



January 27, 2017

SBI Holdings, Inc.

SBI Pharmaceuticals Co., Ltd.

University of Oxford

**Notice on the Start of Phase II Clinical Trial using 5-ALA**  
**by University of Oxford and SBI Pharmaceuticals**

SBI Pharmaceuticals Co., Ltd., (Head office: Minato-ku, Tokyo; Representative Director & President: Yoshitaka Kitao; “SBI Pharmaceuticals”), a subsidiary of SBI Holdings, Inc., engaged in research and development of pharmaceuticals, health foods and cosmetics using 5-aminolevulinic acid (“5-ALA”)\*<sup>1</sup> and the University of Oxford in the United Kingdom hereby announce that the phase II clinical trial using 5-ALA is about to start to evaluate the benefit of 5-ALA in preventing a reduction in cardiac output\*<sup>2</sup> after heart bypass surgery.

SBI Pharmaceuticals and the University of Oxford concluded a joint R&D agreement in 2014 and have been in preparation for the clinical trial using 5-ALA. Last year the approvals of Medicines and Healthcare products Regulatory Agency (MHRA) and National Health Service (NHS) were obtained to perform the clinical trial in the United Kingdom. This is an investigator-initiated clinical trial to be performed by the University of Oxford at the hospitals in Oxford and Birmingham, and SBI Pharmaceuticals will finance the trial.

In coronary artery bypass surgery or aortic valve replacement using a heart-lung machine, cardiac ischemia-reperfusion injury\*<sup>3</sup> occurs, leading to such long-term damage as low cardiac output syndrome after surgery. In pre-clinical studies, 5-ALA administered before surgery showed a preventive effect against cardiac ischemia-reperfusion injury. Based on this knowledge, administration of 5-ALA before surgery is expected to improve the outcome of the surgery by changing the metabolism of myocardial cells, preventing cardiac ischemia-reperfusion injury caused by surgery against myocardial cells, and decreasing the occurrence of low cardiac output syndrome after surgery.

Professor Houman Ashrafian said:

“Heart disease is one of our biggest medical challenges and in UK we currently perform approximately 36,000 cardiac surgical procedures a year. These operations, now performed at relatively low risk, confer substantial and durable benefits for the patients they treat.



Unfortunately, collateral damage caused by surgery can lead to serious complications, impacting on recovery and quality of life. We believe the addition of a pre-surgical treatment approach using 5-ALA would not only improve the outcome of the surgery itself, but limit long term damage.”

SBI Pharmaceuticals will continue to pursue various potential applications of 5-ALA, and focus on research and development to provide pharmaceuticals that satisfy the unmet medical needs of as many people as possible around the world.

(\*1) 5-aminolevulinic acid (5-ALA)

An amino acid produced in mitochondria. It is an important substance that serves as a functional molecule related to energy production in the form of heme and cytochromes, and its productivity is known to decrease with age. 5-ALA is contained in food such as shochu lees, red wine and Asian ginseng. It is also known as a material forming chloroplasts in plants.

(\*2) Cardiac output

The volume of blood pumped by heart per stroke

(\*3) Cardiac ischemia-reperfusion injury

The tissue damage caused at reperfusion (when blood supply returns to the tissue) after a period of ischemia (shortage of oxygen)

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