PFS as assessed by blinded independent central review (BICR), results showed a trend toward improved PFS in patients treated in the 2nd and later-line setting but did not reach statistical significance.

The majority of patients with gastric/GEJ cancers are diagnosed at an advanced or metastatic stage, where the prognosis is especially poor and treatment options are limited, with less than 20% surviving more than one year.[1,2] CLDN18.2 has emerged as an important therapeutic target for these patients, with an estimated 60% of gastric/GEJ cancers expressing CLDN18.2 in 25% or more of tumour cells.[3] Each year, there are roughly 183,500 patients in the US, EU, China and Japan treated in the 2nd and later-line setting for advanced or metastatic CLDN18.2-positive, non-HER2-positive gastric/GEJ cancers.[4]

Rui-Hua Xu, M.D., Ph.D., Professor in the Department of Medical Oncology, Sun Yat-Sen University Cancer Center, Guangzhou, China, and principal investigator of the trial said: "Metastatic gastric cancer is an aggressive disease with very limited options once patients progress after first-line treatment. Sone-Ve is the first CLDN18.2-targeted antibody drug conjugate to demonstrate an overall survival benefit in this setting and has the potential to establish a new precision treatment for a broader population of patients with CLDN18.2 expression."

Susan Galbraith, Executive Vice President, Oncology Haematology R&D, said: "Sone-Ve has the potential to reshape the treatment of gastric cancer by replacing classic chemotherapy with this novel targeted antibody drug conjugate to improve outcomes for patients. These transformative results from the first Phase III readout for Sone-Ve, together with our broad development programme, highlight the potential for Sone-Ve to become an important new medicine in CLDN18.2-positive cancers."

Sone-Ve was well tolerated, and its profile was consistent with the known safety profile of Sone-Ve with no new safety signals identified.

Sone-Ve is a potential global first-in-class CLDN18.2-targeting antibody drug conjugate (ADC) with a monomethyl auristatin E (MMAE) payload.

These data will be presented at a forthcoming medical meeting and shared with global regulatory authorities.

Sone-Ve has received Orphan Drug Designation from the US Food and Drug Administration and the European Commission for the treatment of gastric and GEJ cancers. It has also received Breakthrough Designation in China for the 2nd-line treatment of gastric cancer.

## Notes

### Gastric and GEJ cancers

Gastric (stomach) cancer is the fifth most common cancer worldwide and the fifth-leading cause of cancer-related death.[5] Nearly one million new patients were diagnosed with gastric cancer in 2024, with approximately 650,000 deaths reported globally. In many regions, its incidence has been increasing in patients younger than 50 years old, along with other gastrointestinal (GI) malignancies.[5]

GEJ cancer is a type of gastric cancer that arises from and spans the area where the oesophagus connects to the stomach.[6]

Most advanced gastric cancer patients will eventually experience disease progression after standard 1st-line therapies, and subsequent lines yield poor outcomes, with median survival of 5-9 months for patients receiving 2nd and later-line systemic treatments.[7-9]

### CLARITY-Gastric01

CLARITY-Gastric01 is a randomised, open-label, sponsor-blinded, multicentre, global Phase III trial evaluating Sone-Ve as a 2nd and later-line therapy for patients with advanced or metastatic gastric cancer, GEJ cancer, or EAC with CLDN18.2 expression in 25% or more of tumour cells, with IHC+ of any intensity. In the trial, patients were randomised 1:1:1 in Stage 1 (dose selection) to Sone-Ve monotherapy 2.2 mg/kg or 1.8 mg/kg every three weeks, or investigator's choice of therapy, the comparator arm. In Stage 2, the trial continued with Sone-Ve 2.2 mg/kg as the recommended Phase III dose.

The efficacy analyses from this study will also provide the basis to evaluate the clinical performance of the Ventana SP455 assay for the identification of patients with advanced or metastatic gastric, GEJ or EAC cancers expressing CLDN18.2 who may benefit from Sone-Ve.

The trial is being conducted in 175 centres across 19 countries, including in North America, Europe, South America and Asia. Its dual primary endpoints are PFS as assessed by BICR in the 2nd and later-line setting and OS in the 3rd and later-line setting. A key secondary endpoint is OS in the 2nd and later-line setting.

