To our shareholders and investors,

Thank you sincerely for your ongoing support of Heartseed Inc. I am Keiichi Fukuda, President and CEO. In this TOP MESSAGE, I would like to share, to the extent possible, my reflections on the 30th Annual Scientific Meeting of the Japanese Heart Failure Society (JHFS), held in Toyama, Japan from October 23, 2026.

■ **Symposium 4: "Cutting-edge medicine originating from Japan"**

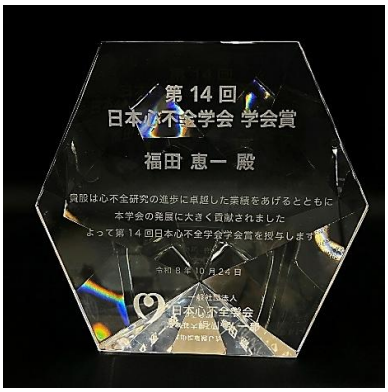


On the first day of the meeting, I had the honor of serving as a co-chair for Symposium 4, where five distinguished speakers gave presentations. Among them, the presentation titled "Clinical implementation of severe heart failure treatment using iPS cells: The world's first catheter-based cardiomyocyte transplantation for dilated cardiomyopathy" delivered by Dr. Hideki Kobayashi from the Department of Cardiovascular Medicine at Shinshu University Hospital, drew significant attention from the audience. He reported the 6-month post-transplantation progress of the first patient enrolled in the EMERALD study—our clinical trial evaluating catheter-based administration of our proprietary iPS cell-derived ventricular cardiomyocyte spheroids. In addition to the absence of serious complications, he reported an improvement in left ventricular ejection fraction (LVEF) and evidence of reverse remodeling (reduction in left ventricular end-diastolic/end-systolic volumes) as early as one month post-transplantation, with these therapeutic effects maintained at six months.
What astonished the attending physicians, including myself as co-chair, were the echocardiogram video recordings. The footage clearly captured how the left ventricle—which had been severely dilated with exceedingly weak contraction prior to the transplantation—gradually contracted and showed marked improvement in systolic function over time. This presentation prompted enthusiastic questions and expressions of astonishment from the session co-chair, Prof. Yuichi Tamura (International University of Health and Welfare Mita Hospital), as well as from physicians across the hall. While it is far too early to draw definitive conclusions based solely on 6-month data from a single patient, the suggestion that this therapy may be effective for dilated cardiomyopathy, coupled with favorable 6-month efficacy data in a setting without concomitant coronary artery bypass grafting (CABG), represents tremendously encouraging news—not only for HS-005 (catheter-based delivery), but also for HS-001 (open-chest delivery).

■ **Symposium 12: "What incentives can we offer cardiologists to persevere in the era of work-style reform?"**

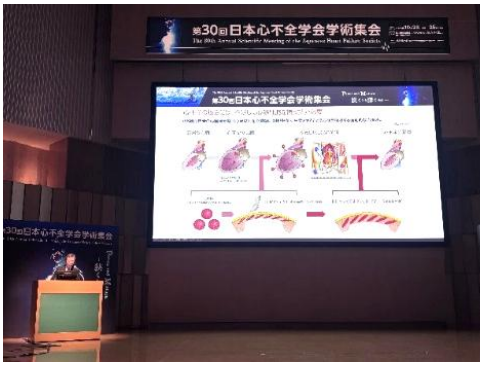
On the morning of the following day, October 24, I gave a lecture in Symposium 12 titled "The advantages of cardiologists: Perspectives from a basic researcher turned entrepreneur." This symposium was organized out of growing concern over the current decline in applicants entering cardiology and cardiovascular surgery due to demanding workloads and frequent emergency duties. Reflecting on my origins in founding an academic-origin startup, I shared my enduring conviction: "To create novel therapies based on our own research findings and contribute to the well-being of humanity." Furthermore, I emphasized that successfully translating research findings into society requires assembling people, capital, and information into an organization. I offered words of encouragement to the audience, noting that by acquiring management acumen, physicians can become highly capable and successful entrepreneurs. While I still consider myself an executive mid-journey, I hope my own career path demonstrates new avenues of opportunity for young researchers and inspires many of them to step forward as entrepreneurs.

