To our shareholders and investors,

Thank you for your continued support of Heartseed Inc. I am Keiichi Fukuda, President and CEO. This is my second message since launching this column in March, and I would like to share my thoughts on our current situation and progress over the past few months.

<Regarding the termination of our partnership with Novo Nordisk A/S and our mid-to-long-term direction>

First, I need to take up this topic, the partnership termination with Novo Nordisk A/S (hereafter "Novo Nordisk") disclosed on September 30, 2025, which should be one of the biggest concerns and interests of our shareholders regarding the company's future direction.

■ Notification of the partnership termination from Novo Nordisk and our response on the day

On the Monday afternoon of September 29, 2025, a letter arrived from Novo Nordisk via international courier about the partnership termination without prior communication. It appears the system was set up so that the time of our receipt was notified to Novo Nordisk right away. After reviewing the letter myself, the first thing that came to my mind was urgent timely disclosure. We prioritized understanding the situation as fact findings with Novo Nordisk, and worked through the night to prepare for disclosure. To ensure fair disclosure and foster investors' understanding, the materials and Q&As were released on our website over three days.

■ Novo Nordisk business re-organization and our perspective on it

Subsequent media reports and public disclosures revealed that Novo Nordisk's structural reforms were of a scale and urgency exceeding our expectations. Many Novo Nordisk employees, despite facing the threat of restructuring for themselves, too, made every effort to ensure the appropriate transfer of the substantial information discussed during our

collaboration, in accordance with our contract. Besides, Heartseed had received approximately total JPY 6B in the upfront and milestone payments designated in the partnership agreement, which contributed the transition of our development stage from pre-clinical to pre-commercial through the conduct of the clinical trial. We would like to express sincere gratitude for all the experience in the collaboration journey with Novo Nordisk.

■ Strategic direction going forward

Since the business development in Japan has been planned under our leadership from the beginning, the partnership termination by Novo Nordisk should not have negative impact on this. As we had planned to entrust overseas expansion to Novo Nordisk, the strategy in ex-Japan region should be re-structured. Given the positive clinical trial progress and the significant advancement in our business stage, coupled with the fact that the development and marketing rights previously granted to Novo Nordisk are now 100% returned to us, we can select the best options to build a medium- to long-term strategy that maximizes our corporate value over the period, without rushing.

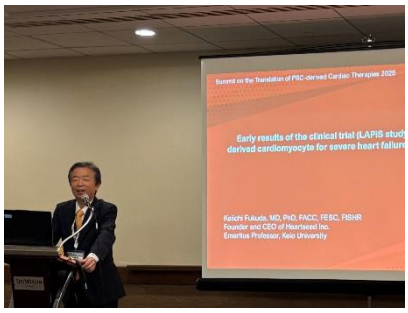
<Report about the clinical trial progress in international conferences>

In this November, I had opportunities to explain the progress of our on-going clinical trial at international academic conferences. Thanks to the tremendous support and dedication of investigators and stakeholders in clinical sites toward our cardiomyocyte replacement therapy, I was able to present at the international conferences. We would like to take this opportunity to express our sincere gratitude.

■ Summit on the Translation of PSC-Derived Cardiac Therapies(Ottawa, Canada)

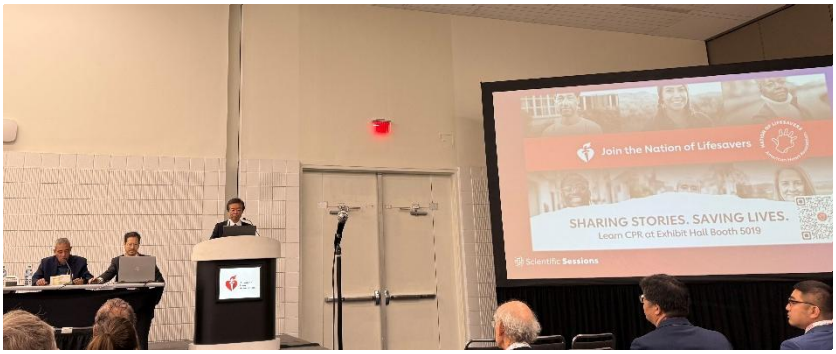
The Summit on the Translation of PSC-Derived Cardiac Therapies was held in Ottawa, Canada, in November 5th-6th, 2025. Approximately 20 global leaders driving research and development toward the clinical application and societal implementation of cardiac regenerative medicine gathered for two days and I was invited to represent Japan for the presentation and discussion of our HS-001 (Heartseed's lead pipeline therapy for heart

failure patients with ischemic heart disease by administration of allogeneic iPS cell-derived cardiomyocytes spheroids in conjunction with open heart surgery) and its ongoing Phase I/II clinical trial (LAPiS study) having enrolled a total of 10 patients (5 patients in the low-dose cohort and 5 patients in the high dose cohort).



