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)

October 17, 2023

To Shareholders,

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

Notice of Allowance of New Use and Dosage Patent for PAI-1 Inhibitor (Title of the Invention: Drug for Enhancing Fibrinolytic System, and Use Thereof)

The Company is pleased to announce that the following use and dosage patent have been granted in Japan.

Title of Invention	: Drug for enhancing fibrinolytic system, and use thereof
Region	: Japan
Application No.	: Patent Application 2021-556350
Registration Number	: Not yet determined
Applicant	: Renascience Inc.

The plasminogen activator inhibitor 1 (PAI-1) inhibitors activate endogenous tissue plasminogen activator[*1] and enhance the blood fibrinolytic system[*2], by inhibiting PAI-1. The PAI-1 inhibitors are involved in the pathogenesis of thrombotic diseases as well as age-related diseases[*3], lung diseases such as acute respiratory distress syndrome[*4], and cancers such as chronic myeloid leukemia[*5].

This patent not only protects inventions relating to pharmaceutical uses of the PAI-1 inhibitors in these diseases, but also protects inventions relating to dosage of the PAI-1 inhibitors.

The Company's patents (including substance patents and use patents) for the PAI-1 inhibitors including RS5614 have been granted in Japan, the United States, Europe, and other countries. This patent will further strengthen the intellectual property rights for the PAI-1 inhibitors including RS5614 and will also allow for the patent term extensions.

There is currently no material impact of this matter on our business performance.

End

*1 Tissue plasminogen activator

It is a type of endopeptidases. Tissue plasminogen activator activates the enzyme precursor, plasminogen, to convert it into a proteolytic enzyme called plasmin. Plasmin then degrades fibrin that forms blood clots and promotes thrombolysis.

*2 Blood fibrinolytic system

When blood vessels are damaged or tissues are destroyed, the coagulation system works to prevent blood from flowing out of the area and the blood clots. When bleeding stops and tissue repair is completed, the blood clot is quickly dissolved and removed by the blood fibrinolytic system. The tissue plasminogen activator or urokinase-type plasminogen activator activates plasminogen, and the resulting plasmin degrades the fibrin of the blood clot.

*3 Age-related diseases

With aging, various diseases develop, including cancer, vascular (atherosclerosis), pulmonary (emphysema, chronic obstructive pulmonary disease), metabolic (diabetes, obesity), renal (chronic kidney disease), bone and joint (osteoporosis, osteoarthritis), and brain (cerebrovascular disease, Alzheimer's disease, and dementia). PAI-1 expression is extremely high in the tissues of these diseases, and through collaborations with domestic and overseas research institutions, the Company has shown that the PAI-1 inhibitors can improve these pathological conditions.

*4 Acute respiratory distress syndrome

The condition is defined as a sudden onset of shortness of breath or dyspnea during the course of sepsis (a condition in which bacteria and other organisms enter the bloodstream and multiply) or pneumonia, or after aspiration (when food or other substances accidentally enter the airways when swallowed) or multiple trauma (when multiple body parts are injured), etc., and a chest X-ray examination shows shadows (infiltrative shadows) on the right and left lungs. The partial pressure of oxygen (PaO2) in the arterial blood decreases (hypoxemia), and the condition is defined as mild, moderate, or severe, depending on the degree of hypoxemia.

*5 Chronic myeloid leukemia

Chronic myeloid leukemia, a type of hematological cancer, is caused by an abnormality in the genes of the source of blood cells (hematopoietic stem cells), resulting in the unrestricted growth of cancerous leukemia cells. The prognosis of chronic myeloid leukemia has been greatly improved by anticancer drugs (molecular target drugs) that inhibit the intracellular protein (tyrosine kinase) that causes the disease. However, these drugs act on chronic myeloid leukemia

cells but not on the source of chronic myeloid leukemia cells (chronic myeloid leukemia stem cells) that lie dormant in the bone marrow, and, when the anticancer drugs are withdrawn, these stem cells turn into chronic myeloid leukemia cells and relapse.

It was reported that the fibrinolytic system is required to activate the hematopoietic stem cells and chronic myeloid leukemia stem cells latent in the bone marrow from their quiescent state. Through collaboration with Tokai University, the Company discovered that PAI-1 plays an important role in the quiescence of the stem cells in the bone marrow and that the PAI-1 inhibitors activate the stem cells to promote their differentiation into chronic myeloid leukemia cells. Therefore, the combination of the PAI-1 inhibitor RS5614 and the anticancer drugs may lead to a radical cure of chronic myeloid leukemia by depleting the chronic myeloid leukemia stem cells. This concept was demonstrated in a late phase II study of long-term RS5614 dosing in combination with the anticancer drugs.