■ **2026 Society Award / Scientific Award Lecture**



On the afternoon of October 24, at the General Assembly of the Japanese Heart Failure Society, I was deeply honored to receive the 14th Society Award, presented by Prof. Koichiro Kinugawa, President of the Japanese Heart Failure Society (Professor, Second Department of Internal Medicine, Faculty of Medicine, University of Toyama). In the subsequent award commemorative lecture, I outlined Heartseed's platform technologies spanning from iPS cell manufacturing to cardiomyocyte spheroid generation. I also reviewed the clinical outcomes of the LAPiS study presented at the European Society of Cardiology (ESC Congress 2026) this past August, as well as the clinical outcomes of the first case in the catheter-based EMERALD study.

Regarding the LAPiS study, I publicly disclosed, for the first time, case-by-case analysis results using SPECT (evaluation of myocardial perfusion and tissue viability using nuclear imaging) to clearly differentiate between "ischemic regions" (reduced blood



perfusion alone) and "infarcted regions" (loss of myocardial tissue). Normally, ischemic myocardium holds potential for functional recovery following coronary revascularization with CABG. However, our analysis revealed that most of the left ventricle in these enrolled patients had already transitioned into infarcted tissue. Notably, in four out of five patients in the high-dose cohort, ischemic regions were undetectable both before and after procedure. Despite these patients being considered CABG non-responders, marked improvements in LVEF were observed. We believe this strongly suggests a direct therapeutic effect driven by the cardiomyocyte spheroids themselves. Concluding the lecture, I shared lessons learned from my own experiences regarding key considerations for the social implementation of basic research, and once again expressed my sincere gratitude to all the laboratory members at Keio University who have dedicated themselves to our research.

■ **President's Special Program 8: "The dawning era of cardiac regenerative medicine before us (iPS sheets & iPS spheroids)"**

At the conclusion of the day, I spoke at President's Special Program 8. Organized by Congress President Prof. Kinugawa, this session featured in-depth discussions on two leading clinical-stage approaches: "iPS cell-derived cardiomyocyte sheets" and "iPS cell-derived cardiomyocyte spheroids." The venue was packed to full capacity with standing room only, allowing me to directly feel the tremendous level of enthusiasm surrounding this field. While their mechanisms of action differ, I believe expanding the range of future treatment options for patients will be immensely valuable.

Over the course of that single day, I served as a chair or speaker across four distinct sessions, speaking for more than 70 minutes in total until my voice was hoarse. It was an intense yet deeply rewarding day.

■ **Closing Remarks**

At this meeting, where physicians leading the field of heart failure management assembled, seeing such high levels of interest directed toward the follow-up data of the first case of the EMERALD study and our corporate presentations served as immense encouragement. Precisely because regenerative medicine entails many uncharted frontiers, it is crucial that we rigorously build robust science, present it transparently to academic experts in the field for debate, and continually acquire new perspectives. Building

upon the favorable overall data from the LAPiS study, I found it profoundly meaningful to share our process of meticulously analyzing each case via SPECT to verify what worked and how.

Furthermore, regarding the EMERALD study, each clinical trial site has been advancing the trial with utmost rigor and dedication, providing tremendous collaboration toward realizing this novel therapy. I would like to take this opportunity to extend our deepest gratitude to all of them. Humbled and motivated by this Society Award, I will continue to make every effort to contribute to the advancement of heart failure research and cardiovascular medicine, and to deliver this therapy to patients as promptly as possible. We sincerely appreciate your continued warm encouragement and support.

Heartseed Inc.　President and CEO　Keiichi Fukuda



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