To our shareholders and investors,

Following my message in November, I would like to share highlights from two major academic conferences where I recently presented: the Keystone Symposia and the 90th Annual Scientific Meeting of the Japanese Circulation Society (JCS2026). I hope this message conveys the enthusiasm of these conferences and the growing momentum behind cardiomyocyte replacement therapy.

■ Keystone Symposia: iPSCs: Progress, Opportunities, and Challenges

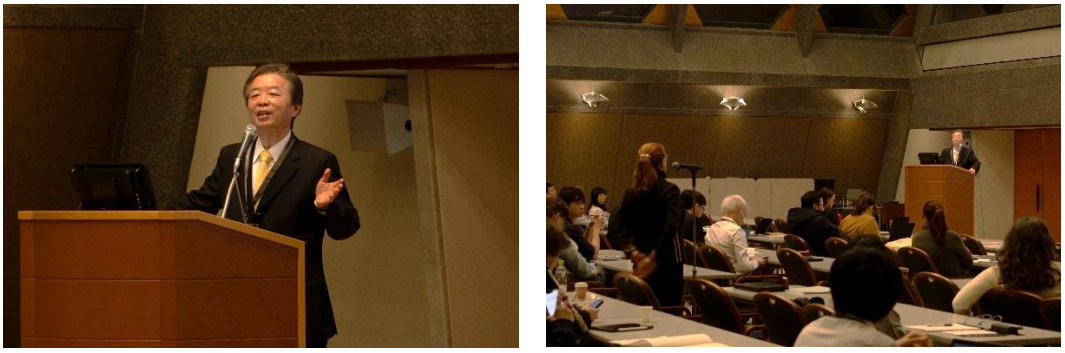
The first conference was Keystone Symposia, an international academic meeting held at the Kyoto International Conference Center from January 27 to 29. Keystone takes its name from a well-known ski resort in Colorado, USA, where these prestigious symposia are typically held during the winter season. Researchers gather at resort venues for intensive, discussion-focused meetings across a wide range of topics in biology and medicine. It was a great honor to be invited to speak at this symposium, which brings together leading researchers from around the world. This year's meeting was exceptionally held in Kyoto, reflecting several factors: the focus on iPSC (induced pluripotent stem cell) research, the leadership of Professor Shinya Yamanaka of Kyoto University - who pioneered iPSCs - and the fact that 2026 marks the 20th anniversary of their discovery. As such, the most important theme was how far clinical applications have progressed.

The first day of the symposium, January 27, opened with a special lecture by Professor Yamanaka. He delivered a comprehensive review of the history of iPSC research, from its very beginnings to subsequent advances and the present day and spoke of his expectations for the future of regenerative medicine, which has now reached clinical application two decades after iPSC development. Lectures on day one focused on using iPSC-based disease models to investigate the underlying causes of illness, featuring presentations on the elucidation of disease mechanisms and development of therapies using iPSCs derived from patients with various genetic disorders. Professor Fred Gage of the Salk Institute in San Diego presented on the pathological analysis of neurological diseases and drug discovery using patient-derived iPSCs, while Professor Deepak Srivastava of the Gladstone Institutes at UC San Francisco spoke on cardiac disease pathology and drug discovery. Highly compelling lectures from these world-leading researchers continued throughout the day － content that could only be heard at a conference of this caliber. In the afternoon, research on disease modeling using three-dimensional organoid structures derived from iPSCs was also presented.

On the second day, January 28, presentations were given on iPSC-based therapeutic approaches that, while still at the basic research stage, are expected to advance toward clinical application in the future. A series of reports covered the latest research in iPSC-based treatment of myelin diseases (Beckman Research Institute), microglial diseases (University of California), autologous iPSC therapy (Cellino Biotech), and thymic immune cells (Stanford University). Results from a collaborative project between Takeda Pharmaceutical Company and the CiRA (Center for iPS Cell Research and Application) at Kyoto University were also introduced, covering regeneration of pancreatic beta cells and cardiomyocyte-based drug screening technology. In the afternoon, presentations were made on the current state of lung regeneration research using iPSCs (UCLA) and on studies examining the interaction between neural tissue and tumors. The highlight of the day was a report by Professor Hideyuki Okano of Keio University on a clinical study in which neural stem cells derived from iPSCs were transplanted into four patients with subacute spinal cord injury. Professor Okano noted that a corporate clinical trial (K Pharma) with a larger number of cases is planned for the future. He is a classmate of mine from Keio University and serves as President of the International Society for Stem Cell Research (ISSCR) - I am always struck by the depth of his science. One evening during the conference, the three of us engaged in wide-ranging discussions with Professor Seigo Izumo - former Professor of Medicine at Harvard Medical School and former Global Head of the Regenerative Medicine Unit at Takeda - about what strategies are needed to advance regenerative medicine in Japan and how we ourselves can contribute to that progress.

