Press Release

# Astellas' VYLOY™ (zolbetuximab) Approved in Japan for Treatment of Gastric Cancer

*VYLOY approved in combination with chemotherapy for patients with human epidermal growth factor receptor 2 (HER2)-negative, CLDN18.2 positive, unresectable, advanced or recurrent gastric cancer*

*MHLW approval makes VYLOY the first and only CLDN18.2-targeted therapy approved in the world*

**TOKYO, March 26, 2024** – Astellas Pharma Inc. (TSE: 4503, President and CEO: Naoki Okamura, "Astellas") today announced that on March 26, 2024, Japan's Ministry of Health, Labour and Welfare (MHLW) approved VYLOY™ (zolbetuximab), an anti-claudin 18.2 (CLDN18.2) monoclonal antibody for patients with CLDN18.2 positive, unresectable, advanced or recurrent gastric cancer. VYLOY is the first and only CLDN18.2-targeted therapy approved by any regulatory agency in the world.

Gastric cancer is frequently diagnosed in the advanced or metastatic stage due to overlapping early-stage symptoms with other more common stomach conditions.[1] Despite efforts to reduce its impact, gastric cancer is the third deadliest cancer in Japan, with 126,724 cases diagnosed in 2022.[2]

**Moitreyee Chatterjee-Kishore, Ph.D., M.B.A., Senior Vice President and Head of Immuno-Oncology Development, Astellas**
"The approval of VYLOY by the MHLW marks a new era in the treatment of gastric cancer, offering the first and only targeted therapy option for CLDN18.2-positive patients living with this devastating disease. Astellas is proud to help address the urgent therapeutic need for this hard-to-treat cancer in Japan, where incidence rates are among the highest globally. Importantly, this approval holds the potential to provide eligible patients with more precious time with their loved ones, delivering on our commitment to improve patient outcomes."

**Kohei Shitara, MD, Primary Investigator for the SPOTLIGHT Trial and Head, Department of Gastrointestinal Oncology, the National Cancer Center Hospital East in Kashiwa, Japan**
"Developing new targeted therapies is critical for diseases like advanced gastric adenocarcinoma, which has had very limited treatment options and is often discovered at an advanced stage. As the primary investigator for the Phase 3 SPOTLIGHT clinical trial, I witnessed firsthand the significant improvement in progression-free survival and overall survival for patients treated with VYLOY in combination with chemotherapy compared to those treated with placebo plus chemotherapy. These results support VYLOY as a new treatment option for the CLDN18.2-positive population in Japan, where there were nearly 44,000 deaths caused by gastric cancer in 2022 alone."

The approval is based on results from the Phase 3 SPOTLIGHT and GLOW clinical trials for first-line treatment in patients with locally advanced unresectable or metastatic HER2-

negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors were CLDN18.2 positive.[3,4] The SPOTLIGHT study evaluated VYLOY plus mFOLFOX6 (a combination chemotherapy regimen that includes oxaliplatin, leucovorin, and fluorouracil) compared to placebo plus mFOLFOX6.[4] The GLOW study evaluated VYLOY plus CAPOX (a combination chemotherapy regimen that includes capecitabine and oxaliplatin) compared to placebo plus CAPOX.[3] Both trials met their primary endpoint, progression-free survival (PFS), as well as a key secondary endpoint, overall survival (OS), showing statistical significance in patients treated with VYLOY plus chemotherapy compared to placebo plus chemotherapy. The most frequent treatment-emergent adverse events (TEAEs) ≥20% for VYLOY in combination with mFOLFOX6 or CAPOX were nausea, vomiting, decreased appetite, neutropenia, and decreased weight. In clinical trials, adverse reactions were managed by antiemetics, dose interruptions, and infusion rate adjustments.[3,4]

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 showing moderate-to-strong membranous CLDN18 staining, which should be confirmed by a pathologist or laboratory with adequate experience using the approved in-vitro diagnostic agent or medical device.[3,4] Astellas collaborated with Roche Diagnostics on the newly approved VENTANA® CLDN18 (43-14A) RxDx Assay, an immunohistochemistry (IHC) companion diagnostic (CDx) test, to identify patients who may be eligible for VYLOY.[5] Testing will be available in Japan at multiple central laboratories and is expected to expand to additional laboratories over time.

Astellas has also submitted applications for VYLOY to regulatory agencies around the world, and review is ongoing.

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

**About VYLOY™**
VYLOY™ (zolbetuximab) is an anti-claudin 18.2 (CLDN18.2) monoclonal antibody that is approved by Japan's Ministry of Health, Labour and Welfare (MHLW) for patients with CLDN18.2 positive, unresectable, advanced or recurrent gastric cancer. VYLOY is used in combination with chemotherapy for patients whose tumors are human epidermal growth factor receptor 2 (HER2)-negative. VYLOY is the first and only CLDN18.2-targeted therapy approved by any regulatory agency in the world. CLDN18.2 positivity should be confirmed by a pathologist or laboratory with adequate experience using the approved in-vitro diagnostic agent or medical device. As an antibody directed against human CLDN18.2, VYLOY binds to CLDN18.2 expressed on cell membrane in cancer cells such as gastric cancer and shows antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC), leading to tumor growth inhibition.[3,4]

**Important Safety Information**
For important Safety Information for VYLOY, please see the Package Insert.

**About Unresectable, Advanced or Recurrent Gastric Cancer**
Gastric cancer, also known as stomach cancer, is the fifth most commonly diagnosed cancer worldwide.[6] Gastric cancer killed 43,807 people in Japan in 2022, making it the third deadliest cancer by number of deaths in the country.[2] 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.[1] Signs of more advanced gastric cancer can include unexplained weight loss, weakness and fatigue, and vomiting blood or having blood in the stool.[7] Risk factors associated with gastric cancer can include older age, male gender, family history, *H. pylori* infection, and smoking.[8] 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.[1] The five-year relative survival rate for patients at the metastatic stage is 6.6%.[9]

**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 gastroesophageal junction (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, including Japan. 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, 2023, and were subsequently published in *The Lancet* on April 14, 2023.[4]

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.[3]

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

**Investigational Pipeline in Targeting CLDN18.2**
An expanded Phase 2 trial of zolbetuximab 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 1/1b 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 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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