Press Release:
Taiho Oncology and Servier Present LONSURF® (trifluridine and tipiracil) Metastatic Colorectal Cancer (mCRC) Data at ASCO 2018 Gastrointestinal Cancers Symposium

PRINCETON, N.J., January 20, 2018 – Taiho Oncology, Inc. and Servier today announced clinical data for LONSURF® (trifluridine and tipiracil) for the treatment of patients with metastatic colorectal cancer (mCRC) who have been previously treated with fluropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild type, an anti-EGFR therapy. These data are being presented at the ASCO 2018 Gastrointestinal Cancers Symposium (ASCO-GI) in San Francisco during Poster Session C: Cancers of the Colon, Rectum, and Anus on Saturday, January 20 from 7:00 AM to 7:55 AM PT and 11:30 AM to 1:00 PM PT.

“These studies expand our knowledge of the safety and efficacy profile of LONSURF for the treatment of mCRC,” said Martin Birkhofer, senior vice president and Chief Medical Officer, Taiho Oncology, Inc. “By looking at various aspects of LONSURF therapy, we are able to better understand patient experience and how we can best help address the needs of people with mCRC.”

“We’re pleased to continue to add to the body of evidence that supports the clinical value of LONSURF for the treatment of mCRC” said Patrick Therasse, Head of R&D Oncology at Servier. “The data to be presented confirm the efficacy and safety profile of LONSURF as assessed in the controlled pivotal clinical RECOURSE trial in daily clinical practice.”

A phase I multicenter, open-label study examined the maximum tolerated dose (MTD) of a LONSURF and oxaliplatin combination in patients with mCRC. Taiho and Servier plan to further investigate the combination of oxaliplatin and LONSURF with bevacizumab or nivolumab in mCRC. The abstract for this presentation is available on the ASCO website: https://meetinglibrary.asco.org/record/155688/abstract.

A safety and tolerability assessment was conducted among elderly patients (age ≥65 years) with mCRC that participated in a LONSURF expanded access program in the US. The results of the analysis showed that the safety profile and treatment duration of LONSURF in patients aged 65 and older with mCRC were similar to those in patients aged under 65. The abstract for this presentation is available on the ASCO website: https://meetinglibrary.asco.org/record/155490/abstract.

A post-hoc analysis of the pivotal phase 3 RECOURSE study was conducted to assess the correlation between baseline neutrophil-to-lymphocyte ratios (NLR) in the blood of patients with refractory mCRC treated with LONSURF and clinical outcomes. Further research is warranted to assess if NLR can be a stratification factor in mCRC clinical trials. The abstract for this presentation is available on the ASCO website: https://meetinglibrary.asco.org/record/155625/abstract.

Preliminary data on the first 300 European and Australian patients in the international phase 3b early access program on LONSURF show a heavily pretreated mCRC population still seeking additional anti-cancer therapy. Baseline evaluations also indicated that pretreated mCRC patients can have impaired quality of life even if they have an ECOG PS of 0 or 1. Preliminary prospective safety, efficacy, and quality of life results from patients treated with LONSURF in this program are expected later in 2018. The abstract for this presentation is available on the ASCO website: https://meetinglibrary.asco.org/record/155528/abstract.

A retrospective study compared real-world treatment patterns with LONSURF and regorafenib for patients with mCRC from a large, representative U.S. claims database. A total of 1,630 LONSURF patients and 1,425 regorafenib patients were identified. The abstract for this presentation is available on the ASCO website: https://meetinglibrary.asco.org/record/155541/abstract.

About Metastatic Colorectal Cancer

Colorectal cancer is the third most common type of cancer, excluding skin cancers, in the United States, with an estimated 135,430 new patients diagnosed in 2017.[1] It is the second and third leading cause of cancer-related deaths among men and women, respectively.[1]

Colorectal cancers that have spread to other parts of the body are often harder to treat and tend to have a poorer outlook.[2] Metastatic, or stage IV colon and rectal cancers, have a five-year relative survival rate of about 11 and 12 percent, respectively.[2] Still, there are often many treatment options available for people with this stage of cancer.[2] Further, treatments have improved over the last few decades.[1] As a result, there are now more than one million survivors of colorectal cancer in the United States.[1]

About LONSURF (TAS-102)

LONSURF is a combination of trifluridine, a nucleoside metabolic inhibitor, and tipiracil, a thymidine phosphorylase inhibitor, indicated in US 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.[3] LONSURF is also available in EU[4], Japan, and other countries.

Important Safety Information[3]

WARNINGS AND PRECAUTIONS

Severe Myelosuppression: In RECOURSE Study, 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 RECOURSE Study, 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 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 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 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 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 45,000[*2] employees across 180 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 2016

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 148 countries and a turnover of 4 billion euros in 2016, Servier employs 21 000 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, cancers and diabetes, as well as by its activities in high-quality generic drugs.

Becoming a key player in oncology is part of Servier's long-term strategy. Currently, there are nine molecular entities in clinical development in this area, targeting gastric 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, immune and cellular therapies, to deliver life-changing medicines to patients.

More information: www.servier.com.

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[1] American Cancer Society; What are the key statistics about colorectal cancer? http://www.cancer.org/cancer/colonandrectumcancer/detailedguide/colorectal-cancer-key-statistics. Accessed December 2017.
[2] American Cancer Society; What Are the Survival Rates for Colorectal Cancer, by Stage? https://www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/survival-rates.html. Accessed December 2017.
[3] LONSURF [US prescribing information]; Princeton, NJ: Taiho Oncology, Inc.; 2017. 2017
[4] Lonsurf EU Summary of Product Characteristics (SmPC) ; August 2017: http://www.ema.europa.eu/ema/.

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