September 25, 2026

To Shareholders,

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

Announcement of Orphan Drug Designation for Cutaneous Angiosarcoma

We would like to inform you that RS5614, which we are developing as a treatment for cutaneous angiosarcoma, was designated as an orphan drug[1)] by the Minister of Health, Labour and Welfare on September 25, 2026.

Cutaneous angiosarcoma is a type of soft-tissue tumor arising from malignant transformation of vascular endothelial cells[2)]. It is an extremely rare and highly aggressive skin cancer, with a five-year survival rate of less than 10%. Its incidence in Japan is higher than that in Western countries, at approximately 2.5 cases *per* million population, and has been increasing in recent years. Paclitaxel[3)], an apoptosis[4)]-inducing agent, is currently used as the first-line therapy for angiosarcoma. However, median overall survival is only 649 days, and even with combined chemotherapy and radiotherapy, achieving long-term tumor shrinkage or disappearance remains difficult for the majority of patients. Pazopanib[5)], which is used as the second-line therapy, has a response rate of only 3% in angiosarcoma (Cancer, 2022), while eribulin[6)] has demonstrated modest efficacy but is associated with serious adverse events in 64% of patients. Thus, effective treatment options following failure of paclitaxel remain limited, creating an urgent need for new therapeutic agents.

Plasminogen activator inhibitor-1 (PAI-1) is produced by vascular endothelial cells and is therefore highly expressed in angiosarcoma, a cancer that originates from these cells. PAI-1 is known to play a key role in tumor growth, metastasis, tumor immunity, and resistance to immunotherapy. Because cancer cells with high PAI-1 expression are less susceptible to paclitaxel-induced apoptosis, we have been developing RS5614, a PAI-1 inhibitor, in combination with paclitaxel, based on the hypothesis that inhibition of PAI-1 could enhance the therapeutic efficacy of paclitaxel against angiosarcoma.

A Phase II clinical trial was conducted in patients with cutaneous angiosarcoma whose disease had become refractory to paclitaxel, in collaboration with seven universities and medical institutions in Japan, including Tohoku University Hospital.

The combination of paclitaxel and RS5614 demonstrated promising results, including an objective response rate of 13.3% (95% confidence interval: 1.7%–40.5%), disease control rate of 86.7%, median progression-free survival of 4.0 months, and median overall survival of 20.8 months. These results exceeded the median progression-free survival of 2.8 months and median overall survival of 12.1 months reported for pazopanib in JCOG1605, a prospective clinical trial conducted in Japan. Regarding safety, no Grade 5 adverse events occurred, and no serious adverse events considered to be causally related to the investigational drugs were observed. The combination therapy was therefore confirmed to be well tolerated (disclosed on February 10, 2026). In addition, the Clinical Study Report (CSR) for this trial was finalized as of September 7,

2026, and the final results have been confirmed to be identical to the preliminary results reported above.

Based on the results of the Phase II trial, we are currently in discussions with the Pharmaceuticals and Medical Devices Agency (PMDA) regarding a Phase III trial toward regulatory approval for the treatment of cutaneous angiosarcoma.

With this orphan drug designation, RS5614 will be eligible for preferential measures, including a marketability premium in drug price calculation, an extension of the post-marketing re-examination period following approval (thereby extending the product's period of market exclusivity), and grant funding through the National Institutes of Biomedical Innovation, Health and Nutrition (NIBOHN).

There is no change to the Company's earnings forecast for the fiscal year ending March 31, 2027 as a result of this matter. If any matter requiring disclosure arises in the future, we will disclose it promptly.

[1)] Orphan Drug

An orphan drug is a pharmaceutical product intended primarily for rare diseases for which the number of patients is small, and effective treatments have not yet been established. Criteria for designation include an estimated patient population of fewer than 50,000 in Japan, the seriousness of the targeted disease such as an intractable disease, high medical need, the absence of an appropriate alternative drug or treatment, the expectation of significantly greater efficacy or safety compared with existing therapies, and a high likelihood of successful development. Orphan drug designation provides various incentives, including priority review by the PMDA (resulting in a shorter review period), a marketability premium in drug price calculation, an extension of the post-marketing re-examination period following approval, thereby extending the period of market exclusivity for the product, and grant funding through the National Institutes of Biomedical Innovation, Health and Nutrition.

[2)] Vascular Endothelial Cells

Vascular endothelial cells are cells that line the inner surface of blood vessels. In addition to forming a structural component of blood vessels, they serve as the interface through which oxygen, nutrients, and other substances are exchanged between the blood and tissues. They also produce various physiologically active substances that help maintain the functions of tissues and organs.

[3)] Paclitaxel

Paclitaxel is a chemotherapeutic anticancer agent whose antitumor activity was originally identified in the bark of the Pacific yew tree, and which is now produced synthetically. It binds to microtubules, which play an important role in cell division, thereby inhibiting cancer cell proliferation and ultimately inducing cell death.

[4)] Apoptosis

Apoptosis is a form of programmed cell death in which cells are eliminated through an internally regulated process when they are no longer needed.

[5] Pazopanib

Pazopanib is a type of molecularly targeted therapy that inhibits tumor growth by suppressing blood supply to cancer cells. It is primarily used for the treatment of renal cell carcinoma and soft-tissue sarcoma. The incidence of adverse events is high, at 93.5%, with major adverse events including diarrhea, hypertension, fatigue, nausea and vomiting, liver dysfunction, and taste disturbances.

[6] Eribulin

Eribulin is an anticancer agent developed from a marine-derived natural product. It acts on microtubules, which are essential cellular components involved in cell division, thereby inhibiting cancer cell proliferation and inducing cell death. Serious adverse events include infections associated with bone marrow suppression, fatigue, and numbness of the hands and feet.