PRESS RELEASE

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FOR IMMEDIATE RELEASE

First Patient Dosed in the World's First Clinical Trial of Catheter Administration of iPSC-Derived Cardiomyocyte Spheroids

Phase I/II EMERALD Study Advances Toward Realizing Minimally Invasive Next-Generation Cardiac Regenerative Medicine

TOKYO, JAPAN, June 12, 2026 - Heartseed Inc. (Headquarters: Minato-ku, Tokyo; CEO: Keiichi Fukuda; hereinafter referred to as "Heartseed") announced today the successful dosing of the first patient in its domestic Phase I/II clinical trial (EMERALD study) of HS-005, allogeneic iPS cell-derived cardiomyocyte spheroids administered via catheter, targeting severe heart failure caused by ischemic heart disease or dilated cardiomyopathy. This study marks the world's first clinical trial to administer iPS cell-derived cardiomyocyte spheroids using a catheter.

HS-005 is a therapeutic program currently under development, in which allogeneic iPS cell-derived cardiomyocyte spheroids (micro-tissues of cardiomyocytes) produced based on Heartseed's proprietary technology are administered into the patient's myocardium using a dedicated delivery catheter system. While Heartseed's lead pipeline, HS-001, requires open-heart surgery, HS-005 utilizes a catheter for delivery from the inside of the heart (endocardial delivery), aiming to realize a next-generation, minimally invasive cardiac regenerative medicine.

Heartseed has been advancing the EMERALD study in Japan aiming at the development of HS-005, and the administration to the first patient suffering from heart failure due to dilated cardiomyopathy was successfully completed in late March 2026 at Shinshu University Hospital. The patient's postoperative course has been generally uneventful, and the patient has already been discharged from the hospital. In addition, the independent Safety Monitoring Committee has evaluated 4-week data on this patient and has given approval for the study to continue in the dilated cardiomyopathy cohort. Heartseed will continue to advance the clinical evaluation of HS-005.

Professor Koichiro Kuwahara, Department of Cardiovascular Medicine, Shinshu University School of Medicine, who performed the first administration, stated:

"The administration of the cardiomyocyte spheroids using a catheter was completed in a relatively short time without any complications. The postoperative course has been uneventful. I believe this is a significant step toward realizing a new, minimally invasive therapy option for the increasing number of patients suffering from heart failure. I would like to express my deepest gratitude to the patient and their family, as well as to everyone involved in this clinical trial."

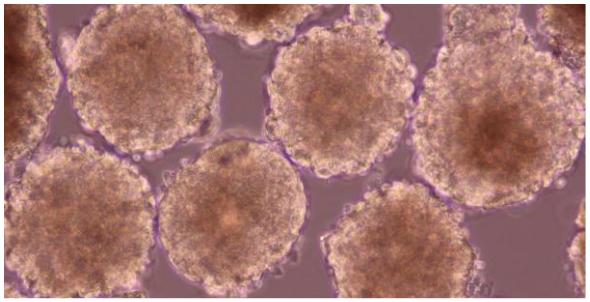
Keiichi Fukuda, CEO of Heartseed, commented on the successful dosing of the first patient:
"I am very pleased that the administration to the first patient in the EMERALD study of our next-generation product, HS-005, using a catheter system, has been successfully completed. Catheter administration enables the minimally invasive delivery of cardiomyocytes. In addition, the inclusion of patients with dilated cardiomyopathy as a new target is a highly significant milestone in our goal to save more patients with severe heart failure. I would like to express my deepest gratitude to the dedicated team at Shinshu University Hospital who contributed to the implementation of this study, and above all, to the patient and their families who participated in the clinical trial."

Through the development of cardiac regenerative medicine using iPS cell-derived cardiomyocyte spheroids, Heartseed aims to establish new treatment options for severe heart failure. Heartseed will continue to steadily advance the clinical development of HS-005 as a next-generation cardiac regenerative medicine with a minimally invasive administration method.

