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FOR IMMEDIATE RELEASE

Notice Regarding Completion of 30-Day Review for Clinical Trial Notification for Phase I/II Study of Cardiac Remuscularization Therapy HS-005 (Catheter Administration) Targeting Severe Heart Failure

- Progressing toward the Study Commencement

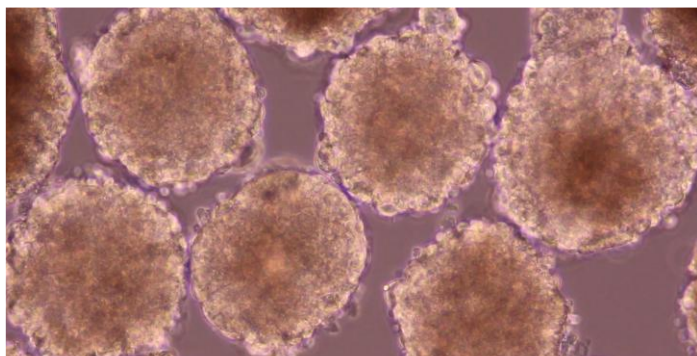
TOKYO, JAPAN, November 4, 2025 - Heartseed Inc. (Headquarters: Minato-ku, Tokyo; CEO: Keiichi Fukuda; hereinafter referred to as “Heartseed”) is pleased to announce that the 30-day review of the clinical trial notification (CTN) submitted to the Pharmaceuticals and Medical Devices Agency (PMDA) for its Phase I/II corporate clinical trial (EMERALD study) of the allogeneic iPS cell-derived cardiomyocyte spheroid has been completed. The clinical trial can now officially commence.

【EMERALD study】

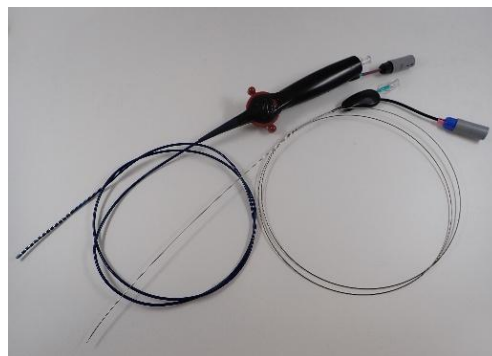
The EMERALD study is the Phase I/II clinical trial to proceed the development of HS-005 program which utilizes a catheter system for endocardial delivery to administer cardiomyocyte spheroids. In the EMERALD study, it aims at treating severe heart failure with reduced ejection fraction (HFrEF) with underlying 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 Endocardial delivery for Mycocardial Regeneration using Allogeneic iPSC-derived Cardiomyocyte Spheroids for Heart Failure with Systolic Dysfunction (**EMERALD study**)

jRCT registration number: jRCT2033250454



Cardiomyocyte spheroids



Delivery catheter system

Technical Platform and Catheter System

Heartseed has partnered with Japan Lifeline Co., Ltd., a medical device manufacturer boasting the top market share in diagnostic catheters for arrhythmia, to jointly develop the delivery catheter system for the HS-005. This system supports 3D mapping visualization within the heart, enabling physicians to manipulate the catheters to the intended location inside the heart while viewing heart's chamber anatomical image. Furthermore, its unique structure featuring electrodes at the tip of the catheter allows for administering the cells while confirming via ECG changes indicating the tip has reached the myocardial layer (for details, please refer to the Company's announcement released on September 11, 2025).

Following approval by the Institutional Review Board (IRB) at clinical trial sites, the Company plans to begin administering the therapies to patients in the clinical trial in 2026. Heartseed, together with Japan Lifeline, aims to realize cardiac remuscularization therapy through minimally invasive administration methods, providing new treatment options for more patients with severe heart failure.

【About HS-005】

The cell utilized by Heartseed in cardiac remuscularization therapy is an allogeneic iPSC-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.

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 iPSC production.

Heartseed announced the global collaboration and license agreement with Novo Nordisk A/S for HS-001 in June 2021. For more information, visit heartseed.jp, [LinkedIn](#) and [YouTube](#).

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