# Solasia Initiates Phase III program for PledOx® in Japan

Tokyo, Japan, December 26, 2018 – Solasia Pharma K.K. (TSE: 4597, Headquarters: Tokyo, Japan, President & CEO: Yoshihiro Arai, hereinafter "Solasia") today announced the initiation of Phase III clinical trial for PledOx® in Japan.

In November 2017, Solasia acquired exclusive development and commercialization rights for PledOx® in Japan, China, Hong Kong, Macau, South Korea and Taiwan from PledPharma.

This Phase III clinical trial in Asia (Japan, South Korea, Taiwan and Hong Kong) is an expansion of the Global Phase III trial led by PledPharma in the rest of the world where the first patient was included in the United States in November. The Asian region including Japan is now officially part of this Global Phase III clinical trial.
Following Japan, Solasia will also initiate in South Korea, Taiwan and Hong Kong successively.

This trial is for colorectal cancer patients treated with mFOLFOX6 (*1) which contains antioxidant drug "oxaliplatin" and to examine the effect of suppressing the development of peripheral neuropathy by administering PledOx®. Oxaliplatin is a platinum-based compound and is indicated for colorectal cancer, pancreatic cancer, gastric cancer etc.
Peripheral neuropathy is known as one of the serious side effects caused by administration of oxaliplatin, and one of the causes is that neurons develop by being damaged due to oxidative stress induced by the drug. Peripheral neuropathy is also known as the main side effect of other platinum-based compound such as cisplatin. There are currently no drugs approved for the treatment of chemotherapy induced peripheral neuropathy. PledOx® is a superoxide dismutase analogue that is an enzyme that degrades active oxygen generated in cells and has the effect of protecting nerve cells from damage caused by drug-induced oxidative stress.
The initiate of this trial is a significant milestone for Solasia as this trial is positioned as a registration trial and its success is expected to contribute to patients suffering from peripheral neuropathy due to cancer chemotherapy.

**Study description:**

- Phase III, International, multicenter, double-blind, randomized, placebo-controlled study

Purpose of the study:
- The effect of reduce the peripheral neuropathy associated with administration of oxaliplatin by PledOx® administration compared with placebo.

Study design:
- POLAR-M study: Colorectal cancer patients who undergo mFOLFOX6 therapy with distant metastases are included.

- POLAR-A study: Colorectal cancer patients who undergo mFOLFOX6 therapy as an adjuvant therapy for postoperative surgery are included.

Primary outcome measures:
- Both the POLAR-M and POLAR-A studies will include subjects with moderate or higher chronic peripheral neuropathy at 9 months after (first day of FOLFOX therapy) the initial administration of PledOx® is evaluated.

Estimated enrollment:
- POLAR-M study: 420 patients (of which 120 patients in Asian region)

- POLAR-A study: 280 patients (of which 80 patients in Asian region)

## About chemotherapy induced peripheral neuropathy (CIPN) in Japan

Cancer chemotherapy has side effects such as nausea and vomiting and onset of stomatitis, but peripheral neuropathy is also a serious side effect. Peripheral neuropathy is known to be markedly expressed in major drugs of cancer chemotherapy such as plant alkaloid preparations and platinum preparations (*2). FOLFOX therapy including oxaliplatin, is a combination of a chemotherapy for advanced and recurrent cancer and a typical anticancer drug for postoperative adjuvant chemotherapy as a treatment for colorectal cancer, which is difficult to heal surgically. Almost all patients (85% - 95%) of oxaliplatin prescribed patients develop peripheral nerve disorder, and the disorder brings about the following symptoms (*2).

- *Acute symptoms: abnormal sensations such as hands, feet and lip peripheral parts, strangulation of pharyngeal larynx accompanied with dyspnea and dysphagia*
- *Chronic symptoms: numbness in the periphery of the limbs, decreased sensation, decreased tendon reflexes, sensory ataxia*

When such side effects occur, it is considered that some symptom improvement is seen in 80% of patients due to discontinuation of medicine and completely recovered in 6 to 8 months in 40% of cases (*2). However, discontinuation of the drug results in discontinuation of cancer treatment or change in treatment regimen which is an important medical issue. There is currently no approved drug to prevent or treat CIPN.

** 1: mFOLFOX6 therapy refers to cancer chemotherapy using three agents, fluorouracil, folinic acid, and oxaliplatin. It is adopted as standard therapy for high risk Stage II colorectal cancer or postoperative adjuvant chemotherapy for Stage III colorectal cancer and systemic chemotherapy for Stage IV recurrent colorectal cancer.*

** 2: Reference: Ministry of Health, Labor and Welfare "Corresponding manual for severe side effects disease Peripheral neuropathy"*

## About PledOx®

PledOx® is a “first in class” drug candidate developed to provide patients, that are treated adjuvantly or for metastatic colorectal cancer, prevention against the nerve damage that can occur in conjunction with chemotherapy treatment. The results from a completed Phase IIb trial (PLIANT), where patients with metastatic colorectal cancer were treated with the chemotherapy combination FOLFOX and PledOx®, indicates that the patients who received PledOx® had a lower risk than the placebo group to suffer from nerve damage during the chemotherapy. The presence of the investigator reported sensory nerve damage, the primary endpoint, was after treatment 38% lower in the group of patients treated with PledOx® compared with the placebo group ($p = 0.16$). This was not statistically significant, but a difference of this magnitude is considered to be clinically relevant. After completion of chemotherapy, the patient-reported incidence of moderate and severe neuropathy was 77% lower in patients treated with PledOx® compared to the placebo group (exploratory analysis; $p = 0.014$). This is considered valuable for the success of the forthcoming POLAR studies, where patient-reported symptoms after completion of treatment will be the primary efficacy parameter. No apparent negative effect on the efficacy of the cancer treatment was observed.

## About Solasia

Solasia is a specialty pharmaceutical company based in Asia, with a mission of "Better Medicine for a Brighter Tomorrow". In order to address the unmet medical needs within the oncology area, we develop innovative medicines to contribute to the patient's healthy living and to provide treatment options for the healthcare providers. Additional information is available at http://www.solasia.co.jp/en/

## About PledPharma

PledPharma develops new drugs that protect the body against oxidative stress – a potentially debilitating and sometimes life-threatening condition that can be caused by chemotherapy treatment and following acetaminophen (paracetamol) overdose. The company's most advanced project PledOx® is being developed to reduce nerve damage associated with chemotherapy. A phase IIb study has been conducted and serves as the basis for the initiated global phase III program. The drug candidate Aladote® is being developed to reduce the risk of acute liver failure associated with acetaminophen poisoning. A proof of principle study has been conducted and will serve as the basis for the continued development. PledPharma (STO: PLED) is listed on Nasdaq First North. Erik Penser Bank is the company's Certified Adviser (tel +46 8 463 80 00). For more information, see https://www.pledpharma.se/

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