December 15, 2025

To Shareholders,

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

Announcement of initiation of a Phase III bridging study for unresectable melanoma in Taiwan

We are pleased to announce that we have signed an agreement with Taipei Medical University[1)] (TMU) to conduct a bridging study[2)] in Taiwan for the Phase III unresectable melanoma[3)] clinical trial currently being conducted in Japan.

In Japan, a Phase III randomized, placebo-controlled, double-blind[4)] trial is being conducted at 18 institutions across Japan, including Tohoku University Hospital, to evaluate the efficacy and safety of combining RS5614 with nivolumab[5)] in 124 patients with unresectable melanoma.

【Outline of the Phase III trial in progress in Japan】

Target	Progressive unresectable melanoma refractory to anti-PD-1 antibody
Clinical trial design	Multicenter, double-blind, placebo-controlled, comparative study
Number of cases	124 cases
Primary endpoint	Overall survival (OS)
Clinical trial site (planned)	Tohoku University Hospital, Sapporo Medical University Hospital, Hirosaki University Hospital, Jichi Medical University Saitama Medical Center, National Cancer Center Hospital East, National Cancer Center Hospital, The Cancer Institute Hospital Of JFCR, Niigata Cancer Center Hospital, Shizuoka Cancer Center, Nagoya City University Hospital, University of Tsukuba Hospital, Gifu University Hospital, Shimane University Hospital, Ehime University Hospital, Kyushu University Hospital, Kyushu Cancer Center, Kumamoto University Hospital, Kagoshima Medical Center.
Implementation Period	February 2025 - July 2029 (Planned registration period: 1.5 years, observation period: 3 years)

【Challenges in melanoma treatment】

In Japan, melanoma is a rare disease with an incidence rate of 1.5-2.0 *per* 100,000 people, representing a total patient population of approximately 5,000. However, in the United States, the incidence rate is 21.0 *per* 100,000 people, and approximately 1.4 million people are affected by melanoma. The introduction of the anti-PD-1 antibody nivolumab, an immune checkpoint inhibitor[6], has significantly improved the treatment of advanced melanoma. Furthermore, the anti-CTLA-4 antibody ipilimumab[7] has been developed, and combination therapy has been implemented to increase the response rate (approximately 20%) of anti-PD-1 antibodies alone. However, due to the severe side effects of autoimmune disease, the incidence of treatment discontinuation is four times higher than with monotherapy. Furthermore, high medical costs remain a challenge. Therefore, the development of a drug that is free of side effects and increases response rates[8] is eagerly awaited.

【Summary of results of Phase II investigator-initiated clinical trial】

Efficacy

- ☐ The primary efficacy endpoint, "response rate after 8 weeks of concomitant use of RS5614," was 24.1%.
- ☐ The disease control rate[9] (complete response (CR), partial response (PR), and stable disease (SD)) was 62.0%.

Safety

- ☐ Of the 34 patients included in the safety analysis, 11 serious adverse events occurred in 9 patients by 8 weeks of treatment, with two cases of liver dysfunction (5.9%) potentially related to the investigational drug.

The PAI-1 inhibitor RS5614 developed by our company is a small-molecule drug with an extremely high safety profile and is conveniently administered orally at home. This bridging study will be undertaken to get the regulatory approval for RS5614 for malignant melanoma in Taiwan. Following discussions with the Taiwan Food and Drug Administration (TFDA), *e.g.*, the number of patients to be included in the bridging study, and approval from the Institutional Review Board (IRB), the investigator-initiated clinical trial is scheduled to begin.

Taipei Medical University (https://eng.tmu.edu.tw) was founded in 1960 and is a top-ranked private medical university in Taiwan, with 3,000 beds. We have entered into a collaborative research agreement with Taipei Medical University regarding the clinical development and practical application of the PAI-1 inhibitor RS5614 (disclosed on November 5, 2024). This bridging study will be conducted as part of this agreement.

We view the overseas expansion of RS5614 as a very important strategy, and hope to use clinical development and commercialization in Taiwan as a foothold for further expansion overseas.

At this time, this matter will have no particular impact on our financial results for the fiscal year ending March 2026.

[1)] Taipei Medical University
Founded in 1960, Taipei Medical University (https://eng.tmu.edu.tw) is a private medical university ranked among the top in Taiwan. Its campus boasts six hospitals with a total of 3,000 beds. Using this vast amount of medical data, data scientists and other researchers are conducting a variety of research and development projects.

