

May 16, 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. I would like to know when the Phase II clinical trial of ET-02 (active ingredient RS5441) developed by Eirion Therapeutics, Inc. (hereinafter "Eirion") will begin.

A1. ET-02 is a topical medication for male pattern baldness and age-related alopecia being developed by Eirion, and we have licensed its active ingredient, RS5441, to Eirion. The completion of the Phase I trial of ET-02 was disclosed in the "Announcement of Phase I Clinical Trial Results of ET-02 (RS5441), a Topical Drug for Male Pattern Baldness and Age-Related Alopecia, by U.S. Company Eirion Therapeutics, Inc." dated January 9, 2025. The Phase II trial will be conducted by Eirion, the licensee, and details such as the start date will be determined by Eirion. According to recent communication from Eirion, they are preparing for Phase II trials, including FDA approval. Once we receive some information from Eirion regarding the start date, we will disclose the details as soon as possible.

Q2. Can Renascience receive royalties from Eirion even if the patent term has expired?

A2. Although we cannot disclose specific royalty figure, we have royalty arrangements in place in our license agreement with Eirion, and we expect to receive royalties upon the commercialization of ET-02. The royalty payment period is set to expire on the later of (a) the last date that the ET-02 product is covered by a valid claim of our licensed patent, (b) the expiration date of any regulatory or data exclusivity for the ET-02 product, and (c) ten years after the first sale of the ET-02 product. Therefore, even if the patent term expires, we expect to receive royalties during these periods.

Q3. What kind of clinical research will be conducted in the XPRIZE Healthspan competition as a Top40 winner?

A3. As humans age, cancer cells and senescent cells develop. These cells must be eliminated by the immune system, but because a molecule called "PAI-1" is expressed and inhibits the immune system, the immune system is unable to effectively eliminate these cells from our body. Experiments on mice and epidemiological studies on humans who were born without the PAI-1 gene have

demonstrated that those without the PAI-1 gene live longer (10 years in humans and 20 % in mice). The efficacy and safety of RS5614 against cancer have been or are currently being tested in human Phase II trials against several types of cancer, including malignant melanoma, lung cancer, and hemangiosarcoma. As promising results were obtained against malignant melanoma, the drug was designated as a orphan disease drug by the Ministry of Health, Labor, and Welfare last year, and Phase III trials for pharmaceutical approval are currently underway.

In the XPRIZE Healthspan trial, we will examine efficacy and safety of RS5614 for anti-aging, not cancer. In developed countries, including Japan, the aging of the population is progressing, and the gap between average life expectancy and healthy life expectancy (the period of time when a person can live independently and in good physical and mental health, and is calculated by subtracting the period of being bedridden or in nursing care conditions such as dementia) from the average life expectancy has become a major issue. The XPRIZE Healthspan is the first global longevity clinical research competition aimed at demonstrating improvements in organ function, particularly immune, muscular and cognitive functions, for 10 years. The goal is not "immortal longevity," which is unscientific and unrealistic, but rather "improvements in immune, muscular and cognitive functions for at least 10 years. ¥

Q4. Why have little clinical studies been conducted for anti-aging in humans until now?

A4. Clinical trials for a drug (for example, a drug to treat melanoma) involve patients with a specific disease (melanoma). On the other hand, the clinical trial for anti-aging will target a broad range of elderly people, including those with multiple lifestyle-related diseases, and therefore the backgrounds of each patient's diseases will vary greatly. In addition, a considerable period of time is required to determine the anti-aging effectiveness of a medicine. In the XPRIZE Healthspan trial, the effectiveness of treatment must be evaluated over a short period of time, such as a few months (semi-final) or a year (final). Furthermore, there are no established clinical endpoints for assessing the effectiveness of anti-aging benefits for individuals or organs. For these reasons, it is extremely difficult to conduct specific clinical trials to confirm the anti-aging effects of medicines. The final trial of the XPRIZE Healthspan will focus on evaluating a few biological functions, including immune, muscle, and cognitive function, and the evaluation criteria will be determined by the XPRIZE Healthspan judging committee. Until now, anti-aging research has mainly been conducted on mice, and the XPRIZE Healthspan will be the first to conduct clinical trials on humans on a global scale. It is expected that the XPRIZE Healthspan will accelerate the scientific, objective and rational development of human anti-aging medicines.

