Taiho Oncology and Servier To Present Data on LONSURF® (trifluridine and tipiracil) at 2021 ASCO Gastrointestinal Cancers Symposium (ASCO GI)

PRINCETON, N.J., January 12, 2021 – Taiho Oncology, Inc. and Servier today announced that data for LONSURF® (trifluridine and tipiracil) in previously treated patients with metastatic gastric cancer (mGC) and metastatic gastroesophageal junction adenocarcinoma (mGEJC) will be presented during the 2021 American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO GI), taking place virtually from January 15-17, 2021. Key presentations include:

- **The impact of prior therapies on outcomes with trifluridine/tipiracil (FTD/TPI) in the phase III TAGS trial:** Kohei Shitara, MD, Chief, Department of Gastrointestinal Oncology, National Cancer Center Hospital East, Kashiwa (Abstract 247). Results will be shared online as a poster presentation on January 15, 2021. The abstract for this presentation is available on the ASCO GI website: https://meetinglibrary.asco.org/record/194068/abstract

- **Trifluridine/tipiracil outcomes in third- or later lines versus placebo in metastatic gastric cancer treatment: An exploratory subgroup analyses from the TAGS study:** Josep Tabernero, MD, PhD, Head of Medical Oncology, Vall d'Hebron Barcelona Hospital, and Director, Vall d'Hebron Institute of Oncology (VHIO). (Abstract 229). Results will be shared online as a poster presentation on January 15, 2021. The abstract for this presentation is available on the ASCO GI website: https://meetinglibrary.asco.org/record/194009/abstract

- **Body weight loss (BWL) as a prognostic/predictive factor in previously treated patients (pts) with metastatic gastric or gastroesophageal junction cancer (mGC/GEJC): Post-hoc analyses of the phase III TAGS trial:** Michele Ghidini, MD, PhD, Medical Oncologist, Department of Oncology, Azienda Ospedaliera di Cremona, Cremona, Italy (Abstract 476). Results will be shared online as a poster presentation on January 15, 2021. The abstract for this presentation is available on the ASCO GI website: https://meetinglibrary.asco.org/record/194263/abstract

Additional information can be found at Taiho Oncology's virtual Medical Booth when the exhibit opens on January 15, 2021.

"We are pleased to facilitate the global collaboration of the TAGS investigators, which is reflected in these abstracts," said Karin Blakolmer, MD, MBA, Senior Vice President and Head of Medical Affairs, Taiho Oncology, Inc. "This partnership is critical as we continue to seek opportunities to optimize the use of LONSURF for patients suffering from advanced gastric cancer."

“These data will continue to broaden our knowledge of how LONSURF performs in patients living with metastatic gastric cancer and gastroesophageal junction adenocarcinoma following previous rounds of treatment,” said François Druguet, Head of Global Medical Affairs Oncology, Servier.

The U.S. Food and Drug Administration (FDA) approved LONSURF in previously treated mGC and mGEJC in February 2019.[1] The approval builds on the initial U.S. approval of LONSURF in 2015 for the treatment of adult patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy.[1]

About TAGS
The TAGS (***TA***S-102 ***G***astric ***S***tudy) trial was a Taiho-sponsored, global, pivotal Phase III, multinational, randomized, double-blind study evaluating LONSURF (trifluridine and tipiracil, FTD/TPI), plus best supportive care (BSC) versus placebo plus BSC in patients with metastatic gastric cancer, including gastroesophageal junction cancer, refractory to standard treatments. The primary endpoint in the TAGS trial was overall survival (OS), and the main secondary endpoint measures included progression-free survival (PFS), safety and tolerability, as well as quality of life.

The TAGS trial enrolled 507 adult patients with metastatic gastric cancer who had previously received at least two prior regimens for advanced disease. The study was conducted in 17 countries and 110 sites around the world.

