Taiho Oncology and Servier Present Data on LONSURF® (trifluridine/tipiracil) at ASCO 2019 Gastrointestinal Cancers Symposium (ASCO GI)

PRINCETON, N.J., January 17, 2019 – Taiho Oncology, Inc. and Servier announced today that the safety and efficacy in patients with gastrectomy from the global Phase 3 TAGS trial evaluating LONSURF® in patients with previously treated metastatic gastric cancer (mGC) are consistent with the overall study results published in *The Lancet Oncology*. These data were highlighted at the ASCO 2019 Gastrointestinal Cancers Symposium (ASCO GI) on Thursday, January 17 during an oral presentation at 2:45 PM PST and during a poster presentation at 11:30 AM-1:00 PM and 5:30 PM-6:30 PM PST. Additional data with LONSURF in metastatic colorectal cancer (mCRC) patients will be presented during a poster session on Saturday, January 19.

In the TAGS trial, 221 (44%) of the 507 randomized mGC patients had undergone prior gastrectomy (147 LONSURF, 74 placebo), which is reflective of the real-world patient population diagnosed with mGC. The results confirmed that LONSURF prolonged survival versus placebo regardless of prior gastrectomy.

“We are pleased to present this subgroup analysis from TAGS in patients with metastatic gastric cancer who had undergone gastrectomy, which further support LONSURF as safe and effective for patients with this life-threatening condition for which treatment options are limited,” said Martin J. Birkhofer, MD, senior vice president and Chief Medical Officer, Taiho Oncology, Inc. “These data further add to the existing body of evidence that already support the benefit of LONSURF for people living with metastatic colorectal cancer.”

The following LONSURF data posters will be presented on Saturday, January 19:

- Exploratory analysis of the effect of FTD/TPI in patients treated in RECOURSE by prognostic factors
- Trifluridine/tipiracil (FTD/TPI) and regorafenib (REG) in patients with metastatic colorectal cancer (mCRC): A single institution retrospective study
- Health-related quality of life in the early-access phase 3b study of trifluridine/tipiracil in pretreated metastatic colorectal cancer (mCRC): Results from PRECONNECT study
- Validation of cost-effectiveness of trifluridine/tipiracil versus best supportive care and regorafenib for previously treated metastatic colorectal cancer in the UK using phase IIIb PRECONNECT early access clinical trial data in the real world setting
- QoI from TASCO1: Health related quality of life of trifluridine/tipiracil-bevacizumab and capecitabine-bevacizumab as first-line treatments in metastatic colorectal cancer patients not eligible for intensive chemotherapy: results from the TASCO1 phase 2 study

LONSURF is indicated in the United States for the treatment of 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
TAGS (***TA***S-102 ***G***astric ***S***tudy) is a Taiho-sponsored pivotal Phase III, multinational, randomized, double-blind study evaluating trifluridine/tipiracil, also known as TAS-102, 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 is overall survival (OS), and the main secondary endpoint measures include progression-free survival (PFS), and safety and tolerability, as well as quality of life.

TAGS 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 Belarus, the European Union, Israel, Japan, Russia, Turkey, and the United States.

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

About Metastatic Colorectal Cancer
Colorectal cancer is the fourth most commonly diagnosed cancer in the United States (U.S.).[2] In 2018, there were an estimated 140,250 new cases and 50,630 deaths in the U.S.[2,3] Approximately 21 percent of U.S. patients with colorectal cancer are diagnosed at the distant or metastasized stage, and between 50 percent and 60 percent of patients develop metastases.[2] Metastatic colorectal cancer (mCRC) is associated with poor prognosis with a five-year survival rate of approximately 14 percent.[2]

Over the last decade, clinical outcomes for patients with mCRC have improved considerably due to the advent of novel treatment agents, predictive biomarkers, and a more strategic approach to the delivery of systemic therapies. Currently, the median overall survival for patients with mCRC being treated both in phase III trials and in large observational series or registries is 30 months – more than double that of 20 years ago.[4,5,6]

About LONSURF
LONSURF consists of a thymidine-based nucleoside analog, trifluridine, and the thymidine phosphorylase inhibitor, tipiracil, at a molar ratio 1:0.5 (weight ratio, 1:0.471). Inclusion of tipiracil increases trifluridine exposure by inhibiting its metabolism by thymidine phosphorylase. Following uptake into cancer cells, trifluridine is incorporated into DNA, interferes with DNA synthesis and inhibits cell proliferation. Trifluridine/tipiracil demonstrated anti-tumor activity against KRAS wild-type and mutant human colorectal cancer xenografts in mice.

In Japan, Taiho Pharmaceutical Co., Ltd. has been marketing LONSURF for the treatment of unresectable advanced or recurrent colorectal cancer since 2014. In the United States, beginning in 2015, Taiho Oncology, Inc., a U.S. subsidiary of Taiho Pharmaceutical, began marketing the drug 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. In June 2015, Taiho Pharmaceutical and Servier entered into 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. In parts of Asia outside of Japan, Taiho Pharmaceutical's business partner TTY Biopharm launched LONSURF in Taiwan in July 2018, and Jeil Pharmaceutical is preparing to bring the drug to market in South Korea.

As of November 2018, LONSURF has been approved as a treatment for advanced mCRC in 62 countries and regions worldwide.

Indications and Use[1]
LONSURF is a combination of trifluridine, a nucleoside metabolic inhibitor, and tipiracil, a thymidine phosphorylase inhibitor, indicated for the treatment of 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.

