Press Release

Astellas Announces Positive Findings from Phase 3 GLOW Trial of Zolbetuximab during March ASCO Plenary Series

Data shows investigational zolbetuximab plus CAPOX reduced risk of progression or death by 31.3% vs CAPOX alone

Study evaluated patients with Claudin 18.2-positive, HER2-negative, locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma

Two statistically significant Phase 3 trials, GLOW and SPOTLIGHT, to serve as the basis for global regulatory submissions

TOKYO, March 22, 2023 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") will present detailed results from the Phase 3 GLOW trial evaluating first-line treatment with zolbetuximab, an investigational first-in-class Claudin 18.2 (CLDN18.2) targeted monoclonal antibody, plus CAPOX (a combination chemotherapy regimen that includes capecitabine and oxaliplatin) versus placebo plus CAPOX in patients with CLDN18.2-positive, HER2-negative, locally advanced unresectable or metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma.

In the study, investigational treatment zolbetuximab plus CAPOX demonstrated a statistically significant improvement in progression-free survival (PFS) compared to placebo plus CAPOX. Specifically, zolbetuximab plus CAPOX reduced the risk of progression or death by 31.3% (n=507; hazard ratio [HR]=0.687; [95% confidence interval [CI]: (0.544-0.866)]; p=0.0007) compared to placebo plus CAPOX, meeting GLOW's primary endpoint. Median PFS was 8.21 months (95% CI: 7.46–8.84) in the treatment arm and 6.80 months (95% CI: 6.14–8.08) in the placebo arm.

The study also showed that zolbetuximab plus CAPOX significantly prolonged overall survival (OS), a key secondary endpoint, reducing the risk of death by 22.9% (HR=0.771; 95% CI: 0.615-0.965; p=0.0118). Median OS was 14.39 months (95% CI: 12.29-16.49) and 12.16 months (95% CI: 10.28-13.67) for the treatment arm and placebo arm, respectively.

The incidence of serious treatment-emergent adverse events (TEAEs) was similar between both arms (47.2% versus 49.8% in the zolbetuximab versus placebo arms, respectively) and consistent with previous studies.[1] The most frequent TEAEs in the GLOW study were nausea (68.5% versus 50.2%), vomiting (66.1% versus 30.9%) and decreased appetite (41.3% versus 33.7%) in the zolbetuximab versus placebo arms.

"The progression-free and overall survival data from GLOW demonstrate the potential of zolbetuximab in patients with CLDN18.2-positive, HER2-negative, locally advanced unresectable or metastatic gastric and gastroesophageal junction cancer," said Rui-Hua Xu, M.D., Ph.D., Professor in the Department of Medical Oncology, Sun Yat-Sen University Cancer Center, Guangzhou, China, and the primary investigator of GLOW. "While the

treatment landscape is continuing to evolve, patients at this stage of the disease are in need of options and the GLOW data are encouraging for this patient population."

These detailed results from the GLOW trial will be presented at the March American Society of Clinical Oncology (ASCO) Plenary Series (Wednesday, March 22, 2023, at 4:00 p.m. ET) by Manish A. Shah, M.D., Medical Oncologist and Director of the Gastrointestinal Oncology Program, Weill Cornell Medicine, New York.

"We are committed to the ongoing clinical development of zolbetuximab and to bringing new therapeutic options for patients with locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma," said Ahsan Arozullah, M.D., M.P.H., Senior Vice President and Head of Development Therapeutic Areas, Astellas. "These two statistically significant Phase 3 trials, GLOW and SPOTLIGHT, will serve as the basis for global regulatory submissions, marking remarkable progress in our gastric cancer development program."

The GLOW and SPOTLIGHT studies are a part of Astellas' gastric cancer development program to investigate targeted treatment options such as zolbetuximab and address patient needs in locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma. In both trials, approximately 38% of these patients had CLDN18.2-positive tumors (≥75% of tumor cells with strong-to-moderate membranous CLDN18.2 staining intensity), as determined by a validated immunohistochemistry assay.[2]

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.[3] 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.[4] Signs of more advanced gastric cancer can include unexplained weight loss, weakness and fatigue and vomiting blood or having blood in the stool.[5] Risk factors associated with gastric cancer can include older age, male gender, family history, H. pylori infection, smoking and gastroesophageal reflux disease (GERD).[4,6] 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.[4] The five-year relative survival rate for patients at the metastatic stage is approximately six percent.[7] Gastroesophageal junction (GEJ) adenocarcinoma is a cancer that starts at the area where the esophagus joins the stomach.[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).[9] The safety and efficacy of zolbetuximab are under investigation in gastric, gastroesophageal junction 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 gastroesophageal junction cancer. The study enrolled 507 patients at 166 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 215 study locations in the U.S., Canada, 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.

Pipeline in Claudin 18.2
In addition to zolbetuximab, ASP2138 is under development in our Primary Focus Immuno-Oncology. ASP2138 is currently in a Phase 1 trial for people with gastric, gastroesophageal junction or pancreatic cancer.

For more information about ASP2138, please visit clinicaltrials.gov under Identifier NCT05365581.

An expanded Phase 2 trial (NCT03816163) in metastatic pancreatic cancer 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 cancer with CLDN18.2-positive tumors (defined as ≥75% of tumor cells demonstrating strong-to-moderate membranous CLDN18.2 staining based on a validated immunohistochemistry assay).

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.

###

Contacts for inquiries or additional information:

Astellas Portfolio Communications
Elysia Wood
+1-703-722-4656
elysia.wood@astellas.com

Astellas Pharma Inc.
Corporate Advocacy & Relations
+81-3-3244-3201

References

[1] Shitara K, Lordick F, Bang YJ, et al: Zolbetuximab + mFOLFOX6 as first-line treatment for patients with claudin-18.2+/HER2− locally advanced unresectable or metastatic gastric or gastroesophageal junction adenocarcinoma: Primary results from phase 3 SPOTLIGHT study. 2023 ASCO GI Cancers Symposium. Abstract LBA292. Presented January 19, 2023.

[2] Data on file. Northbrook, Ill. Astellas Pharma Inc.

[3] Sung H, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49.

[4] American Cancer Society. Signs and symptoms of stomach cancer (01-22-2021). Available at https://www.cancer.org/cancer/stomach-cancer/detection-diagnosis-staging/signs-symptoms.html. Last accessed February 21, 2023.

[5] National Cancer Institute. Gastric cancer treatment (PDQ®): patient version (08-24-2021). Available at https://www.cancer.gov/types/stomach/patient/stomach-treatment-pdq. Last accessed February 21, 2023.

[6] American Cancer Society. Esophageal cancer risk factors (06-09-2020). Available at https://www.cancer.org/cancer/esophagus-cancer/causes-risks-prevention/risk-factors.html. Last accessed February 21, 2023.

[7] National Cancer Institute. Surveillance, Epidemiology, and End Results Program. Cancer stat facts: stomach cancer. Available at https://seer.cancer.gov/statfacts/html/stomach.html. Last accessed February 21, 2023.

[8] American Cancer Society. About esophagus cancer (03-20-2020). Available at https://www.cancer.org/content/dam/CRC/PDF/Public/8614.00.pdf. Last accessed February 21, 2023.

[9] Sahin U, et al. FAST: a randomised phase II study of zolbetuximab (IMAB362) plus EOX versus EOX alone for first-line treatment of advanced CLDN18.2-positive gastric and gastro-oesophageal adenocarcinoma. Ann Oncol. 2021;32(5):609-19.