On the final day of the conference, January 29, a series of important presentations was delivered. Topics included retinal pigment epithelium (Dr. Masayo Takahashi: Vision Care Inc.), Parkinson's disease (Prof. Jun Takahashi: Kyoto University), cardiac disease (Fukuda: Heartseed Inc.), diabetes (Prof. Hongkui Deng: Peking University), and cartilage (Nuwacell Biotechnologies). Dr. Masayo Takahashi is a distinguished researcher who pioneered the world's first transplantation of iPSC-derived retinal pigment epithelium into the retinas of patients with age-related macular degeneration and currently serves as President and CEO of Vision Care Inc., a RIKEN spin-off venture. Her approach has evolved from initial transplantation of sheet-form tissue to suspension of isolated single cells, and most recently to the use of strand-shaped tissue constructs. Dr. Takahashi noted that she is advancing development to enable this therapy to be performed at designated hospitals as advanced medical care or under private medical care in Japan. Prof. Jun Takahashi's approach involves generating dopaminergic neurons from iPSCs and transplanting approximately 10 million cells into the substantia nigra-striatum region of the brain using stereotactic neurosurgery. Prof. Deng reported on development aimed at lowering blood glucose levels through transplantation of beta cells - the insulin-secreting cells of the pancreatic islets of Langerhans.

In my own presentation, I reported an interim clinical trial results from the LAPiS study, in which allogeneic iPSC-derived ventricular cardiomyocytes were produced, purified, and formed into cardiomyocyte spheroids (micro-cardiac muscle tissue clusters) prior to transplantation in patients with severe heart failure due to ischemic heart disease.



(Photo courtesy of Center for iPS Cell Research and Application, Kyoto University)

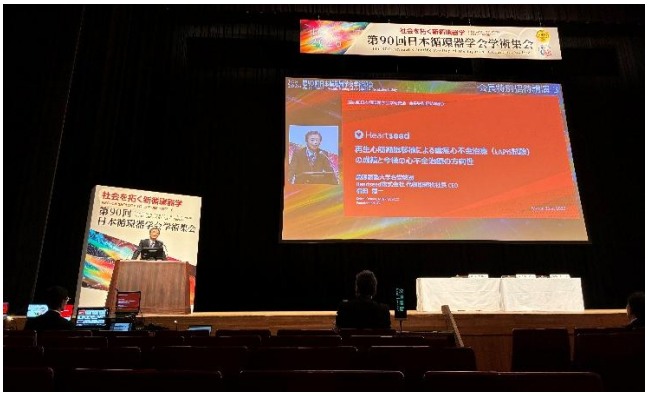
First, I explained that this clinical trial targets patients with severe heart failure for whom existing treatments have not provided sufficiently satisfactory outcomes, by comparing the severity of the enrolled patients with those in previous clinical studies. I then presented one-year clinical data from five patients in the low-dose cohort (50 million cells) and six-month data from five patients in the high-dose cohort (150 million cells). Regarding safety, I explained that no serious adverse events (SAEs) such as tumor formation or lethal arrhythmias have been observed at this stage. Mild adverse events assessed as possibly related to the investigational drug included one case of herpes zoster (likely associated with immunosuppressant use), two cases of mild pneumonia, and transient atrial fibrillation. Regarding efficacy, I reported that data generally showing trends consistent with what was expected, based on pre-specified endpoints, have been obtained across both low- and high-dose cohorts, and engaged in discussion with specialists. In addition, improvements in regional wall motion at the transplantation sites were demonstrated using echocardiography and MRI videos in multiple cases. I believe this presentation constitutes one academic milestone toward the societal implementation of regenerative medicine using ventricular cardiomyocytes. Finally, I reported that we will shortly be initiating a clinical trial using a delivery catheter system co-developed with Japan Lifeline Co., Ltd., which will allow cardiomyocytes to be delivered from within the left ventricular cavity via a catheter-based approach.

In response, I received more than 10 questions from the audience - the highest number at this conference - and an active exchange of views took place regarding specific challenges on the path to practical implementation, including methods for confirming engraftment of

transplanted cells and optimization of immunosuppression protocols. The questions were so numerous that I significantly exceeded my allotted time; fortunately, my presentation happened to fall just before the break, so I did not inconvenience the subsequent presenter. In any case, I was personally delighted to receive such high levels of interest and warm words of academic praise from so many physicians. I believe this conference allowed us to demonstrate the capabilities of Japan's cardiomyocyte replacement therapy and to show that Japan's iPS cell-based regenerative medicine is at the forefront globally.