About Metastatic Gastric Cancer
Gastric cancer, also known as stomach cancer, is the 15th most commonly diagnosed cancer in the U.S.[2] In 2020, there were an estimated 27,600 new cases and 11,010 deaths.[2] Approximately 36 percent of U.S. patients with gastric cancer are diagnosed at advanced disease.[2] Metastatic gastric cancer (mGC) is associated with a five-year survival rate of about 5.5 percent.[2]

In the U.S., standard chemotherapy regimens for advanced gastric cancer include fluoropyrimidines, platinum derivatives, and taxanes (with ramucirumab), or irinotecan. After failure of first- and second-line therapies, subsequent treatment options are limited.

About Gastroesophageal Junction Cancer
Gastroesophageal junction cancer is a type of cancer that begins in cells located near the gastroesophageal junction, the area where the esophagus connects to the stomach.[3] It remains a significant clinical problem that is increasing in incidence and is associated with a poor prognosis. The majority of patients present with advanced disease, and less than 50 percent undergo curative treatment.[4]

About LONSURF[1]

LONSURF is an oral nucleoside antitumor agent discovered and developed by Taiho Pharmaceutical Co., Ltd. LONSURF consists of a thymidine-based nucleoside analog, trifluridine, and the thymidine phosphorylase (TP) inhibitor, tipiracil, which increases trifluridine exposure by inhibiting its metabolism by TP. Trifluridine is incorporated into DNA, resulting in DNA dysfunction and inhibition of cell proliferation.

Since 2015, Taiho Pharmaceutical and Servier have been in an exclusive license agreement for the co-development and commercialization of LONSURF in Europe and other countries outside of the United States, Canada, Mexico, and Asia.

Indications and Use
LONSURF is indicated for the treatment of adult patients with:

- metastatic colorectal cancer previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy
- metastatic gastric or gastroesophageal junction adenocarcinoma previously treated with at least two prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan, and if appropriate, HER2/neu-targeted therapy.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Severe Myelosuppression:

LONSURF caused severe and life-threatening myelosuppression (Grade 3-4) consisting of neutropenia (38%), anemia (18%), thrombocytopenia (5%), and febrile neutropenia (3%). Two patients (0.2%) died due to neutropenic infection. A total of 12% of LONSURF-treated patients received granulocyte-colony stimulating factors. Obtain complete blood counts prior to and on day 15 of each cycle of LONSURF and more frequently as clinically indicated. Withhold LONSURF for febrile neutropenia, absolute neutrophil count less than 500/mm^3, or platelets less than 50,000/mm^3. Upon recovery, resume LONSURF at a reduced dose as clinically indicated.

Embryo-Fetal Toxicity:

LONSURF can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 6 months after the final dose.

USE IN SPECIFIC POPULATIONS

Lactation: It is not known whether LONSURF or its metabolites are present in human milk. There are no data to assess the effects of LONSURF or its metabolites on the

breast-fed infant or the effects on milk production. Because of the potential for serious adverse reactions in breast-fed infants, advise women not to breastfeed during treatment with LONSURF and for 1 day following the final dose.

Male Contraception: Because of the potential for genotoxicity, advise males with female partners of reproductive potential to use condoms during treatment with LONSURF and for at least 3 months after the final dose.

Geriatric Use: Patients 65 years of age or over who received LONSURF had a higher incidence of the following compared to patients younger than 65 years: Grade 3 or 4 neutropenia (46% vs 32%), Grade 3 anemia (22% vs 16%), and Grade 3 or 4 thrombocytopenia (7% vs 4%).

Hepatic Impairment: Do not initiate LONSURF in patients with baseline moderate or severe (total bilirubin greater than 1.5 times ULN and any AST) hepatic impairment. Patients with severe hepatic impairment (total bilirubin greater than 3 times ULN and any AST) were not studied. No adjustment to the starting dose of LONSURF is recommended for patients with mild hepatic impairment.

Renal Impairment: No adjustment to the starting dosage of LONSURF is recommended in patients with mild or moderate renal impairment (CLcr of 30 to 89 mL/min). Reduce the starting dose of LONSURF for patients with severe renal impairment (CLcr of 15 to 29 mL/min) to a recommended dosage of 20 mg/m^2.

