**Taiho Oncology and Servier Present LONSURF® (trifluridine and tipiracil) Data at the 2019 ASCO Annual Meeting**

PRINCETON, N.J., June 3, 2019 – Taiho Oncology, Inc. and Servier announced today clinical data with LONSURF® (trifluridine and tipiracil, TAS-102) in previously treated patients with metastatic gastric cancer (mGC), metastatic gastroesophageal junction adenocarcinoma (mGEJC) and metastatic colorectal cancer (mCRC) were presented at the 2019 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, IL.

"We are pleased to present additional pooled data from two Phase 3 trials, TAGS and RECOURSE, that expand our understanding of the clinical profile of LONSURF in metastatic gastric and colorectal cancers," said Martin J. Birkhofer, MD, Senior Vice President and Chief Medical Officer, Taiho Oncology, Inc. "Data presented at ASCO provide additional evidence that LONSURF is well tolerated and offers consistent efficacy and safety across these gastrointestinal tumors."

Among the data presented were:

- A subgroup analysis from the Phase 3 TAGS trial demonstrates a manageable safety profile and consistent efficacy in patients with previously treated mGEJC. The abstract for this presentation is available on the ASCO website: http://abstracts.asco.org/239/AbstView_239_255129.html

- A second subgroup analysis from the Phase 3 TAGS trial in previously treated mGC and mGEJC patients demonstrates safety and efficacy of LONSURF in patients 65 and older who have a higher incidence of moderate renal impairment vs the overall population. The abstract for this presentation is available on the ASCO website: http://abstracts.asco.org/239/AbstView_239_255071.html

- Health-related quality of life (HRQoL) data from the Phase 3 TAGS trial in previously treated mGC and mGEJC patients shows that treatment with LONSURF is associated with a trend toward a lower risk of QoL deterioration than placebo consistent across all symptoms and functional scales. The abstract for this presentation is available on the ASCO website: http://abstracts.asco.org/239/AbstView_239_258457.html

- A pooled safety analysis of patients receiving at least one dose of LONSURF in the two Phase 3 TAGS and RECOURSE trials demonstrates a consistent safety profile across patients with mGC/mGEJC or mCRC compared with placebo. The abstract for this presentation is available on the ASCO website: http://abstracts.asco.org/239/AbstView_239_255175.html

In February 2019, the U.S. Food and Drug Administration (FDA) approved LONSURF for the treatment of adult patients with 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. LONSURF is also indicated in the U.S. for the treatment of patients with mCRC 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**
TAGS (***TA***S-102 ***G***astric ***S***tudy) is a Taiho-sponsored, global, randomized, double-blind, placebo controlled, Phase 3 study evaluating the efficacy and safety of LONSURF in 507 adult patients with previously treated mGC or mGEJC. The primary endpoint was overall survival (OS), and the key secondary endpoints included progression-free survival (PFS), safety and tolerability, as well as quality of life. LONSURF demonstrated statistically significant improvement in OS and PFS compared with placebo. The median OS improved from 3.6 months with placebo to 5.7 months with LONSURF, HR 0.69 (95% confidence interval [CI], 0·56-0·85; P=0.00058).

For more information on TAGS, please visit www.ClinicalTrials.gov (https://clinicaltrials.gov/ct2/show/NCT02500043). The ClinicalTrials.gov Identifier is NCT02500043.

**About RECOURSE**
The RECOURSE trial is a global, randomized, double-blind, placebo-controlled Phase 3 trial evaluating the efficacy and safety of LONSURF in patients with previously treated mCRC. The trial enrolled 800 patients in North America, Japan, Europe and Australia. Patients were randomized (2:1) to receive LONSURF (35 mg/m$^2$) or placebo, plus BSC, twice daily. The study met its primary and secondary endpoints of OS and PFS versus placebo. The median OS improved from 5.3 months with placebo to 7.1 months with LONSURF, HR 0.68 (95% CI, 0.58 to 0.81; P<0.001).

**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[1]**

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/mm3, or platelets less than 50,000/mm3. 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). Patients with severe renal impairment (CLcr < 30 mL/min) were not studied.

**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: (2% vs 0%) in mCRC and (3% vs 2%) in metastatic gastric cancer and GEJ.

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:** 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 has an oral oncology pipeline consisting of both novel

antimetabolic agents and 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 149 countries and a turnover of 4.2 billion euros in 2018, Servier employs 22 000 people worldwide. Entirely independent, the Group reinvests 25% of its turnover (excluding generics) in research and development and uses all its profits for development. Corporate growth is driven by Servier's constant search for innovation 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.

Becoming a key player in oncology is part of Servier's long-term strategy. Currently, there are twelve molecular entities in clinical development in this area, targeting gastro-intestinal and lung cancers and other solid tumors, as well as different types of leukemia and lymphomas. This portfolio of innovative cancer treatments is being developed with partners worldwide, and covers different cancer hallmarks and modalities, including cytotoxics, proapoptotics, immune targeted therapies, to deliver life-changing medicines to patients. More information: www.servier.com

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[1] LONSURF [US prescribing information]; Princeton, NJ: Taiho Oncology, Inc.; 2019. 2019.