February 10, 2026

To Shareholders,

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

# Flash Report of a Phase II Clinical Trial of RS5614 in Combination with Paclitaxel for Cutaneous Angiosarcoma

We are pleased to announce the flash report of a Phase II investigator-initiated clinical trial conducted with seven medical institutions, including Tohoku University, to evaluate the safety and efficacy of the combination of paclitaxel[1)] and RS5614 for cutaneous angiosarcoma[2)].

Cutaneous angiosarcoma is an extremely rare skin cancer with a poor prognosis, with a 5-year survival rate of less than 10%. It is caused by the canceration of vascular endothelial cells[3)]. The incidence in Japan is higher than in Europe and the United States (2.5 cases per million), and the incidence has been increasing in recent years. Paclitaxel, an apoptosis[4)] inducer, is the first-line treatment for angiosarcoma; however, the overall survival rate is short at 649 days, and even with the combination of paclitaxel chemotherapy and radiation therapy, long-term tumor regression or elimination is difficult in most cases. Pazopanib[5)], used as a second-line treatment, has a 3% response rate[6)] for angiosarcoma (Cancer 2022:128;3516). Furthermore, while eribulin[7)] demonstrates a certain response rate, it suffers from serious side effects in 64% of patients. There are currently no effective second-line treatments for angiosarcoma, making the development of new therapeutic agents urgently necessary.

Plasminogen activator inhibitor (PAI)-1 is produced by vascular endothelial cells, and is particularly highly expressed in angiosarcoma, a malignant tumor of vascular endothelial cells. PAI-1 has been shown to be deeply involved in tumor growth, metastasis, tumor immunity, and resistance to immunotherapy. In fact, it has been reported that paclitaxel is ineffective in patients with angiosarcoma with high PAI-1 expression. Furthermore, while paclitaxel induces apoptosis in angiosarcoma, it has also been shown that cancer cells with high PAI-1 expression are less susceptible to apoptosis. These findings strongly suggest that the combined use of paclitaxel and the PAI-1 inhibitor RS5614 may enhance the therapeutic efficacy of paclitaxel in unresectable angiosarcoma. The anti-tumor effects of the combination therapy with RS5614 are suggested to be related to the suppression of epithelial-mesenchymal transition (EMT)[8)], activation of T lymphocytes, reduction of tumor-infiltrating macrophages (TAM)[9)], increase in the number of T lymphocytes within the tumor, reduction in the expression of immune checkpoint molecules on cancer cells, overcoming cancer cell resistance to immune checkpoint molecule inhibitors, improvement of the tumor immune microenvironment[10)], and activation of tumor

immunity (disclosed in our news release dated November 11, 2025, and in our "Notice of publication of an article related to our company in Nature (Digital edition)" dated December 1, 2025).

This Phase II clinical trial evaluated the efficacy and safety of the combination of paclitaxel and RS5614 in patients with cutaneous angiosarcoma whose first-line treatment was ineffective (unresectable and paclitaxel ineffective). It was conducted as an investigator-initiated multi-center trial involving Tohoku University Hospital, Jichi Medical University Saitama Medical Center, Sapporo Medical University Hospital, Cancer Institute Hospital Ariake, Nagoya City University Hospital, Kyushu University Hospital, and Kumamoto University Hospital (coordinating investigator: Associate Professor Taku Fujimura, Department of Dermatology, Tohoku University Hospital). The trial began in October 2023, enrollment of 16 patients was completed as scheduled on June 19, 2025 (disclosed on June 20, 2025)., and treatment for all enrolled patients was completed on December 12, 2025. The final results will be compiled in a clinical study report.

[Phase II clinical trial flash report]

Sixteen patients were enrolled in this Phase II trial, but one patient was found to be ineligible for the trial. Therefore, efficacy will be evaluated on 15 patients. Safety was evaluated on 16 patients, including those who did not meet the eligibility criteria, due to the administration of medication.

Efficacy

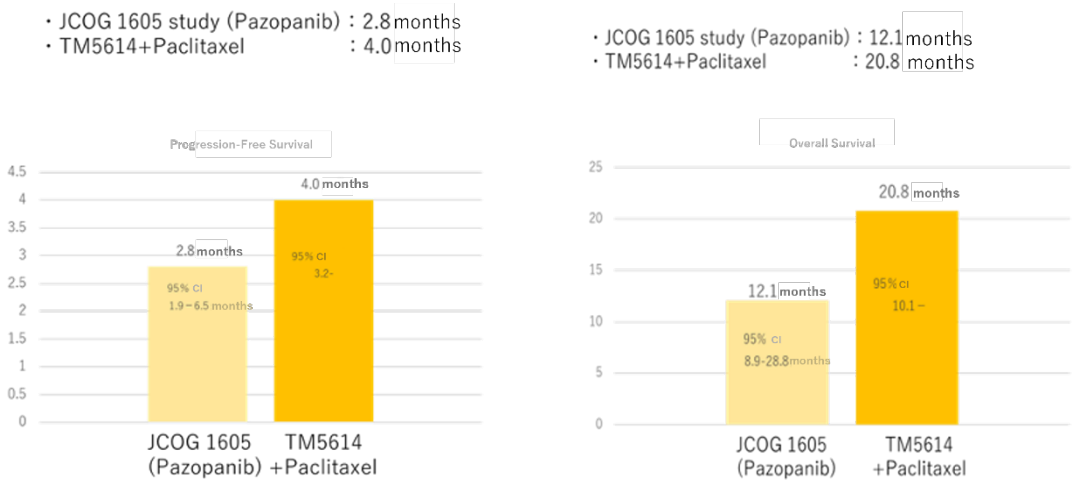
In the 15 patients analyzed for the primary endpoint, the response rate at 28 weeks after the start of treatment, as assessed by imaging (central review), was CR (complete response) 6.67%[11]. Furthermore, the progression-free survival (PFS)[12] and overall survival (OS)[13] were 4.0 months and 20.8 months, respectively, surpassing the 2.8 months and 12.1 months achieved in a prospective clinical trial of pazopanib (JCOG1605)[14] in Japan. Furthermore, disease stabilization was confirmed in 13 of the 15 patients (86.7%), demonstrating a high disease control rate[15].