ADVERSE REACTIONS

Most Common Adverse Drug Reactions in Patients Treated With LONSURF (≥5%): The most common adverse drug reactions in LONSURF-treated patients vs placebo-treated patients with mCRC, respectively, were asthenia/fatigue (52% vs 35%), nausea (48% vs 24%), decreased appetite (39% vs 29%), diarrhea (32% vs 12%), vomiting (28% vs 14%), infections (27% vs 16%), abdominal pain (21% vs 18%), pyrexia (19% vs 14%), stomatitis (8% vs 6%), dysgeusia (7% vs 2%), and alopecia (7% vs 1%). In metastatic gastric cancer or gastroesophageal junction (GEJ), the most common adverse drug reactions, respectively were, nausea (37% vs 32%), decreased appetite (34% vs 31%), vomiting (25% vs 20%), infections (23% vs 16%) and diarrhea (23% vs 14%).

Pulmonary emboli occurred more frequently in LONSURF-treated patients compared to placebo: in mCRC (2% vs 0%) and in metastatic gastric cancer and GEJ (3% vs 2%).

Interstitial lung disease (0.2%), including fatalities, has been reported in clinical studies and clinical practice settings in Asia.

Laboratory Test Abnormalities in Patients Treated With LONSURF: The most common laboratory test abnormalities in LONSURF-treated patients vs placebo-treated patients with mCRC, respectively, were anemia (77% vs 33%), neutropenia (67% vs

1%), and thrombocytopenia (42% vs 8%). In metastatic gastric cancer or GEJ, the test abnormalities, respectively, were neutropenia (66% vs 4%), anemia (63% vs 38%), and thrombocytopenia (34% vs 9%).

Please see full Prescribing Information.
https://www.taihooncology.com/us/prescribing-information.pdf

About Taiho Oncology, Inc. (U.S.)
Taiho Oncology, Inc., a subsidiary of Taiho Pharmaceutical Co., Ltd. and Otsuka Holdings Co., Ltd., has established a world class clinical development organization that works urgently to develop innovative cancer treatments and has built a commercial business in the U.S. Taiho Oncology has an oral oncology pipeline consisting of selectively targeted agents. Advanced technology, dedicated researchers, and state of the art facilities are helping us to define the way the world treats cancer. It's our work; it's our passion; it's our legacy.

For more information about Taiho Oncology, please visit:
https://www.taihooncology.com/us

For more information about Taiho Pharmaceutical Co., Ltd., please visit:
https://www.taiho.co.jp/en/

For more information about Otsuka Holdings Co., Ltd., please visit:
https://www.otsuka.com/en/

About Servier
Servier is an international pharmaceutical company governed by a non-profit foundation, with its headquarters in France (Suresnes). With a strong international presence in 150 countries and a total revenue of 4.6 billion euros in 2019, Servier employs 22,000 people worldwide. Entirely independent, the Group invests on average 25% of its total revenue (excluding generics) every year in research and development and uses all its profits for its development. Corporate growth is driven by Servier's constant commitment in five areas of excellence: cardiovascular, immune-inflammatory, and neurodegenerative diseases, cancer and diabetes, as well as by its activities in high-quality generic drugs. Servier also offers eHealth solutions beyond drug development. More information: www.servier.com

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[1] LONSURF [US prescribing information]; Princeton, NJ: Taiho Oncology, Inc.; 2020. 2020.

[2] National Cancer Institute Surveillance Epidemiology and End Results Program. Cancer Stat Facts: Stomach Cancer. https://seer.cancer.gov/statfacts/html/stomach.html. Accessed December 2020.

[3] The Migration of Gastric Cancer to the GE Junction. *Johns Hopkins Surgery*. Summer 2014. https://www.hopkinsmedicine.org/news/publications/johns_hopkins_surgery/johns_hopkins_surgery_summer_2014/the_migration_of_gastric_cancer_to_the_ge_junction. Accessed December 2020.

[4] Barbour A, Rizk, N, Gonen, M, et al. Adenocarcinoma of the gastroesophageal junction. *Ann Surg*. 2007 Jul; 246(1): 1-8.