



PRESS RELEASE

## Compelling Data for LONSURF® (trifluridine/tipiracil) in Metastatic Colorectal Cancer Presented at ESMO's World Congress on Gastrointestinal Cancer

- *Phase II TASC0-1 trial demonstrates promising progression-free survival results in previously untreated patients*
- *Phase IIIb PRECONNECT study provides further efficacy and safety data for LONSURF® in previously treated patients*

**PARIS, France, 23 June. 2018** – Servier and Taiho Pharmaceutical Co., Ltd. today announced that the TASC0-1 trial demonstrated promising results for LONSURF® (trifluridine/tipiracil) in combination with bevacizumab in patients with previously untreated metastatic colorectal cancer (mCRC) who are not suitable for intensive treatment, with a median progression-free survival (PFS) of 9.2 months (ranging from 7.6 to 11.5 months). A second non-comparative arm in the trial, evaluated the outcome of patients treated with the current standard of care of capecitabine in combination with bevacizumab. The median PFS of this arm was 7.8 months (ranging from 5.5 to 10.1 months).

“Colorectal cancer is the third most common cancer in the world. While there has been some progress in treatment, there are still few options for patients with metastatic disease who are not suitable for intensive treatment,” said Professor Eric Van Cutsem, Head of Digestive Oncology at the University of Leuven, Belgium. “These compelling results suggest that trifluridine/tipiracil, in combination with bevacizumab, can improve progression-free survival in advanced disease, offering a new option to metastatic colorectal cancer patients. These results are an important first step and will need to be investigated further in a global Phase III study.”

Servier has announced the results of a large interim analysis of the Phase IIIb early access study PRECONNECT which is assessing trifluridine/tipiracil in 462 patients with mCRC who have been previously treated with standard therapy. The study showed median progression-free survival of 2.8 months, consistent to that seen in the Phase III RECOURSE trial, which was used as the basis for the European Commission approval of trifluridine/tipiracil in 2016. A similar disease control rate (36.8%) and time to ECOG deterioration (8.7 months) compared to RECOURSE were also shown.



“The incidence of colorectal cancers is growing globally and for those diagnosed with metastatic disease the five-year survival is just 11%,” said Ali Zeaiter, Head of Servier Oncology clinical development department. “For patients with metastatic disease not candidates for intensive therapy or for those who have been pre-treated with chemotherapy and targeted therapies, there are limited options that can extend their survival. We are committed to improving outcomes for people living with cancer, and both TASC0-1 and PRECONNECT studies demonstrate the potential of LONSURF® to provide a substantial benefit to patients with metastatic colorectal cancer.”

### **About TASC0-1**

TASC0-1 is an international, randomized, non-comparative Phase II trial designed to evaluate efficacy of trifluridine/tipiracil in combination with bevacizumab and the current standard of care (capecitabine and bevacizumab) for patients with untreated metastatic colorectal cancer, who are not suitable for intensive therapy.

In addition to the primary endpoint of PFS, secondary endpoints of the trial included overall survival and disease control rate. The combination of trifluridine/tipiracil and bevacizumab was manageable, with the most frequently observed toxicities being gastrointestinal and hematologic. There was a 3.9% serious febrile neutropenia event rate reported in both arms of the trial.

Servier and Taiho Pharmaceutical are committed to exploring all possible combinations of LONSURF® in the treatment of metastatic colorectal cancer, with a number of ongoing clinical trials.

### **About PRECONNECT**

PRECONNECT is an ongoing international, multicentre, Phase IIIb study designed to further assess safety and efficacy of trifluridine/tipiracil in daily practice by giving eligible adult metastatic colorectal cancer patients access to trifluridine/tipiracil. The study aims to treat 1,000 patients in 20 countries; as of 29<sup>th</sup> May 2018 the study had recruited 794 patients across 14 countries.

The PRECONNECT trial gives early access to trifluridine/tipiracil for adult patients with mCRC who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents. PRECONNECT will also assess the quality of life of patients; preliminary data are anticipated in 2019.

### **About colorectal cancer**

Colorectal cancer is the third most common cancer worldwide with approximately 1.4 million new diagnoses in 2012.<sup>1</sup> Each year there are over 690,000 deaths making it the fourth biggest cancer killer worldwide (after lung, liver and gastric cancer).<sup>2</sup> Those with metastatic disease (where the cancer has spread from the primary site) the average five-year survival is approximately 11%.<sup>3</sup> Standard

chemotherapy regimens for advanced metastatic colorectal cancer include fluoropyrimidines, oxaliplatin, irinotecan or targeted treatments, such as those that target vascular endothelial growth factors (VEGF) or endothelial growth factor receptors (EGFR).

#### **About LONSURF<sup>®</sup> (trifluridine/tipiracil)**

LONSURF<sup>®</sup> is an oral anticancer drug, comprising a combination of trifluridine (FTD) and tipiracil (TPI), whose dual mechanism of action is designed to maintain clinical activity. LONSURF<sup>®</sup> is registered in Japan, USA, European Union and in many other countries. In the European Union, LONSURF<sup>®</sup> is indicated for the treatment of adult patients with metastatic colorectal cancer (CRC) who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, oxaliplatin- and irinotecan- based chemotherapies, anti-VEGF agents, and anti-EGFR agents.<sup>4</sup>

LONSURF<sup>®</sup> is recommended by the National Institute for Health and Care Excellence (NICE),<sup>5</sup> NCCN<sup>6,7</sup> and ESMO Guidelines<sup>8</sup> for the treatment of adult patients with metastatic colorectal cancer.

In June 2015, Servier and Taiho Pharmaceutical entered into an exclusive license agreement for the co-development and commercialization of LONSURF<sup>®</sup>.

#### **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 4.152 billion euros in 2017, Servier employs 21,600 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 nine molecular entities in clinical development in this area, targeting gastric 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, cellular and targeted therapies, to deliver life-changing medicines to patients.

More information: [www.servier.com](http://www.servier.com)

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### About Taiho Pharmaceutical Co., Ltd. (Japan)

Taiho Pharmaceutical, a subsidiary of Otsuka Holdings Co., Ltd. (<https://www.otsuka.com/en/>), 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 visit: <https://www.taiho.co.jp/en/>

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<sup>1</sup> World Health Organisation. Globocan (2012), colorectal cancer. Available at:

[http://globocan.iarc.fr/Pages/fact\\_sheets\\_cancer.aspx?cancer=colorectal](http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx?cancer=colorectal) Last accessed June 2018

<sup>2</sup> Cancer Research UK. Worldwide cancer statistics. Available at: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/worldwide-cancer/mortality#heading-One> Last accessed June 2018

<sup>3</sup> American Cancer Society. Survival Rates for Colorectal Cancer, by Stage. Available at: <https://www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/survival-rates.html> Last accessed June 2018

<sup>4</sup> European Medicines Agency. EPAR Lonsurf. Available from: <http://www.ema.europa.eu/ema/>. Last accessed June 2018.

<sup>5</sup> NICE TA405. Available at: [www.nice.org.uk/guidance/TA405](http://www.nice.org.uk/guidance/TA405).

<sup>6</sup> National Comprehensive Cancer Network (NCCN). NCCN Guidelines Insights: Colon Cancer, Version 2.2018.

<sup>7</sup> National Comprehensive Cancer Network (NCCN). NCCN Guidelines for Patients: Rectal Cancer, Version 1.2017.

<sup>8</sup> ESMO consensus guidelines for the management of patients with metastatic colorectal cancer: Van Cutsem E et al. Ann Oncol. 2016;27:1386-422.