■ AHA Scientific Sessions 2025 (New Orleans, USA)

Subsequently, in November 7th -10th, I participated in the AHA Scientific Sessions 2025, the world's largest academic conference in the field of cardiology, held in New Orleans, Louisiana, USA. Even there, I presented the progress and interim dataset of our clinical trial. Other than Heartseed, a Chinese company presented its method of transplanting regenerated cardiac muscle cells (a mixture of single cells of ventricular and atrial cardiomyocytes, rather than forming cardiomyocytes spheroids like Heartseed) but did not report on details of clinical efficacy. Regarding non-clinical research, researchers from the US and Canada reported studies on suppressing arrhythmias through regenerative cardiomyocyte transplantation. Additionally, German researchers announced plans for a multi-center clinical trial concerning a technique to apply cardiomyocytes as patches to the heart surface.



<Heartseed's Presentations>

The presentations at both conferences attracted a large audience and were very lively sessions. In this chapter, I will share an overview of the content to the extent possible.

■ Mechanism and background of our cardiac remuscularization therapy

First, I explained the HS-001 mechanism and patients' baseline characteristics of LAPiS study. In the past large-scale U.S. study "STICH trial" (Surgical Treatment for Ischemic Heart Failure) reported 10-years survival data of the severe heart failure patients after undergoing coronary artery bypass surgery; approximately 60% of the patients died within 10 years. Compared to the patient population in the STICH trial, the patients enrolled in our LAPiS study were older, had lower left ventricular ejection fractions, and exhibited greater cardiac enlargement, indicating a higher severity of disease.

■ Case presentation for the low-dose group

I presented MRI videos of left ventricular wall motion for two of the five cases in the low-dose group of the LAPiS study as examples. In the third case (an improvement case), wall motion in the transplanted site was enhanced, leading to increasing of left ventricular systolic function (LVEF: left ventricular ejection fraction) and reduction in its size (referred to as reverse remodeling). In these changes, shrinkage of the left atrium, right ventricle, and right atrium were also found. In the second case (a worsening case) which originally had mitral regurgitation in the patient, although the wall motion of the left ventricle at the transplantation sites improved, this improvement was accompanied by an increase in the backflow of blood from the left ventricle to the left atrium and caused the symptoms of heart failure to worsen.

By presenting these two cases, I demonstrated that: (i) wall motion in the transplanted area of our cardiomyocytes improved, and (ii) while this improvement led to reduced heart failure when it increased cardiac output, it could potentially worsen heart failure when a heart structural problem was not treated before, such as mitral regurgitation due to valve problem. I emphasized that understanding the specific pathology of each individual case is crucial for our heart failure treatment. I felt that many of the attending physicians gained a deeper understanding.

■ Low-dose group (5 cases): interim clinical results at 1 year post-transplantation

After presenting these two cases, the interim data at 1 year (52 weeks) post-transplant for the 5 low-dose group was presented. Excluding the second case where heart failure worsened due to the aforementioned mitral regurgitation, improvements were generally observed across multiple heart failure indicators. Furthermore, tumor formation, refractory arrhythmias, and serious adverse events were not observed. Additionally, the only patient who required re-admission after the operation was the second case who developed mitral regurgitation.

■ High-dose group : interim findings from 6-month post-transplant case analysis

Next, for the high-dose group, I presented detailed changes in condition for two of the three cases with data available for 6 months post-transplantation. This was done using MRI and echocardiography videos for each case. Image analysis of MRI data from the seventh trial case demonstrated increased systolic wall thickness in the left ventricle at 6 months post-transplantation, precisely at the sites where our cardiomyocytes were transplanted. Furthermore, echocardiographic image analysis of the eighth case showed improved systolic function at 6 months post-transplantation specifically at the sites where our cardiomyocytes were transplanted, without coronary artery bypass grafting.

■ Safety findings confirmed to date

I also presented the current safety status, noting that it is interim. No refractory arrhythmias or uncontrollable serious adverse events were observed. Additionally, while the association with immunosuppressants remains unclear, we noted temporary pneumonia in two cases and temporary shingles and temporary hair loss in another case.

■ Conclusion and thoughts

At the conclusion of the presentation, I prefaced that the data are still interim, and concluded by stating that our cardiac remuscularization therapy has been conducted without major safety concerns to date, and that improved cardiac wall motion has been observed at the sites where regenerated cardiomyocytes were transplanted, including sites not benefiting from bypass surgery.

My impressions from both conferences were reinforced: cardiac regenerative medicine,

which was at purely basic research level just a few years ago, has now entered clinical trials involving actual human subjects. Clinical efficacy is being reported in greater detail at conferences, evolving through mutual critique among researchers. On the way of discussions and challenges in safety and clinical efficacy, only universally recognized therapy will be selected. In this context, Heartseed's technology and the clinical results from initial trials are approaching a level that attracts scientific interest worldwide. We will pursue steady business progress without complacency or overconfidence, while continuously incorporating cutting-edge science to deliver the latest and best solutions. I will continue to share updates on our business progress through PR and IR communications. We sincerely appreciate your continued support.

Heartseed Inc. President and CEO Keiichi Fukuda

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