Press Release

China's National Medical Products Administration (NMPA) Approves VYLOY™ (zolbetuximab) for First-Line Treatment of Advanced Gastric or Gastroesophageal Junction Adenocarcinoma

- China has the highest number of cases and deaths from gastric cancer of any country worldwide[1] -

- Zolbetuximab is the first and only therapy approved in China to target claudin 18.2, a biomarker expressed by 35% of Chinese patients with advanced gastric and gastroesophageal junction (GEJ) cancer[2] -

- Treatment with the claudin 18.2-targeted monoclonal antibody shown to significantly extend both progression-free survival and overall survival in the Phase 3 GLOW and SPOTLIGHT trials[3,4] -

TOKYO, Jan. 06, 2025 – Astellas Pharma Inc. (TSE:4503, President and CEO: Naoki Okamura, "Astellas") today announced that China's National Medical Products Administration (NMPA) has approved VYLOY™ (zolbetuximab), in combination with fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of patients 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. Zolbetuximab is the first NMPA-approved monoclonal antibody to target gastric tumor cells that express the biomarker CLDN18.2, offering a highly targeted approach to cancer treatment.

Gastric cancer is the third leading cause of cancer-related mortality in China, with more than 260,000 deaths reported from the disease in 2022.[5] As early symptoms are often hard to detect, approximately 60% of Chinese patients are diagnosed at the advanced stage of the disease[6] where treatment options are limited and outcomes are often poor. The average five-year survival rate for patients with advanced gastric cancer in China is 9.1%, driving the urgent need for novel therapeutic options that can slow disease progression and extend lives.[7]

Professor Xu Ruihua, Lead Primary Investigator of the Phase 3 GLOW Study, Director of the Cancer Prevention and Treatment Center of Sun Yat-sen University, President of the Chinese Society of Clinical Oncology (CSCO):

“Approximately 30% of patients enrolled in the global Phase 3 GLOW trial were from mainland China. The results of this study demonstrated that the combination of zolbetuximab and chemotherapy provided significant survival benefits to patients with CLDN18.2-positive, HER2-negative advanced gastric and gastroesophageal junction (GEJ) cancers. The analysis of the China subgroup data showed that Chinese gastric cancer patients benefited substantially in terms of both survival and quality of life. We are excited that the NMPA has approved zolbetuximab, which will provide a valuable and effective first-line treatment option for patients with advanced gastric cancer in China.”

Professor Xu Jianming, Lead Primary Investigator of the Phase 3 SPOTLIGHT Study in China, Fifth Medical Center of the Chinese People's Liberation Army General Hospital:
“We are extremely encouraged that the NMPA has approved zolbetuximab in China. The SPOTLIGHT study explored the efficacy and safety of zolbetuximab combined with chemotherapy as a first-line treatment for patients with CLDN18.2-positive, HER2-negative advanced gastric and gastroesophageal junction cancer. The results showed statistically significant differences in key endpoints such as progression-free survival and overall survival. The survival and safety benefits seen in the China subgroup were consistent with the global trial population, and the results are expected to have far-reaching implications for meeting the clinical needs of Chinese patients with advanced gastric cancer. The trial provides valuable insights to guide the first-line treatment of advanced gastric cancer in China.”

Moitreyee Chatterjee-Kishore, Ph.D., M.B.A., Senior Vice President and Head of Immuno-Oncology Development, Astellas:
“*Approximately 35% of Chinese patients with advanced and metastatic gastric and GEJ cancers have tumors that positively express CLDN18.2. By specifically targeting this biomarker with zolbetuximab we are able to stimulate selective cell death, reducing the overall number of CLDN18.2-positive cells in a tumor. The NMPA approval of zolbetuximab offers a new precision medicine for first-line use in China, supporting our ongoing ambition to drive progress and innovation in cancer care.”*