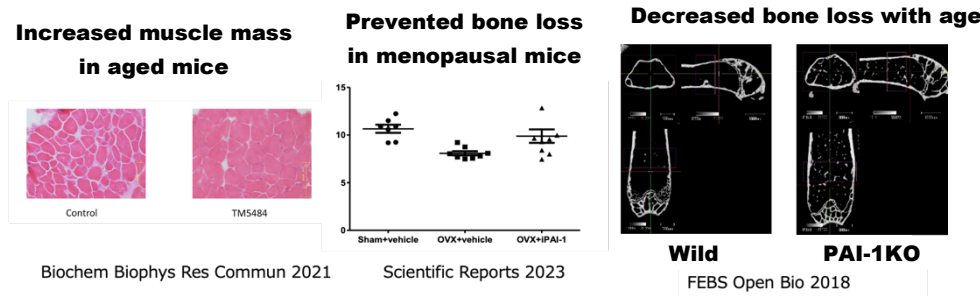
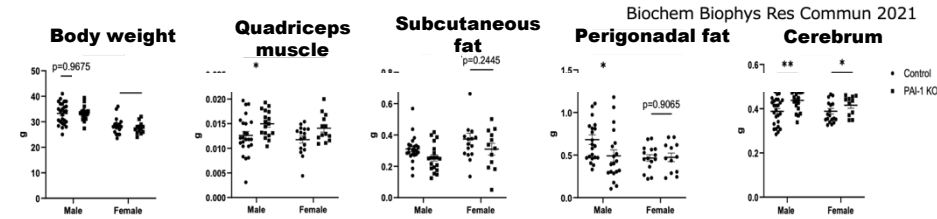
Q5. The XPRIZE Healthspan project aims to improve immune, muscle and cognitive function. Can RS5614 be expected to have an effect on improving these functions?

A5. Preclinical studies (in animal models) have confirmed that RS5614 treats cancers by inhibiting PAI-1 and immune checkpoint molecules expressed in cancer cells, thereby activating the immune system against cancer. In a human clinical trial for malignant melanoma (Phase II), therapeutic effects were confirmed despite the short administration period of two months, demonstrating at the very least the improvement of immune function against cancer. In this XPRIZE Healthspan, we will

be examining improvements in immune function for anti-aging but we believe that this will be relatively easy to examine as there are many biomarkers and other indicators for evaluating immune function.

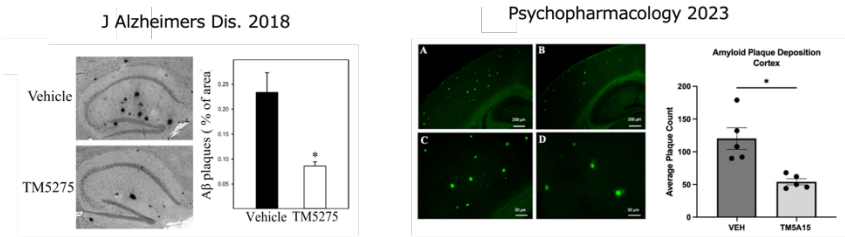
Regarding muscle function, as shown in the figure below, we have confirmed an increase in muscle and bone mass in PAI-1 gene-deficient mice and aged mice administered a PAI-1 inhibitor.

Increased brain and quadriceps muscle weight, decreased fat mass(PAI-1 knockout mice)

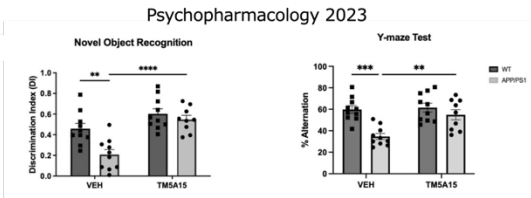


Regarding cognitive function, administration of a PAI-1 inhibitor to a mouse model of Alzheimer's disease reduced amyloid deposition and improved cognitive function and learning disabilities.

Reduce amyloid deposits(PAI-1 inhibitors)



Preventing cognitive and learning impairments in mice



As such, improvements in immune, muscle, and cognitive function were observed in mice, and these results have been reported in scientific journals. However, it is unclear whether short-term oral

administration can be shown to improve these functions in humans through clinical studies. We plan to have experts in the immune system, muscles, and cognitive function take part in this program.

Q6. How will participating in XPRIZE Healthspan impact Renascience business?

A6. Renascience aims to develop pharmaceuticals to treat age-related diseases and extend healthy lifespan. If we treat various age-related diseases in a multifaceted way, such as cancer, cardiovascular disease (arteriosclerosis), lung disease (emphysema, chronic obstructive pulmonary disease), metabolic disease (diabetes, obesity), chronic kidney disease, bone and muscle diseases (osteoporosis, sarcopenia), and cranial nerve diseases (cerebrovascular disease, Alzheimer's disease, dementia), we can extend healthy lifespan. Preclinical studies have shown that RS5614 is effective against many of these age-related diseases, in addition to cancer. For cancer, we are conducting several clinical trials with the aim of commercializing it as a medical drug (a drug used based on a doctor's diagnosis and prescription, also known as a prescription drug). On the other hand, longevity is difficult to verify through clinical trials, so it is not eligible for medical drugs. However, longevity and anti-aging are important themes in the self-medication field and OTC drugs, which is growing rapidly against the backdrop of the super-aging population. There is also an example of RS5441 being used as a treatment for alopecia, and if the XPRIZE Healthspan clinical study further advances our anti-aging research on PAI-1 inhibitors, we would like to think it can be expanded other business other than medical drugs, *e.g.*, OTC drugs, veterinary drugs, etc.