■ 90th Annual Scientific Meeting of the Japanese Circulation Society (JCS2026)

I was invited to deliver a Special Lecture at the Annual Scientific Meeting of the Japanese Circulation Society, held from March 20 to 22 at the Fukuoka International Congress Center, Fukuoka Sunpalace, and other venues. Thanks to the kind consideration of Professor Koichi Node, President of Saga University, I was given the opportunity to present in the largest hall during the prime time slot following the luncheon seminar on March 21, the second day of the conference. This time slot attracts the largest audience, and a full one-hour session was arranged. In addition to my longstanding relationship with Professor Node, I strongly felt the urgent expectations surrounding regenerative medicine as it enters the clinical stage, and I was once again reminded of the high level of attention from the academic community. The session was chaired by Prof. Koichiro Kinugawa (University of Toyama), the President of the Japanese Heart Failure Society, with Prof. Takayuki Inomata (Niigata University) and Prof. Masaru Hatano (Tottori University) - both leading authorities in heart failure - serving as discussants, enabling an exceptionally stimulating exchange of views.



The content of the presentation was essentially the same as that delivered at Keystone Symposia; however, given the additional time available, I was able to include materials

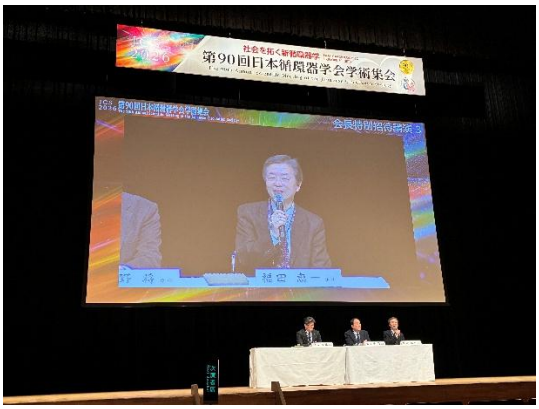
previously presented at several conferences by investigators from the trial sites, showing pre- and post-operative (6-month or 1-year) analyses of regional wall motion at transplantation sites on a case-by-case basis. I believe these findings will provide important academic insights for evaluating objective assessment methods in cardiomyocyte replacement therapy going forward.

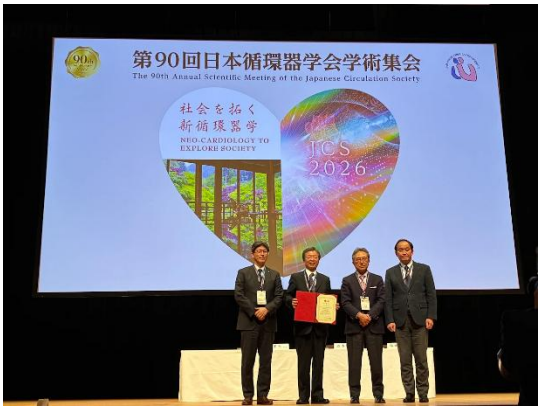
During the Q&A session, Prof. Inomata raised a sharp question regarding the relationship between increases in myocardial mass observed through imaging and changes in wall motion, including the underlying biological mechanisms. In response, I discussed several possible scientific explanations, including in vivo maturation and physiological changes of transplanted cardiomyocytes, as well as the potential paracrine effects of humoral factors released by the cells. We also engaged in a detailed discussion, based on careful case analyses, on the scientific significance of myocardial transplantation as a novel therapeutic approach distinct from bypass surgery.

Prof. Hatano raised a specialized question regarding the progression of transient ventricular arrhythmias (AIVR) observed during postoperative follow-up and their relationship to the engraftment process of transplanted cells. In response, I discussed the intrinsic immunological characteristics of cardiomyocytes, such as low HLA expression, as well as the possibility that these arrhythmias represent physiological responses during the process of electrical integration with surrounding myocardial tissue.

I also referred to comparisons with cases reported overseas and shared the importance of our company’s approach of selectively transplanting high-purity ventricular cardiomyocytes, established through our proprietary technology, which may contribute to reducing post-transplant arrhythmia risk and achieving more stable engraftment.

Prof. Hatano further raised questions regarding the management of acute arrhythmia and improvements in subjective symptoms. While I will omit the details, I believe I was able to respond to most questions with reasonable clarity. Each discussant is an opinion leader in heart failure care in Japan, and a number of incisive questions were posed.





Following the presentation, I received direct feedback from more than 10 physicians, representing a wide range of reactions: surprise at the progress of current cardiomyocyte replacement therapy, and heartfelt voices from the front lines of care expressing eager anticipation for its practical implementation. Hearing these perspectives from cardiologists and cardiovascular surgeons at the forefront of heart failure treatment, I once again recognized the magnitude of the role that Heartseed is expected to play. At the same time, I reinforced my commitment to advancing our clinical trials and regulatory approval processes with even greater care and diligence.

Heartseed Inc.　President and CEO　Keiichi Fukuda

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