### Sonesitatug Vedotin (Sone-Ve)

Sone-Ve is a novel ADC targeting CLDN18.2, a protein found in the stomach lining and a validated therapeutic target in oncology, particularly for GI cancers. Sone-Ve consists of an anti-CLDN18.2 monoclonal antibody, a protease-degradable linker and a cytotoxic small molecule MMAE payload.

AstraZeneca entered into a global exclusive licence agreement with KYM Biosciences to develop and commercialise Sone-Ve in March 2023.

In addition to CLARITY-Gastric01, Sone-Ve is being evaluated in the CLARITY-Gastric02 Phase III trial in combination with capecitabine, with or without rilvegostomig, as a 1st-line treatment for advanced or metastatic gastric cancer, GEJ cancer and EAC. In Phase II development, Sone-Ve is being evaluated in patients with advanced solid tumours in multiple combinations across settings, including in CLDN18.2-positive pancreatic and biliary tract cancers (BTC).

### AstraZeneca in GI cancers

AstraZeneca has a broad development programme for the treatment of GI cancers across several medicines and a variety of tumour types and stages of disease. In 2024, GI cancers collectively represented approximately 5 million new cancer cases leading to approximately 3.3 million deaths.[10]

Within this programme, the Company is committed to improving outcomes in gastric, liver, biliary tract, oesophageal, pancreatic and colorectal cancers.

*Imfinzi* (durvalumab), an anti-PDL1 antibody, is approved in the US, China, EU, Japan and other countries in combination with chemotherapy in locally advanced or metastatic BTC, in combination with *Imjudo* (tremelimumab) in unresectable hepatocellular carcinoma (HCC) and in combination with FLOT chemotherapy (fluorouracil, leucovorin, oxaliplatin, and docetaxel) in early-stage and locally advanced gastric and GEJ cancers. *Imfinzi* is also approved as a monotherapy in unresectable HCC in Japan, China and the EU.

*Enhertu* (trastuzumab deruxtecan), a HER2-directed ADC is approved in the US, China, EU, Japan and several other countries for HER2-positive advanced gastric cancer. *Enhertu* is jointly developed and commercialised by AstraZeneca and Daiichi Sankyo.

*Lynparza* (olaparib), a first-in-class PARP inhibitor, is approved in the US and several other countries for the treatment of BRCA-mutated metastatic pancreatic cancer. *Lynparza* is developed and commercialised in collaboration with MSD (Merck & Co., Inc. inside the US and Canada).

*Orpathys* (savolitinib), an oral, potent, and highly selective MET tyrosine kinase inhibitor (TKI), has received conditional approval in China for the treatment of patients with locally advanced or metastatic gastric cancer or GEJ adenocarcinoma harbouring MET amplification who have progressed on at least two prior lines of systemic therapy. *Orpathys* is being jointly developed and commercialised by AstraZeneca and HUTCHMED.

The Company is also assessing rilvegostomig, a PD-1/TIGIT bispecific antibody, in combination with chemotherapy as an adjuvant therapy in BTC, and in combination with *Enhertu* in previously untreated, HER2-expressing, locally advanced or metastatic BTC. Rilvegostomig is also being evaluated in combination with bevacizumab with or without *Imjudo* as a 1st-line treatment in patients with advanced HCC, and as a 1st-line combination treatment in patients with HER2-positive, or CLDN18.2-positive and HER2-negative, locally advanced unresectable or metastatic gastric and GEJ cancers.

In addition to Sone-Ve, AstraZeneca is also advancing AZD5863, a novel CLDN18.2/CD3 T-cell engager bispecific antibody licensed from Harbour Biomed in Phase I development.

In early development, AstraZeneca is developing AZD7003, a Glypican 3 armoured CAR T, in HCC. The Company is also advancing a pan-KRAS inhibitor programme licensed from Jacobio Pharma, which is being evaluated in Phase I trials in advanced solid tumours with KRAS alterations, including in pancreatic ductal adenocarcinoma.

**AstraZeneca in oncology**
AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients.

The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyse changes in the practice of medicine and transform the patient experience.

AstraZeneca has the vision to redefine cancer care and, one day, eliminate cancer as a cause of death.

**AstraZeneca**
AstraZeneca (LSE/STO/NYSE: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Disease, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Social Media @AstraZeneca.

**Contacts**

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