

Results from Astellas' Phase 3 SPOTLIGHT Trial of Investigational Zolbetuximab Published in *The Lancet*

TOKYO, April 14, 2023 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, “Astellas”) today announced that *The Lancet* published detailed data from the Phase 3 SPOTLIGHT trial evaluating first-line treatment with zolbetuximab, an investigational first-in-class Claudin 18.2 (CLDN18.2) targeted monoclonal antibody, plus mFOLFOX6 (a combination regimen that includes oxaliplatin, leucovorin and fluorouracil) versus placebo plus mFOLFOX6 in patients with CLDN18.2-positive, HER2-negative, locally advanced unresectable or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma. The study data was first published online on April 14 in *The Lancet*.¹ Initial results from SPOTLIGHT, which met its primary endpoint of progression-free survival (PFS) and a key secondary endpoint of overall survival (OS), were presented at the 2023 American Society of Clinical Oncology (ASCO) Gastrointestinal (GI) Cancers Symposium.

“Patients with HER2-negative, CLDN18.2-positive, locally advanced unresectable or metastatic gastric or gastroesophageal junction cancers have limited first-line treatments available that are biomarker-based,” said Kohei Shitara, MD, Primary Investigator for the SPOTLIGHT trial and Head, Department of Gastrointestinal Oncology, the National Cancer Center Hospital East in Kashiwa, Japan. “*The Lancet’s* decision to publish the SPOTLIGHT study reinforces the value this data provides to the gastrointestinal cancer scientific community.”

“The publication of the SPOTLIGHT study is an important report of the first Phase 3 trial to demonstrate clinical benefit following CLDN18.2-targeted therapy in any tumor type, and we are honored that it has been published in *The Lancet*,” said Pranob Bhattacharya, DrPH, MS, MBA, Executive Director and Interim Head of Immuno-oncology, Astellas. “This manuscript, which provides further insight into the investigational use of zolbetuximab, reinforces Astellas’ commitment to patients with advanced-stage gastric/GEJ cancer.”

The SPOTLIGHT and GLOW studies are part of Astellas’ gastric cancer development program to investigate targeted treatment options, such as zolbetuximab, and address patient needs in locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma. These two statistically significant Phase 3 trials will serve as the basis for global regulatory submissions. In both trials, approximately 38% of these patients had CLDN18.2-positive tumors ($\geq 75\%$ of tumor cells with strong-to-moderate membranous CLDN18 staining intensity), as determined by a validated immunohistochemistry assay.² GLOW study data were presented at the March American Society of Clinical Oncology (ASCO) Plenary Series.

About Locally Advanced Unresectable Metastatic Gastric and Gastroesophageal Junction Cancer

Gastric cancer, also commonly known as stomach cancer, is the fifth most commonly diagnosed cancer worldwide.³ Signs and symptoms can include indigestion or heartburn, pain or discomfort in the abdomen, nausea and vomiting, diarrhea or constipation, bloating of the stomach after meals and loss of appetite and sensation of food getting stuck in the throat while eating.⁴ Signs of more advanced gastric cancer can include unexplained weight loss, weakness and fatigue and vomiting blood or having blood in the stool.⁵ Risk factors associated with gastric cancer can include older age, male gender, family history, *H. pylori* infection, smoking and gastroesophageal reflux disease (GERD).^{4,6} Because early-stage gastric cancer symptoms frequently overlap with more common stomach-related conditions, gastric cancer is often diagnosed in the advanced or metastatic stage, or once it has spread from the tumor’s origin to other body tissues or organs.⁴ The five-year relative

survival rate for patients at the metastatic stage is approximately six percent.⁷ Gastroesophageal junction (GEJ) adenocarcinoma is a cancer that starts at the area where the esophagus joins the stomach.⁸

About Zolbetuximab

Zolbetuximab is an investigational, first-in-class chimeric IgG1 monoclonal antibody (mAb) that targets and binds to CLDN18.2, a transmembrane protein. Zolbetuximab acts by binding to CLDN18.2 on the cancer cell surface of gastric epithelial cells. In pre-clinical studies, this binding interaction then induces cancer cell death by activating two distinct immune system pathways — antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC).⁹ The safety and efficacy of zolbetuximab are under investigation in gastric, gastroesophageal junction and pancreatic cancers and have not been established. There is no guarantee the agent will receive regulatory approval or become commercially available for the uses being investigated.

About SPOTLIGHT Phase 3 Clinical Trial

SPOTLIGHT is a Phase 3, global, multi-center, double-blind, randomized study, assessing the efficacy and safety of zolbetuximab (IMAB362) plus mFOLFOX6 (combination regimen of oxaliplatin, leucovorin and fluorouracil) compared to placebo plus mFOLFOX6 as a first-line treatment of patients with CLDN18.2-positive, HER2-negative, locally advanced unresectable or metastatic gastric/GEJ cancer. 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 is progression-free survival of participants treated with combination of zolbetuximab plus mFOLFOX6 compared to those treated with placebo plus mFOLFOX6. Secondary endpoints include overall survival, objective response rate, duration of response, safety and tolerability and quality-of-life parameters.

