

October 5, 2026

To Shareholders,

Company Name: Renascience Inc.
Representative: Toshio Miyata, Chairman and CEO
(Code: 4889 TSE Growth)
For inquiries, please contact Administration Dept.

Completion of Patient Enrollment in an Investigator-Initiated Phase III Clinical Trial of Nivolumab in Combination with the PAI-1 Inhibitor RS5614 for Unresectable Malignant Melanoma

We are pleased to announce that enrollment of all 124 planned patients was completed on October 5, 2026, in the investigator-initiated, randomized, placebo-controlled, double-blind Phase III clinical trial evaluating the efficacy and safety of RS5614 in combination with nivolumab in patients with unresectable malignant melanoma. The trial is being conducted at 18 medical institutions across Japan, including Tohoku University Hospital. Following a follow-up period of up to three years, the Company plans to evaluate the primary endpoint and compile the results of the data analysis in a clinical study report.

Malignant melanoma¹⁾ is one of the most aggressive forms of skin cancer and is associated with a high risk of metastasis. In Japan, the incidence of malignant melanoma is estimated at 1.5–2 cases per 100,000 population, and the total number of patients is approximately 5,000, making it a rare disease in Japan. By contrast, in the United States, the incidence is 21.0 cases per 100,000 population, and the number of people living with the disease is estimated at approximately 1.4 million.

The advent of immune checkpoint inhibitors²⁾, particularly the anti-PD-1 antibody nivolumab³⁾, has substantially improved the treatment of advanced malignant melanoma. In addition, the anti-CTLA-4 antibody ipilimumab⁴⁾ has been developed, and combination therapy is used to improve response rates beyond those achieved with anti-PD-1 monotherapy alone (approximately 20%). However, severe immune-related adverse events can lead to treatment discontinuation at a rate approximately four times higher than with monotherapy, and the high cost of treatment remains another challenge. There is therefore a strong unmet need for an affordable combination therapy that can improve response rates while causing fewer adverse events.

This investigator-initiated, randomized, placebo-controlled, double-blind Phase III clinical trial is evaluating the efficacy and safety of nivolumab in combination with RS5614, a PAI-1 inhibitor, in patients with advanced malignant melanoma refractory to anti-PD-1 antibody therapy. The trial commenced on February 18, 2025, and enrollment of all 124 planned patients was completed on October 5, 2026.

Following the achievement of proof of concept (POC) in a Phase II investigator-initiated clinical trial, in which the objective response rate, the primary efficacy endpoint, was 24.1% and the disease control rate was 62.0%, RS5614 was designated as an orphan drug by Japan's Minister of Health, Labour and Welfare on August 28, 2024. RS5614, a small-molecule PAI-1 inhibitor developed by the Company, has demonstrated a favorable safety profile and is an orally administered therapy that can be taken at home. This Phase III trial is a pivotal study intended to support regulatory approval of RS5614 for malignant melanoma. If efficacy is confirmed, RS5614 is expected to offer a new treatment option for patients with unresectable malignant melanoma refractory to anti-PD-1 antibody therapy.

[Impact on Earnings]

No material impact on the Company's financial results for the fiscal year ending March 2027 is currently expected as a result of this matter.

¹⁾ Malignant melanoma

Malignant melanoma is a type of skin cancer arising from the malignant transformation of melanocytes, the pigment-producing cells responsible for skin color. It is one of the most aggressive forms of skin cancer and is associated with a high risk of metastasis. The incidence of malignant melanoma is relatively low in Japan, at 1.5–2 cases per 100,000 population, compared with 21.0 per 100,000 in the United States and 33.6 per 100,000 in Australia, both higher than in Japan. Malignant melanoma is highly aggressive: the five-year survival rate is approximately 50% for tumors greater than 4 mm in thickness, approximately 40% in patients with regional lymph node metastasis, and only a few percent in patients with distant metastasis. The extent of disease progression at diagnosis has also been reported to be approximately three times greater in Japan than in the United States. This has been attributed to genetic differences between melanoma in Japanese and Western populations that may contribute to lower treatment responsiveness in Japan.

²⁾ Immune checkpoint inhibitor

A class of drugs that inhibit the activity of immune checkpoint molecules. All agents in this class currently used therapeutically are antibody drugs that bind directly to immune checkpoint molecules and inhibit their function.

³⁾ Nivolumab

An antibody drug (a fully human anti-PD-1 monoclonal antibody) that targets programmed cell death protein 1 (PD-1), an immune checkpoint molecule, thereby restoring antitumor immune activity. Nivolumab is a representative immune checkpoint inhibitor. In Japan, the response rate to nivolumab in malignant melanoma is 22.2%, underscoring the need for new combination therapies.

⁴⁾ Ipilimumab

An antibody drug (a fully human anti-CTLA-4 monoclonal antibody) that targets cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), an immune checkpoint molecule distinct from the target of nivolumab. In Japan, combination therapy with nivolumab and ipilimumab is reimbursed for patients who do not respond to nivolumab monotherapy, with response rates reported at approximately 21% overseas and 13.5% in Japan. However, nivolumab/ipilimumab combination therapy causes severe adverse events in more than half of patients, and treatment discontinuation due to severe immune-related adverse events occurs approximately four times as often as with monotherapy. These events

may require hospitalization for several months and interruption of cancer treatment. Together with the high cost of treatment, these challenges create a need for an affordable, orally administered combination agent with a modality distinct from antibody therapy that can improve response rates while causing fewer adverse events.

⁵⁾ PAI-1

PAI-1 is an abbreviation for Plasminogen Activator Inhibitor-1, a factor that suppresses the fibrinolytic system responsible for dissolving blood clots. In addition to being expressed in vascular endothelial cells, PAI-1 has recently been shown to be involved in the egress of hematopoietic stem cells from the bone marrow niche and in cell differentiation. PAI-1 is also a major component of the senescence-associated secretory phenotype (SASP), a group of inflammatory factors secreted by senescent cells, and recent research has linked it to tissue aging and age-related functional decline. Based on these findings, PAI-1 inhibitors are expected to have potential applications not only in oncology but also in the anti-aging and longevity fields through the clearance of senescent cells (senolysis).

⁶⁾ Placebo-controlled, double-blind

A clinical trial design in which patients are randomly assigned to receive either the investigational drug (in this case, RS5614) or a control (in this case, an inactive placebo), with neither the physician nor the patient aware of the assigned treatment. The two groups are treated concurrently. This design reduces the risk of selection bias, such as preferentially administering the investigational drug to patients expected to benefit, and minimizes the influence of preconceptions about efficacy or knowledge of treatment assignment on treatment response and assessment.

⁷⁾ Proof-of-Concept (POC)

Confirmation, through non-clinical or clinical studies, that a new drug candidate demonstrates the anticipated efficacy. When the expected results are obtained, the candidate is considered to have achieved POC.

⁸⁾ Orphan drug

A designation for medicines intended primarily for serious diseases that affect a small number of patients and for which established treatment options are limited or unavailable. Designation criteria include a target patient population of fewer than 50,000 in Japan; a serious condition, such as an intractable disease; high medical need; the absence of an appropriate alternative drug or treatment; the expectation of markedly higher efficacy or safety than existing treatments; and a high likelihood of successful development. Orphan drug designation provides benefits including priority review by the Pharmaceuticals and Medical Devices Agency (PMDA), resulting in a shorter review period; a marketability premium in NHI drug price calculation; and an extended post-approval re-examination period, which effectively extends the period of market exclusivity. Designated products may also be eligible for support measures such as subsidies administered through the National Institute of Biomedical Innovation, Health and Nutrition.