TAIHO ONCOLOGY

Taiho Oncology, Inc. Announces FDA Approval of LONSURF® (trifluridine and tipiracil) for Refractory Metastatic Colorectal Cancer (mCRC)

– LONSURF represents the first FDA-approved product for Taiho Oncology, setting the stage for the company's oncology pipeline –

PRINCETON, N.J., Sept. 22, 2015 – Taiho Oncology, Inc. (U.S.), a subsidiary of Taiho Pharmaceutical Co., Ltd. (Japan), today announced that the U.S. Food and Drug Administration (FDA) approved LONSURF® (trifluridine and tipiracil), formerly known as TAS-102, for the treatment of patients with metastatic colorectal cancer (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]

"Patients with metastatic colorectal cancer, whose disease has progressed after treatment with standard therapies, have had limited therapeutic options to treat their disease," said Eric Benn, Taiho Oncology's President and Chief Executive Officer. "LONSURF helps address this unmet medical need by providing patients with a new therapeutic option that can help extend their overall survival. As the first FDA approval for Taiho Oncology, LONSURF also represents a major milestone for our company."

"Metastatic colorectal cancer cells often become resistant to previously effective treatment, underscoring the importance of identifying new therapeutic options for patients with the disease," said Robert J. Mayer, MD, Faculty Vice President for Academic Affairs at the Dana Farber Cancer Institute, Professor of Medicine at Harvard Medical School, and Principal Investigator of the RECOURSE study. "In a pivotal clinical trial, LONSURF demonstrated that it can extend overall survival, providing patients and their oncologists with a novel oral therapy."

Pivotal Phase III Study Demonstrates Improvement in Overall Survival (OS)
The FDA approval of LONSURF is based on results from the global Phase III RECOURSE trial in 800 patients who have been previously treated for mCRC.[1]

The trial met the primary efficacy endpoint of statistically significant improvement in OS compared to placebo (HR = 0.68, CI: 0.58, 0.81, $p < 0.001$). LONSURF reduced the risk of death by 32 percent when compared to placebo. Median OS was 7.1 months (95 percent CI: 6.5, 7.8) and 5.3 months (95 percent CI: 4.6, 6.0) for LONSURF and placebo, respectively.[1]

LONSURF caused severe and life-threatening myelosuppression (Grade 3-4) consisting of anemia (18%), neutropenia (38%), thrombocytopenia (5%), and febrile neutropenia (3.8%). Complete blood counts should be obtained prior to and on Day 15 of each cycle of LONSURF and more frequently as clinically indicated. One patient (0.2%) died due to neutropenic infection.[1]

The most common adverse drug reactions or laboratory abnormalities were anemia, neutropenia, asthenia/fatigue, nausea, thrombocytopenia, decreased appetite, diarrhea, vomiting, abdominal pain, and pyrexia. The most common adverse reactions leading to dose reduction were neutropenia, anemia, febrile neutropenia, fatigue, and diarrhea.[1]

“Data from the pivotal RECOURSE study demonstrated a significant survival benefit for patients with refractory metastatic colorectal cancer, whose disease had progressed after standard therapies, reducing the risk of death in these patients by 32 percent,” said Fabio Benedetti, MD, Taiho Oncology’s Senior Vice President and Chief Medical Officer. “This significant milestone underscores our longstanding commitment to patients challenged by metastatic colorectal cancer and to bringing new treatment options to them.”

LONSURF was approved in Japan in March 2014 and is indicated to treat unresectable advanced or recurrent colorectal cancer.[2]

About Metastatic Colorectal Cancer
Colorectal cancer is the third most common type of cancer and is the second leading cause of cancer-related deaths in the U.S.[3] In the U.S., there were an estimated 136,830 patients diagnosed with cancer of the colon or rectum in 2014, and in 2012, there were an estimated 1.1 million individuals living with the disease.[4,5] Of those, about 27,400 patients will have had their cancer spread to another part of the body.[5]

About LONSURF
LONSURF is 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.[1]

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 percent 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.

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

Male Contraception: 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: Grade 3 or 4 neutropenia and thrombocytopenia and Grade 3 anemia occurred more commonly in patients 65 years old or older who received LONSURF.

Renal Impairment: Patients with moderate renal impairment may require dose modifications for increased toxicity. No patients with severe renal impairment were enrolled in Study 1.

Hepatic Impairment: Patients with moderate or severe hepatic impairment were not enrolled in Study 1.

ADVERSE REACTIONS

Most Common Adverse Drug Reactions in Patients Treated with LONSURF (≥ 5 percent): 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%).

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 Prescribing Information.

www.taihooncology.com/us/prescribing-information.pdf

To view the FDA Press Release, please see the following link.

http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm463650.htm

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: 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, allergies 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 and around the world for developing innovative medicines for the treatment of cancer. In areas other than oncology, as well, the company creates quality products that effectively treat medical conditions and can help improve people's quality of life. Always putting customers first, Taiho Pharmaceutical aims to also offer over-the-counter medicinal products that support people's efforts to lead fulfilling and rewarding lives.

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

About Otsuka Holdings Co., Ltd. (Japan)
The Otsuka Group is a global organization of 176 healthcare companies with nearly 43,000 employees (including unconsolidated subsidiaries). Otsuka Holdings Co., Ltd. is the Group's holding company. The Group operates in 27 countries and regions, conducting diversified businesses in four segments all connected by a focus on health: pharmaceuticals, nutraceuticals, consumer products, and others.[6]

The Group's corporate philosophy of "Otsuka-people creating new products for better health worldwide," is supported by the corporate ethic of "JISSHO (Proof through Execution) and SOZOSEI (Creativity)." The Otsuka Group thus seeks to foster a culture and vitality appropriate to an enterprise involved with human health and to create innovative products that contribute to the health and wellness of people worldwide.

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

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References

1. LONSURF [prescribing information]; Princeton, NJ: Taiho Oncology, Inc.; 2015.
2. Taiho Pharma; Taiho's Lonsurf® (trifluridine and tipiracil hydrochloride) Tablets Approved in Japan for Treatment in Advanced Metastatic Colorectal Cancer. March 24, 2014. http:/www.taiho.co.jp/english/news/20140324.html. Accessed September 2015.
3. American Cancer Society; What are the key statistics about colorectal cancer? http://www.cancer.org/cancer/colonandrectumcancer/detailedguide/colorectal-cancer-key-statistics. Accessed September 2015.
4. American Cancer Society; Cancer Facts & Figures 2014. http://www.cancer.org/acs/groups/content/@research/documents/webcontent/acspc-042151.pdf. Accessed September 2015.
5. National Cancer Institute; Surveillance, Epidemiology, and End results Program Fact Sheet: Colon and Rectum. http://seer.cancer.gov/statfacts/html/colorect.html. Accessed September 2015.
6. Otsuka Holdings Annual Report for the year ending December 2014; http://www.otsuka.com/en/ir/library/pdf/2014/2014dec_all.pdf. Accessed September 2015.