Notice: This is a translation of a notice in Japanese and is made solely for the convenience of foreign shareholders. In the case of any discrepancy between the translation and the Japanese original, the latter shall prevail.

(Translation)

February 6, 2024

To Shareholders,

Company Name: Renascience Inc.
Representative: Koji Naito, President & CEO
(Code: 4889 TSE Growth)
For inquiries, please contact Administration Dept.

Completion of Treatment of Final Patient in Phase II Investigator-Initiated Clinical Trial of RS8001 (pyridoxamine) for Premenstrual Syndrome with Psychiatric Symptoms/Premenstrual Dysphoric Disorder

The Company has been conducting a phase II investigator-initiated clinical trial of RS8001 (pyridoxamine) for premenstrual syndrome (PMS) with psychiatric symptoms/premenstrual dysphoric disorder (PMDD)[*1] in collaboration with Kinki University, Tohoku University, Tokyo Medical and Dental University, Tokyo Women's Medical University, and several other private medical institutions. The Company is pleased to announce that the treatment of the last patient was completed on February 5, 2024.

As society becomes more complex, many people live under stress, but compared to physical illnesses, medical treatment for mental illnesses is still insufficient. The Company had been engaged in the research and development of the drug to treat PMS/PMDD, which makes it difficult for women to lead a social life. PMS is a disorder unique to women in which mental and physical symptoms last for 3-10 days before menstruation, and then improve or disappear with the onset of menstruation. More severe mental symptoms are classified as PMDD, but it is now common to consider PMS and PMDD as a continuum of illnesses. While 70-80% of women of reproductive age have some premenstrual symptoms, they are eligible for medical treatment when that their daily and social life are affected. Studies in Japan have reported that the frequency of PMS with social difficulties is 5.4% and that of PMDD is 1.2%. As drug treatment, antidepressants (SSRIs)[*2] and low-dose pills[*3] are used in off-label prescriptions, but they are not widespread enough due to the side effects and resistance to their use.

The neurotransmitters GABA[*4] and serotonin[*5] have the structure of amino group in their chemical structure and are collectively called monoamines. RS8001 (pyridoxamine) is a type of water-soluble

vitamin B6 that is important for the production of these monoamines, but it has not been approved as a drug in Japan and other developed countries.

The Company has been conducting a phase II investigator-initiated clinical trial of RS8001 for PMS/PMDD in collaboration with several universities and medical institutions (placebo lead-in[*6] , placebo-controlled, double-blind, three-arm comparative study with a target number of 105 patients). The Company was selected by the Japan Agency for Medical Research and Development (AMED) for the Cyclic Innovation for Clinical Empowerment (CiCLE) project in fiscal 2019 and began clinical trials in November 2020. Since there were difficulty to secure the enrollment due to a significant decrease in the number of patient visits at the time of the spread of the novel coronavirus infection, the measures have been taken to ensure the enrollment: five (5) private medical institutions were added to the study; in-hospital posters and educational booklets were created; webinars for pharmacists by a coordinating physician were conducted; and volunteer panels have been utilized. As a result, the number of enrolled patients reached the target of 105 in September 2023, and the treatment of the final patient was completed on February 5, 2024. The study report will be compiled around June 2024, after the analysis of the results.

This matter will have no impact on the forecast of business results.

End

*1 Premenstrual syndrome (PMS) with psychiatric symptoms/premenstrual dysphoric disorder (PMDD)

PMS is a mental and/or physical symptom that lasts for 3 to 10 days before menstruation and improves or disappears with the onset of menstruation. In women who have a rhythm of ovulation, follicular and luteal hormones are secreted in large quantities during the period between ovulation and menstruation (luteal phase). It is believed that the cause of PMS is a sudden drop in these hormones during the latter half of the luteal phase, causing abnormalities in the hormones and neurotransmitters in the brain. Psychoneurotic symptoms include emotional instability, irritability, depression, anxiety, drowsiness, difficulty in concentration, and sleep disturbances; autonomic disorders (including hot flash, anorexia and overeating, dizziness, and fatigue); and physical symptoms (including abdominal pain, headache, back pain, swollenness, bloated stomach, and breast tenderness).

PMDD is the severe case in which psychiatric symptoms, such as depression, agitation, anxiety, compulsion, and loss of identity, are apparent and become a serious obstacle to social life.

*2 Antidepressants (SSRIs)

SSRI stands for selective serotonin reuptake inhibitor. They inhibit the reuptake of serotonin, a neurotransmitter, in the brain, thereby increasing the serotonin concentration in the brain and

facilitating neurotransmission, which is thought to exert antidepressant and anti-anxiety effects.

*3 Low-dose pills

The pill is a hormonal drug that contains female hormones (follicular and luteal hormones) that control the menstrual and ovulatory cycles. A low-dose pill is one in which the amounts of hormones are kept as low as possible to minimize the side effects. Although the purpose of the pill is to suppress ovulation and provide contraception, it also has several positive effects such as improving PMS as well as making the menstrual cycle more regular.

*4 GABA

It is one of the natural amino acids widely present in our bodies and is called GABA (gamma amino butyric acid). GABA acts mainly as an inhibitory neurotransmitter.

*5 Serotonin

It is one of the neurotransmitters in the brain, biosynthesized from the essential amino acid tryptophan, and works to stabilize the mind by controlling the effects of other neurotransmitters such as dopamine (involved in joy, pleasure, etc.) and noradrenaline (involved in fear and surprise).

*6 Placebo lead-in

A placebo does not contain active ingredients, but it may improve disease symptoms due to psychological effects (placebo effect). Therefore, the phase II study was conducted with a study design in which the subjects were asked to take a placebo for a certain period of time prior to administration of the active drug, and the trial was conducted after excluding the subjects with a large placebo effect (placebo lead-in).