Safety

No serious or unknown side effects were observed. Adverse events of Grade 3 or higher (liver dysfunction and leukopenia), for which a causal relationship to the study drug could not be ruled out, occurred in 5 of 16 cases (31.25%), all of which resolved. No serious adverse events related to the study drug were observed. Compared to the 70% of adverse events of Grade 3 or higher in JCOG1605, this drug appears to have better tolerability.

The high progression-free survival (PFS) and overall survival (OS) figures in this study are data that support clinical significance. This drug is considered a potential new treatment option for advanced cutaneous angiosarcoma, which has not responded adequately to existing treatments, demonstrating a survival benefit and a favorable safety profile. Given the extremely

short overall survival rate of this disease and the extremely small number of patients, making it difficult to develop new treatments, the development of this drug is considered to be an extremely high medical need. Going forward, we will compile the results of this clinical trial into a clinical study report and proceed with preparations for the next phase of trials and commercialization.




There is currently no impact on our financial results for the fiscal year ending March 31, 2026. However, we will make timely disclosures if any matters arise in the future.

[1] Cutaneous Angiosarcoma

Angiosarcoma is a type of skin cancer. Scalp angiosarcoma is particularly rare, occurring in approximately 2.5 cases per million. However, it is highly malignant, rapidly progressing, and the five-year disease-free survival rate is reported to be less than 20%, with no established standard treatment.

[2] Paclitaxel

This chemotherapy drug was discovered to have anticancer properties in the bark of the Pacific yew tree and is now chemically synthesized. It is thought to bind to microtubules, which are involved in cell division, thereby halting cancer cell division and causing cell death.

[3] Vascular Endothelial Cells

Cells lining the lumen of blood vessels. Vascular endothelial cells not only constitute blood vessels but also function as a site for the exchange of oxygen, nutrients, and other substances between blood and tissues. They also produce various physiologically active substances to maintain tissue and organ function.

[4] Apoptosis

Apoptosis is a process in which cells self-programmedly commit suicide in order to eliminate unnecessary cells.

[5] Pazopanib

This drug is a type of molecular targeted therapy that prevents cancer cells from growing by reducing blood flow to them. It is primarily used to treat renal cell carcinoma and soft tissue sarcoma. The side effect rate is high at 93.5%, with the main side effects being diarrhea, high blood pressure, fatigue, nausea/vomiting, liver dysfunction, and taste abnormalities.

[6] Response Rate

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

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|---|---|
| Complete response (CR) | Disappearance of all target lesions or reduction of the short axis of lymph nodes to less than 10 mm |
| Partial response (PR) | More than 30% reduction compared to before treatment |
| Progression (PD) | During treatment, the tumor grows by 20% or more from its smallest size or grows by 5 mm or more in diameter |
| Stable (SD) | Between partial response (PR) and progressive disease (PD) |

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

[7] Eribulin

Developed from a marine natural product, this anticancer drug acts on microtubules, a cellular component necessary for cell division, inhibiting the growth and killing of cancer cells. Serious side effects include bone marrow suppression, infections, fatigue, and numbness in the hands and feet.

[8] Epithelial-Mesenchymal Transition (EMT): This phenomenon occurs when epithelial cells, which form tissue through cell-cell adhesion, transform into highly mobile mesenchymal cells. This can promote tissue fibrosis, cancer invasion, and metastasis.

[9] Tumor-infiltrating Macrophages (TAMs)

Tumor-infiltrating macrophages are a type of immune cell that accumulates in cancer tissue. High levels of these cells are associated with poor patient prognosis. Specifically, they promote the production of cell growth factors and cancer cell proliferation, the release of angiogenic factors and increased blood supply to tumors, and the invasion and metastasis of cancer cells into surrounding tissues.

[10] Tumor Immune Microenvironment
This refers to a tissue state that differs from normal tissue due to interactions between cancer cells and surrounding cells. Anticancer drugs render cancer cells less susceptible to immune attack, and is thought to be one factor in the acquisition of resistance.

[11] Complete Response (CR)
This refers to a state in which all target lesions have disappeared and no new lesions have appeared (based on the RECIST guidelines).

[12] Progression-Free Survival (PFS)
This is one of the indicators used to evaluate the effectiveness of cancer treatment. It refers to the period from the start of treatment until cancer progression or recurrence is confirmed, or until the patient dies. The longer this period, the more effective the treatment.

[13] Overall Survival (OS)
This refers to the period from the start of treatment to the patient's death, and is one of the main indicators used to evaluate the effectiveness of cancer treatment.

[14] JCOG1605
This study evaluated the efficacy and safety of pazopanib therapy as second-line chemotherapy for patients with primary cutaneous angiosarcoma that had progressed or recurred after first-line chemotherapy with paclitaxel.

[15] Disease Control Rate
This is an indicator used in cancer treatment clinical trials. It indicates the percentage of patients who achieved complete response (CR), partial response (PR), or stable disease (SD), and evaluates the state of suppression of cancer progression.