

January 27, 2025

To Shareholders,

Company Name: Renascience Inc.
Representative: Keisuke Furuta, President & CEO
(Code: 4889 TSE Growth)
For inquiries, please contact Administration Dept.

Frequently Asked Questions and Answers

We would like to disclose the main questions and answers we have received from investors recently as follows. This disclosure is intended to strengthen information dissemination to investors and to ensure fair disclosure.

Q1. Could you please tell us about the milestone payments and royalties for ET-02 (active ingredient, RS5441) developed by Eirion Therapeutics, Inc. (hereinafter referred to as "Eirion")?

A1. ET-02 is a topical medication for male pattern baldness and age-related alopecia developed by Eirion, and we have licensed its active ingredient, RS5441, to Eirion.

As for future milestones, as stated in the timely disclosure on January 9, 2025, "Announcement of the results of the Phase I clinical trial with ET-02 (Active Ingredient RS5441) for the for the treatment of androgenetic alopecia (AGA) and age-related hair loss at Eirion Therapeutics, Inc., USA," we will receive a milestone of US\$200,000 when the first patient is enrolled in the Phase II trial, and we plan to receive subsequent milestone payments accordingly.

We cannot disclose specific figures, but as there is a royalty agreement in the license agreement with Eirion, we plan to receive royalties upon commercialization of ET-02.

Q2. Is Renascience a company that develops medicines for alopecia?

A2. As stated in A1 above, we have licensed RS5441, the active ingredient of ET-02, a topical medication for male pattern baldness and age-related alopecia. RS5441 is a drug developed by our company, but the development of male pattern baldness and age-related alopecia is carried out by Eirion.

Our company has many R&D pipelines, and treatment modalities are diverse, including pharmaceuticals, medical devices, and medical softwares. In addition to small molecule drugs (PAI-1

inhibitors such as RS5614 and RS5441), we are also developing biopharmaceuticals (nucleic acid drugs) in our pharmaceutical pipeline. PAI-1 inhibitors are small molecule drugs that we are focusing on, and we are developing them for the treatment of cancer (chronic myeloid leukemia and melanoma in phase 3 trials, non-small cell lung cancer and angiosarcoma in phase 2 trials) and aging-related diseases (lung diseases, etc.). We are developing alopecia (RS5441) in collaboration with Eirion as one of our pipelines for aging-related diseases. We are very excited about this pipeline, but it is only one of our pipelines.

Q3. Is Renascience a company that develops anti-aging medicines?

A3. In developed countries, including Japan, the super-aging society is progressing, and the difference between average life expectancy and healthy life expectancy (the period during which one can live independently in both body and mind and is healthy, minus the period of nursing care such as bedriddenness or dementia) is about 10 years, which is a major issue. We aim to develop drugs to treat aging-related diseases and extend healthy life expectancy. Various diseases that occur with aging, such as cancer, blood vessels (arteriosclerosis), lungs (emphysema, chronic obstructive pulmonary disease), metabolism (diabetes, obesity), kidneys (chronic kidney disease), bones and muscles (osteoporosis, sarcopenia), and brain (cerebrovascular disease, Alzheimer's disease, dementia), can be improved in a multifaceted way to extend healthy lifespan. In that sense, we are working on developing anti-aging medicines, but our goal is to extend healthy lifespan by treating aging-related diseases, not to develop drugs that will make us immortal.

The following series of scientific findings have been obtained through collaborative researches with Northwestern University and Tohoku University.

- Cells in living organisms cannot proliferate indefinitely due to a phenomenon called cellular senescence. This phenomenon involves shortening of the telomere length of genes and cellular senescence factors such as p53, p21, and p16. It has been found that senescent cells have extremely high expression of plasminogen activator inhibitor (PAI)-1. The PAI-1 inhibitor developed by our company inhibits p53, p21, and p16, inhibiting cellular senescence in cardiomyocytes, fibroblasts, and vascular endothelial cells (Oncotarget, 2016).
- The PAI-1 inhibitor developed by our company reduces DNA damage in fibroblasts of Hutchinson-Gilford syndrome (designated intractable disease 333), a human premature aging disease, improves mitochondrial disorders, and corrects cellular abnormalities in Hutchinson-Gilford syndrome (Cell Death and Disease, 2022).
- It is known that PAI-1 expression is high not only in cells but also in aged tissues and individuals (mice and humans). In a non-clinical study using *klotho* mice, a well-known aging model, in a

joint research project between Tohoku University and Northwestern University in the United States, the PAI-1 inhibitor improved the main symptoms of aging in klotho mice (Proc Natl Acad Sci USA. 2014).

- We tested the blood of Amish people living in the United States and confirmed that many of them have a PAI-1 gene deficiency. We reported that these PAI-1 gene deficiency individuals live about 10 years longer than those with the same gene (Science Advances, 2017). This human epidemiological study is consistent with the results of experiments on cells and mice. This fact was introduced in an article in the New York Times on November 21, 2017 (November 11, 2021).
- PAI-1 expression is extremely high in organs with age-related diseases shown above, and it has become clear through collaborative researches with many universities in Japan and abroad that administering our PAI-1 inhibitors can improve the pathology.

RS5614, which we are developing, has been confirmed in non-clinical trials to have the potential to improve various aging-related diseases, and is being examined in clinical trials. At present, RS5614 is being developed as a medical drug (a drug used based on a doctor's diagnosis and prescription, also known as a prescription drug), so clinical trials are being conducted to determine the suitability of the drug for each individual disease. Our goal in anti-aging is to scientifically extend healthy lifespan by overcoming various age-related diseases, and we do not advocate the development of a drug that will make us immortal.

Longevity is difficult to verify in clinical trials, so it is not a target for medical drugs. On the other hand, the longevity and anti-aging will be important themes in the self-medication field and OTC drug market¹⁾, which is growing rapidly against the backdrop of super-aging. As mentioned above, RS5441 has been used as a treatment for alopecia, and if our anti-aging researches on PAI-1 inhibitors progress, we would like to consider applications other than prescription drugs in the future.

¹⁾ OTC drugs

Over-the-counter (OTC) drugs that can be purchased at pharmacies and drugstores without a prescription.