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)

December 5, 2023

To Shareholders

Company Name Renascience Inc.
Name of Representative: Koji Naito, President & 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: Inhibitor against Expression of Immune Checkpoint Molecule)

The Company is pleased to announce that the following use patent has been granted a patent in Japan.

Title of Invention	: Inhibitor of expression of immune checkpoint molecules
Region	: Japan
Application No.	: Patent Application 2021-551413
Registration Number	: Not yet determined.
Applicant	: Renascience Inc.

The basic treatment for cancer is (1) surgical therapy, (2) radiation therapy, (3) chemotherapy (anticancer drugs), and (4) immunotherapy. The human body has a system called immunity that protects the body from foreign viruses, bacteria, and microorganisms, but the body is also equipped with a brake called an immune checkpoint molecule[*1] that suppresses excessive immunity. Cancers abuses these immune checkpoint molecules to prevent the immune system from working against themselves. Immune checkpoint inhibitors[*2], a typical immunotherapy, inhibit the immune checkpoint molecules, thereby releasing the brake and allowing the immune system to attack cancers.

The Company has discovered that plasminogen activator inhibitor 1 (PAI-1) inhibits cancer immunity via the immune checkpoint molecules. Non-clinical studies using animal models have shown that oral administration of RS5614, a PAI-1 inhibitor developed by the Company, regresses malignant melanoma, colorectal cancer, and lung cancer, and that this effect is significantly enhanced when RS5614 is combined with nivolumab, the immune checkpoint inhibitor. Based on these findings,

the Company has completed a phase II study for malignant melanoma (the results were disclosed on August 16, 2023) and is also conducting phase II studies for non-small cell lung cancer (disclosed on September 26, 2023) and cutaneous angiosarcoma (disclosed on October 26, 2023).

The patent protects the inventions relating to pharmaceutical uses of the PAI-1 inhibitors as immune checkpoint inhibitors. To date, the Company has several patents for the PAI-1 inhibitors, including RS5614, that were already granted in several major countries including Japan, the US and Europe (composition of matter, use, and dosage patents). This patent will further strengthen the patent portfolio for the PAI-1 inhibitors including RS5614, and will also enable the patent term extension for 10 years.

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

End

1 Immune checkpoint molecule

It is a molecule that inhibits the immune response to self and suppress excessive immune responses to maintain immune homeostasis. Immune checkpoint molecules exist to prevent lymphocytes from attacking self by suppressing their excessive activation, but cancer cells abuse immune checkpoint molecules to evade attacks from the immune system. Various immune checkpoint molecules have now been identified, including PD-1 and CTLA-4.

2 Immune checkpoint inhibitor

It is a pharmaceutical that inhibits immune checkpoint molecule(s). All drugs currently used as therapeutic agents are antibody therapeutics that bind directly to immune checkpoint molecules and inhibit them.