

Astellas Announces U.S. FDA Grants Priority Review for Zolbetuximab Biologics License Application

If approved, the investigational therapy would offer a new treatment option for patients with advanced gastric and gastroesophageal cancers

TOKYO, July 6, 2023 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, “Astellas”) today announced that the U.S. Food and Drug Administration (FDA) has accepted and granted Priority Review for the company’s Biologics License Application (BLA) for zolbetuximab, a first-in-class investigational Claudin 18.2 (CLDN18.2)-targeted monoclonal antibody, for first-line treatment of patients with locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors are CLDN18.2-positive. If approved, zolbetuximab would be the first CLDN18.2-targeted therapy available in the U.S. for these patients.

Under the Prescription Drug User Fee Act (PDUFA), the FDA has set a target action date of January 12, 2024. The FDA reviewed the application under its Real-Time Oncology Review (RTOR) program, which aims to explore a more efficient review process to ensure that safe and effective treatments are available to patients as early as possible.

In the U.S., it is estimated that 26,500 people will be diagnosed with gastric cancer and 11,130 will die from the disease in 2023.¹ Early-stage gastric cancer symptoms frequently overlap with more common stomach-related conditions, often resulting in gastric cancer diagnosis in the advanced or metastatic stage, or once it has spread from the tumor’s origin to other body tissues or organs.² The five-year relative survival rate for patients at the metastatic stage is 6.6%.¹

“Astellas is committed to bringing innovative therapies to patients with hard-to-treat cancers, including gastric cancer. While rare in the U.S., gastric cancer can be deadly when diagnosed in the late stages,” said Moitreyee Chatterjee-Kishore, PhD, MBA, Senior Vice President and Head of Immuno-Oncology Development, Astellas. “The FDA’s acceptance of the Biologics License Application filing and Priority Review designation for zolbetuximab confirms the urgent therapeutic need and brings us one step closer to delivering on this commitment to patients, families and caregivers.”

The BLA is based on results from the Phase 3 SPOTLIGHT and GLOW clinical trials. The SPOTLIGHT study evaluated zolbetuximab plus mFOLFOX6 (a combination regimen that includes oxaliplatin, leucovorin and fluorouracil) compared to placebo plus mFOLFOX6. The GLOW study evaluated zolbetuximab plus CAPOX (a combination chemotherapy regimen that includes capecitabine and oxaliplatin) compared to placebo plus CAPOX.

In both SPOTLIGHT and GLOW, approximately 38% of patients screened for the trials had tumors that were CLDN18.2-positive ($\geq 75\%$ of tumor cells with moderate-to-strong membranous CLDN18 staining intensity), as determined by a validated immunohistochemistry assay.^{3,4}

Astellas has already reflected the impact from this acceptance in its financial forecast of the current fiscal year ending March 31, 2024.

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.⁵ In the U.S., it is estimated that 26,500 people will be diagnosed with gastric cancer and 11,130 will die from the disease in 2023.¹ 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, loss of appetite, and sensation of food getting stuck in the throat while eating.² Signs of more advanced gastric cancer can include unexplained weight loss, weakness and fatigue, and vomiting blood or having blood in the stool.⁶ Risk factors associated with gastric cancer can include older age, male gender, family history, *H. pylori* infection, smoking and gastroesophageal reflux disease (GERD).^{2,7} 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.² The five-year relative survival rate for patients at the metastatic stage is 6.6%.¹ 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 Claudin 18.2 (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 Zolbetuximab has not been approved by any regulatory bodies for the treatment of patients with gastric and GEJ cancers, and there is no guarantee the agent will receive regulatory approval or become commercially available for the uses being investigated.

INVESTIGATIONAL STUDIES

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 (a combination 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 is progression-free survival (PFS) in participants treated with the combination of zolbetuximab plus mFOLFOX6 compared to those treated with placebo plus mFOLFOX6. Secondary endpoints include 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 and were subsequently published in *The Lancet* on April 14.³

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 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. The primary endpoint is PFS in participants treated with the combination of zolbetuximab plus CAPOX compared to those treated with placebo plus CAPOX. Secondary endpoints include OS, ORR, DOR, safety and tolerability and quality-of-life parameters.

Data from the GLOW study were initially presented at the March 2023 American Society of Clinical Oncology (ASCO) Plenary Series with an updated oral presentation at the 2023 ASCO Annual Meeting on June 3.⁴

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

Investigational Pipeline in CLDN18.2

An expanded Phase 2 trial in metastatic pancreatic adenocarcinoma 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 adenocarcinoma with CLDN18.2-positive tumors (defined as ≥75% of tumor cells demonstrating moderate-to-

strong membranous CLDN18 staining based on a validated immunohistochemistry assay). For more information, please visit clinicaltrials.gov under [Identifier NCT03816163](#).

In addition to zolbetuximab, ASP2138 is under development in our [Primary Focus Immuno-Oncology](#). ASP2138 is a bispecific monoclonal antibody that binds to CD3 and CLDN18.2, and it is currently in a Phase 1 trial for people with gastric, GEJ or pancreatic adenocarcinoma. The safety and efficacy of the agent under investigation have not been established for the uses being considered. For more information, please visit clinicaltrials.gov under [Identifier NCT05365581](#).

There is no guarantee that the agent will receive regulatory approval and become commercially available for the uses being investigated.

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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³ Shitara K, 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. *The Lancet*. Published online April 14, 2023; S0140-6736(23)00620-7.

⁴ Xu RH, Shitara K, Ajani JA, et al. Updates on Abstract 405736: Zolbetuximab + CAPOX in 1L claudin-18.2+ (CLDN18.2+)/HER2- locally advanced (LA) or metastatic gastric or gastroesophageal junction (mG/GEJ) adenocarcinoma: Primary phase 3 results from GLOW. Presented at: 2023 ASCO Annual Meeting. Abstract 405736.

⁵ 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.

⁶ 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 June 28, 2023.

⁷ 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 June 28, 2023.

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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.