Press Release

U.S. FDA ACKNOWLEDGES ASTELLAS' RESUBMISSION OF BIOLOGICS LICENSE APPLICATION FOR ZOLBETUXIMAB AND SETS NEW ACTION DATE

If approved, the investigational therapy would offer a new treatment option for patients with advanced gastric and gastroesophageal junction cancers as the first and only CLDN18.2-targeted therapy in the U.S.

TOKYO, May 30, 2024 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, "Astellas") today announced that the U.S. Food and Drug Administration (FDA) has acknowledged the company's resubmission of the Biologics License Application (BLA) for zolbetuximab, a first-in-class investigational claudin (CLDN) 18.2-targeted monoclonal antibody, 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 CLDN18.2 positive. If approved, zolbetuximab would be the first CLDN18.2-targeted therapy approved for this patient population in the U.S. Under the Prescription Drug User Fee Act (PDUFA), the FDA has set a new target action date of November 9, 2024.

In the U.S., it was estimated that 26,890 people will be diagnosed with gastric cancer and 10,880 will die from the disease in 2024.[1] Since 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 7%.[1]

Moitreyee Chatterjee-Kishore, Ph.D., M.B.A., Senior Vice President and Head of Immuno-Oncology Development, Astellas
"Astellas is committed to introducing new targeted therapies for hard-to-treat cancers. Those living with advanced gastric or GEJ cancer often face great unmet needs, and the FDA acknowledgment of the zolbetuximab BLA resubmission brings us one step closer to offering this important treatment option to eligible patients in the U.S. facing this deadly disease."

The zolbetuximab BLA was resubmitted on May 9, 2024, following a complete response letter issued on January 4, 2024 by the FDA due to third-party manufacturing deficiencies identified during the pre-license inspection of the facility. The FDA did not raise any concerns related to the clinical data, including efficacy or safety, of zolbetuximab, and did not request additional clinical studies to support the BLA approval.

The zolbetuximab BLA was based on results from the Phase 3 SPOTLIGHT and GLOW clinical trials.[3,4] 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 had tumors that were CLDN18.2 positive[3,4] CLDN18.2 positivity is defined as ≥75% of tumor cells demonstrating moderate-to-strong membranous CLDN18 staining, as determined by a validated immunohistochemistry assay.[3,4]

On March 26, 2024, Japan's Ministry of Health, Labour and Welfare (MHLW) approved zolbetuximab, making it the first and only CLDN18.2-targeted treatment approved for patients with CLDN18.2 positive, unresectable, advanced or recurrent gastric cancer.[5] Astellas has also submitted applications for zolbetuximab to regulatory agencies around the world, and reviews are ongoing.

Astellas has already reflected the impact from the FDA acknowledgment of the BLA resubmission for zolbetuximab in its financial forecast for the current fiscal year ending March 31, 2025.

About Zolbetuximab
Zolbetuximab is a claudin 18.2-directed cytolytic antibody being investigated in combination with fluoropyrimidine- and platinum-containing chemotherapy 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 an investigational first-in-class monoclonal antibody (mAb), zolbetuximab targets and binds to CLDN18.2, a transmembrane protein. In pre-clinical studies, zolbetuximab depleted CLDN18.2-positive cells via antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC).[6] There is no guarantee the agent will receive regulatory approval in the U.S. or become commercially available for the uses being investigated.

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.[7] In the U.S., it is estimated that 130,263 people are living with gastric cancer, classifying it as a rare disease.[1,8] In 2024, it is estimated that 26,890 people will be diagnosed with gastric cancer and 10,880 will die from the disease in the U.S.[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.[9] Risk factors associated with gastric cancer can include older age, male gender, family history, *H. pylori* infection, smoking, and gastroesophageal reflux disease (GERD).[2, 10] Gastroesophageal junction (GEJ) adenocarcinoma is a cancer that starts at the area where the esophagus joins the stomach.[11] 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 7%.[1]

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 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 is progression-free survival (PFS) of 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, 2023.[3]

For more information, please visit clinicaltrials.gov under Identifier 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 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 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 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.[4]

For more information, please visit clinicaltrials.gov under Identifier NCT03653507.

Investigational Pipeline in CLDN18.2
An expanded Phase 2 trial of zolbetuximab in metastatic pancreatic adenocarcinoma is in progress and recruiting patients. 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 area and is currently recruiting patients. ASP2138 is a bispecific monoclonal antibody that binds to CD3 and CLDN18.2, and it is currently in a Phase 1/1b study in participants with metastatic or locally advanced unresectable gastric or GEJ adenocarcinoma or metastatic pancreatic adenocarcinoma whose tumors have CLDN18.2 expression. 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(s) 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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