In the study, investigational treatment zolbetuximab plus mFOLFOX6 demonstrated statistically significant improvements in progression-free survival (PFS) and overall survival (OS) compared to placebo plus mFOLFOX6. Specifically, zolbetuximab plus mFOLFOX6 reduced the risk of progression or death by 24.9% (n=565; Hazard Ratio [HR]=0.751; [95% Confidence Interval [CI]: (0.598-0.942)]; P=0.0066) compared to placebo plus mFOLFOX6. Median PFS was 10.61 months (95% CI: 8.90-12.48) in the treatment arm and 8.67 months (95% CI: 8.21-10.28) in the placebo arm. The study also showed that zolbetuximab plus mFOLFOX6 significantly prolonged OS, reducing the risk of death by 25.0% (HR=0.750; 95% CI: 0.601-0.936; P=0.0053). Median OS was 18.23 months (95% CI: 16.43-22.90) and 15.54 months (95% CI: 13.47-16.53) for the treatment arm and placebo arm, respectively.

The incidence of serious treatment-emergent adverse events (TEAEs) was similar between both arms (44.8% versus 43.5% in the zolbetuximab versus placebo arms) and consistent with previous studies. The most frequent TEAEs in the SPOTLIGHT study were nausea (82.4% versus 60.8%), vomiting (67.4% versus 35.6%) and decreased appetite (47.0% versus 33.5%).

For more information, please visit clinicaltrials.gov under [Identifier NCT03504397](https://clinicaltrials.gov/ct2/show/study/NCT03504397).

About GLOW Phase 3 Clinical Trial

GLOW is a Phase 3, global, multi-center, double-blind, randomized study, assessing the efficacy and safety of zolbetuximab (IMAB362) plus CAPOX (a combination chemotherapy regimen which includes capecitabine and oxaliplatin) compared to placebo plus CAPOX as a first-line treatment of patients with CLDN18.2 positive, HER2-negative, locally advanced unresectable or metastatic gastric/GEJ cancer. The study enrolled 507 patients at 166 study locations in the U.S., Canada, United Kingdom, Europe, South America and Asia. The primary endpoint is progression-free survival of participants treated with combination of zolbetuximab plus CAPOX compared to those treated with placebo plus CAPOX. Secondary endpoints include overall survival, objective response rate, duration of response, safety and tolerability and quality-of-life parameters.

For more information, please visit clinicaltrials.gov under [Identifier NCT03653507](https://clinicaltrials.gov/ct2/show/study/NCT03653507).

Pipeline in Claudin 18.2

In addition to zolbetuximab, ASP2138 is under development in our [Primary Focus Immuno-Oncology](#). ASP2138 is currently in a Phase 1 trial for people with gastric, gastroesophageal junction or pancreatic cancer.

For more information about ASP2138, please visit clinicaltrials.gov under [Identifier NCT05365581](https://clinicaltrials.gov/ct2/show/study/NCT05365581).

An expanded Phase 2 trial ([NCT03816163](https://clinicaltrials.gov/ct2/show/study/NCT03816163)) in metastatic pancreatic cancer is in progress. The trial is a randomized, multi-center, open-label study, evaluating the safety and efficacy of investigational zolbetuximab in combination with gemcitabine plus nab-paclitaxel as a first-line treatment in patients with metastatic pancreatic cancer with CLDN18.2-positive tumors (defined as ≥75% of tumor cells demonstrating strong-to-moderate membranous CLDN18.2 staining based on a validated immunohistochemistry assay).

About Astellas

Astellas Pharma Inc. is a pharmaceutical company conducting business in more than 70 countries around the world. We are promoting the Focus Area Approach that is designed to identify opportunities for the continuous creation of new drugs to address diseases with high unmet medical needs by focusing on Biology and Modality.

Furthermore, we are also looking beyond our foundational Rx focus to create Rx+® healthcare solutions that combine our expertise and knowledge with cutting-edge technology in different fields of external partners. Through these efforts, Astellas stands on the forefront of healthcare change to turn innovative science into VALUE for patients. For more information, please visit our website at <https://www.astellas.com/en>.

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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References

¹ Shitara K, et al. Zolbetuximab plus mFOLFOX6 in patients with claudin-18 isoform 2-positive, HER2-negative, untreated, locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma (SPOTLIGHT): a multicentre, randomised, double-blind, phase 3 trial. *The Lancet*. Published online April 14, 2023; S0140-6736(23)00620-7.

² Data on file. Northbrook, Ill. Astellas Pharma Inc.

³ Sung H, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209-49.

⁴ American Cancer Society. Signs and symptoms of stomach cancer (01-22-2021). Available at <https://www.cancer.org/cancer/stomach-cancer/detection-diagnosis-staging/signs-symptoms.html>. Last accessed February 21, 2023.

⁵ National Cancer Institute. Gastric cancer treatment (PDQ®): patient version (08-24-2021). Available at <https://www.cancer.gov/types/stomach/patient/stomach-treatment-pdq>. Last accessed March 24, 2023.

⁶ American Cancer Society. Esophageal cancer risk factors (06-09-2020). Available at <https://www.cancer.org/cancer/esophagus-cancer/causes-risks-prevention/risk-factors.html>. Last accessed March 24, 2023.

⁷ National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer stat facts: stomach cancer. Available at <https://seer.cancer.gov/statfacts/html/stomach.html>. Last accessed March 24, 2023.

⁸ American Cancer Society. About esophagus cancer (03-20-2020). Available at <https://www.cancer.org/content/dam/CRC/PDF/Public/8614.00.pdf>. Last accessed March 24, 2023.

⁹ Sahin U, et al. FAST: a randomised phase II study of zolbetuximab (IMAB362) plus EOX versus EOX alone for first-line treatment of advanced CLDN18.2-positive gastric and gastro-oesophageal adenocarcinoma. *Ann Oncol.* 2021;32(5):609-19.