Press Release

# Astellas Announces Zolbetuximab Meets Primary Endpoint in Phase 3 GLOW Trial as First-Line Treatment in Claudin 18.2 Positive, HER2-negative Locally Advanced Unresectable or Metastatic Gastric and Gastroesophageal Junction (GEJ) Cancers

*Astellas' GLOW trial, the second Phase 3 trial in CLDN18.2 positive, HER2-negative locally advanced unresectable or metastatic gastric and GEJ cancer, meets primary endpoint for progression-free survival (PFS) and key secondary endpoint for overall survival (OS)*

*GLOW results, along with SPOTLIGHT topline results, mark progress in Astellas' gastric cancer development program*

**TOKYO, December 16, 2022** – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced positive topline results from the Phase 3 GLOW clinical trial evaluating the efficacy and safety of zolbetuximab in combination with CAPOX (a combination chemotherapy regimen which includes capecitabine and oxaliplatin). Zolbetuximab is an investigational first-in-class Claudin-18.2 (CLDN18.2) targeted monoclonal antibody, for the first-line treatment of patients with CLDN18.2-positive, HER2-negative, locally advanced unresectable or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma.

The GLOW study met its primary endpoint showing statistical significance in progression-free survival (PFS) for patients treated with zolbetuximab plus CAPOX compared to placebo plus CAPOX. In addition, the study met a key secondary endpoint, overall survival (OS), showing statistical significance for patients treated with zolbetuximab plus CAPOX compared to placebo plus CAPOX. The most frequent treatment-emergent adverse events (TEAEs) were nausea and vomiting. Detailed results will be presented at a future scientific congress and submitted for publication.

"Zolbetuximab has the potential to be an innovative therapeutic option for patients with locally advanced unresectable or metastatic gastric or GEJ cancer, a difficult disease for which treatment options are still limited," said Ruihua Xu, MD, PhD, Primary Investigator for the GLOW study and Professor in the Department of Medical Oncology at Sun Yat-Sen University Cancer Center, Guangzhou, China. "I am so pleased with the topline results from GLOW that establish progression-free survival and overall survival in patients treated with zolbetuximab plus CAPOX."

"We are extremely pleased to share positive topline results from GLOW following the positive SPOTLIGHT readout last month. This further confirms the potential role of zolbetuximab in gastric cancer treatment, an important milestone in our gastric cancer development program," said Ahsan Arozullah, M.D., M.P.H., Senior Vice President and Head of Development Therapeutic Areas, Astellas. "We intend to discuss these results with

regulatory authorities as we continue to develop zolbetuximab for the first-line treatment of patients with locally advanced unresectable or metastatic gastric and GEJ cancer."

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).[1] CLDN18.2 is a type of transmembrane protein found in normal gastric cells and is a major component of epithelial tight junctions controlling the flow of molecules between cells.[2] Pre-clinical studies have shown that CLDN18.2, which is frequently present in gastric tumors, may become more exposed and accessible to targeted antibodies as gastric tumors develop.[3,4,5] Based on the SPOTLIGHT and GLOW studies, approximately 38% of these patients have CLDN18.2-positive tumors, meeting the qualification of CLDN18.2 expression in ≥75% of tumor cells with strong to moderate staining intensity based on a validated immunohistochemistry assay.[6]

The Phase 3 GLOW trial (n=507) is a global, multi-center, double-blind, randomized study assessing the efficacy and safety of zolbetuximab plus CAPOX compared to placebo plus CAPOX. This study, and the Phase 3 SPOTLIGHT trial (n=565), which evaluated the efficacy and safety of zolbetuximab plus a combination regimen of oxaliplatin, leucovorin and fluorouracil (mFOLFOX6) compared to placebo plus mFOLFOX6, were conducted to provide foundational data for regulatory submissions in the U.S., Europe, Asia and other countries globally. These studies are part of Astellas' gastric cancer development program to investigate new treatment options such as zolbetuximab and address patient needs in locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma.

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.[7] The five-year relative survival rate for patients at the metastatic stage is approximately six percent.[8,9]

**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).[1] The safety and efficacy of zolbetuximab are under investigation in gastric, gastroesophageal 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 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 or GEJ cancer. The study enrolled 507 patients at 165 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.

**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 or gastroesophageal junction cancer. The study enrolled 565 patients at 220 study locations in the U.S., 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.

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

**About Locally Advanced Unresectable Metastatic Gastric and GEJ Cancer**
Gastric cancer, also commonly known as stomach cancer, is the fifth most commonly diagnosed cancer worldwide.[10] 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.[11] 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, smoking and gastroesophageal reflux disease (GERD).[7,12] 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.[7] The five-year relative survival rate for patients at the metastatic stage is approximately six percent.[8,9] Gastroesophageal junction (GEJ) adenocarcinoma is a cancer that starts at the area where the esophagus joins the stomach.[13]

**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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