Press Release

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

Astellas' SPOTLIGHT trial meets primary endpoint of progression-free survival (PFS)

Full data to be presented at future scientific congress

TOKYO, November 17, 2022 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced positive topline results from the Phase 3 SPOTLIGHT clinical trial evaluating the efficacy and safety of zolbetuximab in combination with mFOLFOX6 (a combination regimen that includes oxaliplatin, leucovorin and fluorouracil). Zolbetuximab is an investigational first-in-class monoclonal antibody targeting Claudin 18.2 (CLDN18.2), 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 SPOTLIGHT trial enrolled 566 patients with CLDN18.2-positive, HER2-negative, locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma. The study met its primary endpoint showing statistical significance in progression-free survival (PFS) for patients treated with zolbetuximab plus mFOLFOX6 compared to placebo plus mFOLFOX6. In addition, the study met a secondary endpoint, overall survival (OS), showing statistical significance for patients treated with zolbetuximab plus mFOLFOX6 compared to placebo plus mFOLFOX6. The most frequent treatment-emergent adverse events (TEAEs) in patients treated with zolbetuximab plus mFOLFOX6 were nausea, vomiting, and decreased appetite. Detailed results will be presented at a future scientific congress and submitted for publication.

"I am excited by the potential for a new treatment option to help patients with advanced-stage gastric cancer or GEJ cancer," said Kohei Shitara, MD, Primary Investigator for the SPOTLIGHT trial and Chief, Department of Gastrointestinal Oncology, the National Cancer Center Hospital East in Kashiwa, Japan. "Gastric and GEJ cancers still have very limited treatment options available for patients with an advanced diagnosis."

"We're delighted and excited about the positive topline results from the SPOTLIGHT trial of zolbetuximab in combination with mFOLFOX6, and we have increased confidence in advancing development of zolbetuximab for the first-line treatment of patients with locally advanced or metastatic gastric cancer," said Ahsan Arozullah, M.D., M.P.H., Senior Vice President and Head of Development Therapeutic Areas, Astellas. "These topline results further support the role of CLDN18.2 as an emerging biomarker in gastric and GEJ cancer. We look forward to presenting the full results at a scientific congress in the near future."

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 toxicity and complement-dependent cytotoxicity.[1] CLDN18.2 is a type of transmembrane protein found in normal gastric cells and is a major component of epithelial and endothelial tight junctions controlling the flow of molecules between cells.[2] Pre-clinical studies have shown that CLDN18.2, which can also be present in gastric tumors, may become more exposed and accessible to targeted therapies with antibodies as gastric tumors develop.[3,4,5] Based on this study, approximately 38% of screened patients have CLDN18.2-positive tumors, defined as CLDN18.2 expression in ≥75% of tumor cells with strong-to-moderate staining intensity based on a validated immunohistochemistry assay.[6]

The Phase 3 SPOTLIGHT trial is a global, multi-center, double-blind, randomized study assessing the efficacy and safety of zolbetuximab plus mFOLFOX6 compared to placebo plus mFOLFOX6. Specifically, this study and the Phase 3 GLOW trial, which is evaluating the efficacy and safety of zolbetuximab plus capecitabine and oxaliplatin (CAPOX) compared to placebo plus CAPOX, are being conducted to provide foundational data for regulatory submissions in the U.S., Europe, Asia and other countries globally.

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]

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 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 566 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 Gastroesophageal Junction Cancer
Gastric cancer, also commonly known as stomach cancer, is the fifth most commonly diagnosed cancer worldwide.[9] 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.[10] 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).[7,11] 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.[7] The five-year relative survival rate for patients at the metastatic stage is approximately six percent.[8] Gastroesophageal junction (GEJ) adenocarcinoma is a cancer that starts at the area where the esophagus joins the stomach.[12]

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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