Press Release

Astellas to Present Positive Findings from Phase 3 SPOTLIGHT Trial of Zolbetuximab during 2023 ASCO GI Cancers Symposium

Data shows investigational zolbetuximab reduced risk of progression or death by 24.9%

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

Data to be featured in late-breaking oral presentation

TOKYO, Jan. 19, 2023 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today will present detailed results from the Phase 3 SPOTLIGHT trial evaluating first-line treatment with zolbetuximab, an investigational first-in-class Claudin 18.2 (CLDN18.2) targeted monoclonal antibody, plus mFOLFOX6 (a combination regimen that includes oxaliplatin, leucovorin and fluorouracil) versus placebo plus mFOLFOX6 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 mFOLFOX6 demonstrated statistically significant improvements in progression-free survival (PFS) and overall survival (OS) compared to placebo plus mFOLFOX6. Specifically, zolbetuximab plus mFOLFOX6 reduced the risk of progression or death by 24.9% (n=565; Hazard Ratio [HR]=0.751; [95% Confidence Interval [CI]: (0.598-0.942)]; P=0.0066) compared to placebo plus mFOLFOX6, meeting SPOTLIGHT's primary endpoint. Median PFS was 10.61 months (95% CI: 8.90-12.48) in the treatment arm and 8.67 months (95% CI: 8.21-10.28) in the placebo arm. The study also showed that zolbetuximab plus mFOLFOX6 significantly prolonged OS, reducing the risk of death by 25.0% (HR=0.750; 95% CI: 0.601-0.936; P=0.0053). Median OS was 18.23 months (95% CI: 16.43-22.90) and 15.54 months (95% CI: 13.47-16.53) for the treatment arm and placebo arm, respectively.

The incidence of serious treatment-emergent adverse events (TEAEs) was similar between both arms (44.8% versus 43.5% in the zolbetuximab versus placebo arms) and consistent with previous studies. The most frequent TEAEs in the SPOTLIGHT study were nausea (82.4% versus 60.8%), vomiting (67.4% versus 35.6%) and decreased appetite (47.0% versus 33.5%).

These new data from the SPOTLIGHT trial will be presented today at the 2023 American Society of Clinical Oncology (ASCO) Gastrointestinal (GI) Cancers Symposium in an oral presentation (Abstract LBA292; January 19, 1:30 p.m. PT) by Kohei Shitara, MD, Primary Investigator for SPOTLIGHT Study and Chief, Department of Gastrointestinal Oncology, the National Cancer Center Hospital East in Kashiwa, Japan.

“For gastric and gastroesophageal junction cancer patients with disease that is locally advanced but inoperable or metastatic, to see a positive progression-free and overall survival response in SPOTLIGHT is very encouraging given the limited treatment options available,” said Dr. Shitara.

“The investigational results from SPOTLIGHT are exciting and support the potential of zolbetuximab as a precision therapy for patients with CLDN18.2-positive gastric/GEJ cancer,” said Ahsan Arozullah, MD, MPH, Senior Vice President and Head of Development Therapeutic Areas, Astellas. “The SPOTLIGHT data, along with the positive topline results from the GLOW Phase 3 trial announced in December, build a strong foundation for our ongoing regulatory discussions for zolbetuximab and mark valuable progress towards our mission of turning innovative science into VALUE for patients.”

The SPOTLIGHT and GLOW studies are a 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 GEJ adenocarcinoma. In both trials, approximately 38% of these patients have CLDN18.2-positive tumors (CLDN18.2 expression in ≥75% of tumor cells with strong-to-moderate staining intensity), as determined by a validated immunohistochemistry assay.1 Based on these findings, an estimated 82,000 patients globally may be eligible for zolbetuximab annually, if approved.[1]

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.[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 and loss of appetite and sensation of food getting stuck in the throat while eating.[3] Signs of more advanced gastric cancer can include unexplained weight loss, weakness and fatigue and vomiting blood or having blood in the stool.[4] Risk factors associated with gastric cancer can include older age, male gender, family history, H. pylori infection, smoking and gastroesophageal reflux disease (GERD).[4,5] 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.[6] Gastroesophageal junction (GEJ) adenocarcinoma is a cancer that starts at the area where the esophagus joins the stomach.[7]

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).[8] 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 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 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 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 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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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

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