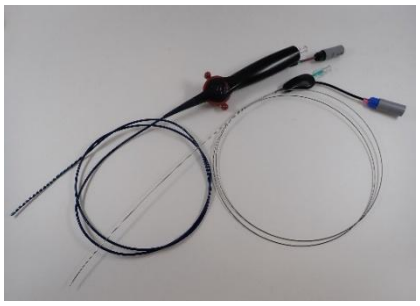
The development of HS-005 utilized data obtained through the following support provided by Japan Agency for Medical Research and Development (AMED):
Basic Technology Development Project for Industrialization of Regenerative Medicine and Gene Therapy (Support for Accelerating the Development of Regenerative Medicine Seeds) "Evaluation of Quality and Safety and Regulatory Affairs for Transitioning to Clinical Trials Toward the Industrialization of iPS cell-Derived Regenerative Cardiomyocyte Transplantation Therapy" (Representative: Keiichi Fukuda) (FY2018-FY2020)

【About HS-005】
The cell utilized by Heartseed in cardiac remuscularization therapy is allogeneic iPS cell-derived, highly purified ventricular cardiomyocyte product formulated in spheroids. The non-clinical studies confirmed that forming micro-tissue-like spheroids enhances the cell retention rate and viability compared to single cells in their administration.
When administering cardiomyocyte spheroids into the myocardial layer of the heart, HS-001 uses a proprietary delivery needle (SEEDPLANTER®) and guide adapter developed in-house for epicardial delivery. In contrast, HS-005 utilizes a catheter system for endocardial delivery. The administered cardiomyocytes are expected to be engrafted into the patient's
myocardium, promoting “remuscularization” and improving cardiac contractility. Additionally,
they are anticipated to secrete various angiogenic factors, promoting neovascularization

(formation of new blood vessels) around the administration sites.



Cardiomyocyte spheroids



Delivery catheter system

【EMERALD study】

The EMERALD study is the Phase I/II clinical trial to proceed the development of HS-005 program which utilizes a catheter system for endocardial delivery to administer cardiomyocyte spheroids. In the EMERALD study, it aims at treating severe heart failure with reduced ejection fraction (HFrEF) with underlying ischemic heart disease as well as dilated cardiomyopathy, planning to enroll 7 patients in each cohort, for a total of 14 patients, to evaluate the safety and efficacy of the therapy.

A phase I/II study of **E**ndocardial delivery for **M**yocardial R**e**gene**r**ation using **A**llogeneic iPS cell-derived Cardiomyocyte Spheroids for Heart Failure with Systolic **D**ysfunction (**EMERALD study**)

jRCT registration number: jRCT2033250454

About Heart Failure

Heart failure is a chronic, progressive condition in which the heart muscle is unable to pump enough blood and oxygen to meet the body's needs, commonly caused by ischemic heart disease or dilated cardiomyopathy. It affects approximately 1.2 million people in Japan and more than 65 million people globally, with the number of patients continuing to rise—a phenomenon often referred to as a "heart failure pandemic." Heart disease, including heart failure, is the second leading cause of death in Japan and the leading cause worldwide. Despite recent advances, therapies for severe heart failure primarily focus on symptom management. Aside from heart transplantation, there are no radical treatment options, and the development of innovative therapies for heart failure is urgently required.

About Heartseed

Heartseed Inc. was founded with the aim of realizing cardiac remuscularization therapy, and it was listed on the Tokyo Stock Exchange Growth Market in July 2024 (Stock Code: 219A). Heartseed has proprietary technologies throughout the entire manufacturing process of the cardiomyocyte cell product, including purification, cell delivery and iPS cell production.

To date, the Company has received numerous awards in Japan and internationally, including the Japan Venture Awards 2021 (Minister of Science and Technology Policy Award), the University Venture Awards

2021 (Minister of Education, Culture, Sports, Science and Technology Award), the Asia-Pacific Cell & Gene Therapy Excellence Awards (Most Promising Pipelines Award), the IP BASE AWARD (Startup Category Grand Prize) presented by the Japan Patent Office, the 7th Japan Medical Research and Development Award – Startup Award (January 2025), and the Intellectual Property Achievement Award – Minister of Economy, Trade and Industry Award (April 2025).

For more information, visit heartseed.jp, LinkedIn and YouTube.

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