The NMPA’s approval of zolbetuximab is supported by data from the global Phase 3 GLOW and SPOTLIGHT clinical trials which included 145 and 36 patients from mainland China, respectively.[3,4] The GLOW trial evaluated zolbetuximab plus CAPOX (a combination chemotherapy regimen that includes capecitabine and oxaliplatin) compared to placebo plus CAPOX.[4] The SPOTLIGHT trial evaluated zolbetuximab plus mFOLFOX6 (a combination regimen that includes oxaliplatin, leucovorin and fluorouracil) compared to placebo plus mFOLFOX6.[3] Treatment with zolbetuximab was shown to provide statistically significant improvements in progression-free survival (PFS) and overall survival (OS) compared to other standard of care chemotherapies in eligible patients with gastric and GEJ cancers.[3,4] In the GLOW trial, a median PFS of 8.21 months was achieved with zolbetuximab plus CAPOX as first-line treatment versus 6.80 months with placebo plus CAPOX. The median OS was 14.39 months versus 12.16 months in the respective treatment groups.[4] Similar efficacy results were seen in the SPOTLIGHT trial, where the median PFS was 10.61 months versus 8.67 months, and the median OS was 18.23 months versus 15.54 months, with zolbetuximab plus mFOLFOX6, compared to placebo plus mFOLFOX6.[3] In both the GLOW and SPOTLIGHT trials, the incidence

of serious treatment emergent adverse events (TEAEs) was similar in the zolbetuximab treatment groups compared to the controls. The most common all-grade TEAEs reported in the zolbetuximab treatment groups were nausea, vomiting and decreased appetite.[3,4]

Astellas has already reflected the impact from the NMPA approval of zolbetuximab in its financial forecast for the current fiscal year ending March 31, 2025.

About Locally Advanced Unresectable Metastatic Gastric and Gastroesophageal Junction Cancer

Gastric and gastroesophageal junction (G/GEJ) cancers are known to be histologically similar, are recommended to be managed in the same way in treatment guidelines, and frequently display aligned responses to treatment.[8] Across China, more than 358,000 new cases of gastric cancer were diagnosed in 2022.[5] Gastric cancer is the third most common cause of cancer-related mortality in China, responsible for more than 260,000 deaths in 2022.[5] GEJ adenocarcinomas start in the first two inches (5 cm) where the esophagus joins the stomach.[9]

Because early-stage cancer symptoms frequently overlap with more common stomach-related conditions, G/GEJ cancers are often diagnosed in the advanced or metastatic stage, or once they have spread from the tumor's origin to other body tissues or organs.[10]

Early signs and symptoms can include indigestion or heartburn, pain or discomfort in the abdomen, nausea and vomiting, bloating of the stomach after meals, and loss of appetite.[10,11] Signs of more advanced G/GEJ cancer can include unexplained weight loss, weakness and fatigue, sensation of food getting stuck in the throat while eating, vomiting blood or having blood in the stool.[10,11,12] Risk factors associated with G/GEJ cancer can include older age, male gender, family history, *H. pylori* infection, smoking, and gastroesophageal reflux disease (GERD).[13,14]

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 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.[4]

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.

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 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.[3]

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.[3]

For more information, please visit clinicaltrials.gov under Identifier NCT03504397.

About Zolbetuximab

Zolbetuximab is a first-in-class monoclonal antibody (mAb) specifically designed to target tumor cells that express CLDN18.2, a transmembrane protein. Zolbetuximab is the only CLDN18.2 targeted therapy to be approved in combination with fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of patients 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.

Zolbetuximab has been approved in a number of countries around the world including Japan, the UK, Korea, the US, Canada, Brazil and China, plus has received marketing authorization from the European Commission which is valid in all 27 EU member states as well as Iceland, Liechtenstein, and Norway. Regulatory approvals were based on the positive results of the SPOTLIGHT and GLOW Phase III trials where zolbetuximab demonstrated statistically significant improvements in progression-free survival and overall survival compared to other standard of care chemotherapies in eligible patients with gastric and GEJ cancers.[3,4] In both the GLOW and SPOTLIGHT Phase 3 clinical trials, approximately 38% of all patients screened, and 35% of patients screened in China, had tumors that were CLDN18.2 positive, defined as ≥75% of tumor cells demonstrating moderate to strong membranous CLDN18 immunohistochemical staining, assessed and confirmed using the VENTANA® CLDN18 (43-14A) RxDx Assay.[3,4]

By binding to CLDN18.2, zolbetuximab induces cancer cell death and tumor growth inhibition by activating two distinct immune system pathways — antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC).[15] This targeted approach that specifically focuses on CLDN18.2, a biomarker shown to be positively expressed in gastric and GEJ cancers, could help to identify patients who are most likely to respond to treatment.

Investigational Pipeline in CLDN18.2

An expanded Phase 2 trial of zolbetuximab in metastatic pancreatic adenocarcinoma is in progress involving 393 patients worldwide. 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 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.

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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