(Translation)

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To Shareholders,

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

Notice of Publication of Results from Phase II Trial of the PAI-1 Inhibitor in Advanced Malignant Melanoma

The Company is pleased to announce that a paper on the results of a phase II study of the PAI-1 inhibitor RS5614 in advanced malignant melanoma has been published in the scientific journal "British Journal of Dermatology".

Fujimura T, Yoshino K, Kato H, Fukushima S, Ishizuki S, Otsuka A, Matsushita, Amagai R, Muto Y, Yamazaki E, Kambayashi Y, Yahata T, Miyata T, Fujisawa Y, Asano Y Fujisawa Y, Asano Y.

Phase II, multicenter study of plasminogen activator inhibitor-1 inhibitor 1 (TM5614) plus nivolumab for treating anti-PD-1 antibody-refractory malignant melanoma: TM5614-MM trial

British Journal of Dermatology 2024 online.

(https://doi.org/10.1093/bjd/ljae231)

The basic treatment for cancer is (1) surgical therapy, (2) radiation therapy, (3) chemotherapy (anticancer drugs), and (4) immunotherapy (immune checkpoint inhibitors). The human body has a system called immunity that protects the body from foreign viruses, bacteria, and microbes. The body is equipped with immune checkpoint molecules[*1] that suppress excessive immunity. Cancers abuse these immune checkpoint molecules to prevent the immune system from working against themselves. Immune checkpoint inhibitors[*2] block these immune checkpoint molecules, thereby releasing the brakes and allowing the immune system to attack cancers. Nivolumab, an antibody therapeutic that targets an immune checkpoint molecule called programmed cell death-1 (PD-1), and ipilimumab, an antibody therapeutic that targets an immune checkpoint molecule called cytotoxic T lymphocyte antigen-4 (CTLA-4), are representative immune checkpoint inhibitors used to treat various types of cancers.

In collaboration with Tokai University and Tohoku University, the Company has discovered that PAI-1 induces expression of programmed cell death ligand 1 (PD-L1), an immune checkpoint molecule, in various cancer cells and cancer-infiltrating cells, thereby interfering with immune responses, and that RS5614, a PAI-1 inhibitor, has an immune checkpoint inhibitory action by inhibiting PD-L1 expression and activates immune responses. Based on the immune checkpoint inhibitory activity of RS5614, a phase II investigator-initiated clinical trial to investigate the efficacy and safety of RS5614 in combination with nivolumab for malignant melanoma that is difficult to surgically resect has been conducted at Tohoku University Hospital, Cancer Institute Hospital of JFCR, University of Tsukuba Hospital, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Nagoya City University Hospital, Kinki University Hospital, and Kumamoto University Hospital. As a result, the efficacy and safety of RS5614 in combination with nivolumab were confirmed in the second-line treatment of malignant melanoma refractory to nivolumab (disclosed on February 22, 2024).

The Company is pleased to report that a paper on the results of this clinical trial has been published in the electronic edition of the British Journal of Dermatology. In addition, the British Journal of Dermatology will separately publish the presentation material and the video message from the first author to publicize this paper.

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1 Immune checkpoint molecules

Immune checkpoint molecules are a group of molecules that inhibit the immune response to self and suppress excessive immune response to maintain immune homeostasis. Immune checkpoint molecules suppress excessive activation of lymphocytes to prevent them from attacking the self, but cancer cells exploit immune checkpoint molecules to evade attacks from the immune system. Various immune checkpoint molecules, such as PD-1 and CTLA-4, have been identified.

2 Immune checkpoint inhibitors

All immune checkpoint inhibitors currently used as therapeutic agents are antibody therapeutics that bind directly to immune checkpoint molecules and inhibit them.