[2)] Bridging study
A bridging study is a clinical trial that examines whether overseas clinical trial data can be used as a substitute for clinical trial data from the country where the trial is being conducted. Also known as a bridging study. In 1998, the International Conference on Harmonisation (ICH), the international standard for new drug applications, allowed overseas clinical trial data to be added to or substituted for domestic clinical trial data. Data substitution is permitted only if the overseas data on the new drug's efficacy, safety, pharmacokinetics, dosage and administration are consistent with that released domestically. A bridging study is a study that investigates whether this data is consistent. By utilizing overseas clinical trial data, duplicate clinical trials can be eliminated in Japan, significantly shortening the time required for new drug approval. It is also expected that the widespread use of bridging studies will eliminate drug lag.

[3)] Melanoma
Melanoma is a type of skin cancer that develops when melanocytes, the skin cells that produce melanin, the pigment responsible for skin color, become malignant. It is considered to be one of the most aggressive skin cancers, with a high rate of metastasis. While the incidence rate of malignant melanoma patients in Japan is low at 1.5-2 *per* 100,000, it is 20.1 in the United States and 33.6 in Australia, several dozen times higher than in Japan. Malignant melanoma is a highly malignant cancer (the 5-year survival rate is approximately 50% for tumors larger than 4 mm, approximately 40% for those with regional lymph node metastasis, and several percent for those with distant metastasis). Furthermore, it has been reported that the progression rate of malignant melanoma in Japan is approximately three times higher than in the United States. This is thought to be due to the genetic differences between malignant

melanoma in Japan and those in Europe and the United States, making treatment less effective.

[4] Randomized, placebo-controlled, double-blind study
In this clinical trial, patients are randomly assigned to either an investigational drug (RS5614 in this case) or a control drug (an inactive placebo). Neither the doctor nor the patient knows which group they are receiving, and both groups are simultaneously administered the drug. This reduces the chances of doctors prescribing the drug to patients who are likely to respond, and also reduces the possibility of preconceived notions of efficacy being reflected in the evaluation, as well as the possibility that patients' reactions to the treatment or their evaluations may be affected if they become aware of the treatment.

[5] Nivolumab
This antibody drug (human anti-human PD-1 monoclonal antibody) targets the immune checkpoint molecule programmed cell death 1 (PD-1). It aims to achieve anti-cancer effects by deactivating immune system suppression. It is a representative immune checkpoint inhibitor. In Japan, the response rate of nivolumab for malignant melanoma is 22.2%, and the development of new combination therapies is desired.

[6] Immune checkpoint inhibitors
Immune checkpoint inhibitors are drugs that block the action of immune checkpoint molecules. All currently used therapeutic agents are antibody drugs that directly bind to and inhibit immune checkpoint molecules.

[7] Ipilimumab
Ipilimumab is an antibody drug (human anti-human CTLA-4 monoclonal antibody) that targets the immune checkpoint molecule cytotoxic T-lymphocyte antigen-4 (CTLA-4). It is an immune checkpoint inhibitor with a different target than nivolumab. For patients who do not respond to nivolumab, the combination of nivolumab and ipilimumab is covered by health insurance, with a response rate of 21% overseas and 13.5% in Japan. However, nivolumab-ipilimumab combination therapy experiences serious side effects in over half of patients, and the incidence of severe immune-related side effects leading to treatment discontinuation is four times higher than with monotherapy, posing problems such as requiring hospitalization for several months or interruption of cancer treatment. Furthermore, given the high cost of medical care, there is a strong demand for inexpensive combination drugs that use different antibody and modalities, are orally administered, have minimal side effects, increase response rates, and are inexpensive.

[8] Response rate

This is a common evaluation criterion used to assess the effectiveness of treatment for solid tumors. Before treatment begins, tumor size is measured using imaging diagnostics such as CT. Large tumors are selected as target lesions, while others are called non-target lesions. The change in size of these lesions during treatment is expressed as "complete response (CR)," "partial response (PR)," "stable disease (SD)," or "progressive disease (PD)."

Complete Response (CR)	Disappearance of all target lesions, or, in the case of lymph nodes, reduction to a minor axis of less than 10 mm.
Partial Response (PR)	Shrinkage of more than 30% from before the start of treatment.
Progressive Disease (PD)	Tumor growth of more than 20% from its smallest size or an increase of more than 5 mm in diameter during treatment.
Stable Disease (SD)	Between partial response (PR) and progressive disease (PD).

The response rate is defined as the ratio of complete response (CR) + partial response (PR).

[9] Disease control rate

This is an indicator showing the percentage of patients whose cancer has shrunk (complete response or partial response) or stopped progressing as a result of treatment. It is used to comprehensively evaluate the effectiveness of treatment.