September 29, 2026

To Shareholders,

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

Notice of Completion of Patient Dosing in a Phase III Trial of PAI-1 Inhibitor RS5614 in Combination with Tyrosine Kinase Inhibitors (TKIs) for Chronic Myeloid Leukemia

The Company, in collaboration with 12 universities and medical institutions in Japan, including Tohoku University, Tokai University, and Akita University, is conducting an investigator-initiated Phase III trial entitled "A Phase III Trial to Verify the Efficacy of RS5614 in Combination with Tyrosine Kinase Inhibitors (TKIs)[2)] for Chronic-Phase Chronic Myeloid Leukemia (CML)[1)]." We are pleased to announce that dosing of all 57 enrolled patients was completed on September 29, 2026. The trial will be evaluated and the data analyzed, and the results will be compiled in a clinical study report.

CML is a blood cancer caused by CML stem cells carrying the BCR-ABL gene, which arises from a genetic mutation in hematopoietic stem cells. It is a rare disease, with an estimated 1,300 new cases diagnosed annually in Japan (approximately 1 per 100,000 population) and a total patient population of approximately 15,000. The current standard of care is treatment with a tyrosine kinase inhibitor (TKI), such as imatinib. However, TKIs have limited efficacy against quiescent CML stem cells residing in the bone marrow niche, and many patients therefore require lifelong TKI therapy, which can result in adverse effects and a substantial economic burden. Recent prospective trials have shown that some patients with CML who receive long-term TKI therapy can achieve treatment-free remission (TFR), without relapse after TKI discontinuation, if they maintain a deep molecular response (DMR[3)]) for a certain period (at least two years). With existing TKI monotherapy, however, the cumulative 1-year DMR achievement rate is only 8–12% (historical control).

RS5614 is a PAI-1[4)] inhibitor under development by the Company. It has a novel mechanism of action distinct from existing therapies: it induces quiescent CML stem cells in the bone marrow niche to enter the cell cycle and promotes their differentiation, allowing the resulting differentiated CML cells to be eliminated by a TKI and thereby depleting the CML stem cell population itself. In an investigator-initiated late Phase II trial, proof of concept (POC) was established, with 48 weeks of combination therapy with RS5614 and a TKI resulting in a cumulative DMR achievement rate of 33.3%, substantially higher than the historical control of 8–12%. No serious adverse events for which a causal relationship with the investigational drug could not be ruled out were observed.

The trial was selected for funding under the fiscal year 2022 "Practical Research for Innovative Cancer Control" program of the Japan Agency for Medical Research and Development (AMED), and the first patient was dosed on August 3, 2022 (disclosed on August 3, 2022). Patient enrollment was completed at the end of December 2023, with 57 patients enrolled, exceeding the number required for analysis. Following AMED's final-year evaluation in December 2024, an extension of the grant period was approved on the basis that the required patient enrollment had been completed (disclosed on

December 3, 2024), and the trial has since progressed as planned.

This trial is a confirmatory study aimed at obtaining regulatory approval for RS5614 for the treatment of CML. If its efficacy is demonstrated in this study, RS5614 could provide a new treatment option for patients with CML.

[Impact on Financial Results]

The Company currently expects this matter to have no material impact on its financial results for the fiscal year ending March 31, 2027.

1) Chronic Myeloid Leukemia (CML)

CML is a blood cancer caused by CML cells carrying the BCR-ABL gene, which arises from a genetic mutation in hematopoietic stem cells. It is a rare disease, with an estimated 1,300 new cases diagnosed annually in Japan and a total patient population of approximately 15,000.

2) Tyrosine Kinase Inhibitors (TKIs)

TKIs are drugs that inhibit the abnormal tyrosine kinase protein produced by the BCR-ABL fusion gene, thereby suppressing the proliferation of CML cells and inducing cell death. Examples include imatinib, nilotinib, dasatinib, and bosutinib. TKI therapy has enabled many patients to avoid progression to blast crisis. However, TKIs have limited efficacy against quiescent CML stem cells residing in the bone marrow niche, and most patients therefore require lifelong TKI therapy.

3) DMR (Deep Molecular Response) and Treatment-Free Remission (TFR)

DMR refers to a deep molecular response in which CML-related genetic abnormalities are barely detectable, defined as a BCR-ABL^{IS} level of 0.0032% or lower on the International Scale (IS). Multiple prospective trials have shown that some patients with CML who maintain DMR for at least two years can achieve treatment-free remission (TFR), meaning that no molecular relapse occurs even after discontinuation of TKI therapy.

4) PAI-1

PAI-1 stands for Plasminogen Activator Inhibitor-1, a factor that suppresses the fibrinolytic system involved in dissolving blood clots. In addition to its role in vascular endothelial cells, recent studies have shown that PAI-1 is involved in the mobilization of hematopoietic stem cells from the bone marrow niche and in cellular differentiation. PAI-1 is also known to be one of the principal components 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 anti-aging and longevity through the clearance of senescent cells (senolysis).