Important Safety Information[1]

WARNINGS AND PRECAUTIONS

Severe Myelosuppression: In Study 1, LONSURF caused severe and life-threatening myelosuppression (Grade 3-4) consisting of anemia (18%), neutropenia (38%), thrombocytopenia (5%), and febrile neutropenia (3.8%). One patient (0.2%) died due to neutropenic infection. In Study 1, 9.4% 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, Grade 4 neutropenia, 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 with LONSURF.

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 (48% vs 30%), Grade 3 anemia (26% vs 12%), and Grade 3 or 4 thrombocytopenia (9% vs 2%).

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. Do not initiate LONSURF in patients with baseline moderate or severe (total bilirubin greater than 1.5 times ULN and any AST) hepatic impairment.

Renal Impairment: In Study 1, patients with moderate renal impairment (CLcr=30 to 59 mL/min, n=47) had a higher incidence (difference of at least 5%) of ≥Grade 3 adverse events, serious adverse events, and dose delays and reductions compared to patients with normal renal function (CLcr ≥90 mL/min, n=306) or patients with mild renal impairment (CLcr=60 to 89 mL/min, n=178).

Patients with moderate renal impairment may require dose modifications for increased toxicity. Patients with severe renal impairment 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 refractory 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%), abdominal pain (21% vs 18%), pyrexia (19% vs 14%), stomatitis (8% vs 6%), dysgeusia (7% vs 2%), and alopecia (7% vs 1%).

Additional Important Adverse Drug Reactions: The following occurred more frequently in LONSURF-treated patients compared to placebo: infections (27% vs 15%) and pulmonary emboli (2% vs 0%).

The most commonly reported infections which occurred more frequently in LONSURF-treated patients were nasopharyngitis (4% vs 2%) and urinary tract infections (4% 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: Laboratory test abnormalities in LONSURF-treated patients vs placebo-treated patients with refractory mCRC, respectively, were anemia (77% vs 33%), neutropenia (67% vs 1%), and thrombocytopenia (42% vs 8%).

Please see full US Prescribing Information.
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.

About Taiho Pharmaceutical Co., Ltd. (Japan)
Taiho Pharmaceutical, a subsidiary of Otsuka Holdings Co., Ltd., is an R&D-driven specialty pharma focusing on the three fields of oncology, allergy and immunology, and urology. Its corporate philosophy takes the form of a pledge: "We strive to improve human health and contribute to a society enriched by smiles." In the field of oncology in particular, Taiho Pharmaceutical is known as a leading company in Japan for developing innovative medicines for the treatment of cancer, a reputation that is rapidly expanding through their extensive global R&D efforts. In areas other than oncology, as well, the company creates and markets quality products that effectively treat medical conditions and can help improve people's quality of life. Always putting customers first, Taiho Pharmaceutical also aims to offer consumer healthcare products that support people's efforts to lead fulfilling and rewarding lives.

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

About Otsuka Holdings Co., Ltd. (Japan)
The Otsuka group of companies is a total-healthcare enterprise that aims to contribute to the health of people around the world under the corporate philosophy, "Otsuka-people creating new products for better health worldwide."

Healthcare is broadly and holistically addressed through the two main pillars – the

pharmaceutical business for the diagnosis and treatment of diseases and the nutraceutical[*1] business to support the maintenance and promotion of everyday health. Our 46,000[*2] employees across 183 companies in 28 countries and regions take on challenges across various fields and themes to help fulfill the universal wish of people to be healthy. Our pursuit of these challenges is motivated by the Otsuka's corporate culture, articulated as "Ryukan-godo" (by sweat we recognize the way), "Jissho" (actualization) and "Sozosei" (creativity), and fostered by successive generations of Otsuka leaders. By striving to provide unique products and services, we seek to achieve sustainable growth and be an indispensable contributor to the world.

For more information, please visit the company's website at https://www.otsuka.com/en/.

*1. Nutraceuticals: nutrition + pharmaceuticals *2. As of end of December 2017

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 4.152 billion euros in 2017, Servier employs 21,700 people worldwide. Entirely independent, the Group reinvests 25% of its turnover (excluding generic drugs) 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 neuropsychiatric 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 various leukemias and lymphomas. This portfolio of innovative cancer treatments is being developed with partners worldwide, and covers different cancer hallmarks and modalities, including cytotoxics, proapoptotics, targeted therapies, to deliver life-changing medicines to patients.

For more information about Servier, please visit www.servier.com.

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[1] LONSURF [US prescribing information]; Princeton, NJ: Taiho Oncology, Inc.; 2017. 2017.
[2] National Cancer Institute Surveillance Epidemiology and End Results Program. Cancer Stat Facts: Colon and Rectum Cancer. https://seer.cancer.gov/statfacts/html/colorect.html. Accessed May 17, 2018.
[3] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA: a cancer journal for clinicians.* 2018;68(1):7-30. https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21442. Accessed December 2018.
[4] Brenner H, Kloor M, Pox CP. Colorectal cancer. *Lancet.* 2014;383(9927):1490-1502.
[5] Price TJ, Segelov E, Burge M, et al. Current opinion on optimal systemic treatment for metastatic colorectal cancer: outcome of the ACTG/AGITG expert meeting ECCO 2013. *Expert review of anticancer therapy*. 2014;14(12):1477-1493.
[6] Van Cutsem E, Cervantes A, Adam R, et al. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. *Ann Oncol*. 2016;27(8):1386-1422.