November 4, 2025

To whom it may concern,

Company name: Heartseed Inc.
Representative: Keiichi Fukuda, MD/PhD/FACC, CEO, Representative Director of the Board
Securities code: 219A, Tokyo Stock Exchange
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Notice of 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 due to ischemic heart disease and dilated cardiomyopathy

Heartseed Inc. (hereinafter "the Company"), as previously announced in its October 2, 2025 press release titled "Notice of submission of clinical trial notification for Phase I/II study of cardiac remuscularization therapy HS-005 (catheter administration) targeting severe heart failure due to ischemic heart disease and dilated cardiomyopathy," had submitted a clinical trial notification (CTN) to the Pharmaceuticals and Medical Devices Agency (PMDA) regarding the commencement of the Japan clinical trial for HS-005, catheter-based administration therapeutic program of allogeneic iPS cell-derived cardiomyocyte spheroids. The Company announces that the 30-day PMDA review of the CTN has been completed and is pleased to report that the clinical trial can now officially commence.

This Company's sponsored Japan clinical trial (hereby called EMERALD study) aims at treating severe heart failure 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. The Company will proceed to contract with the candidate clinical trial sites once the discussions in the Institutional Review Boards (IRBs) at each site are finalized. The Company plans to begin administering the therapies to patients in the clinical trial in 2026.

Please note that, there is no revision to the latest earnings forecast for the fiscal year ending December 31, 2025.

(Cautionary notice on forward-looking information)
The financial results forecasts and other forward-looking information contained in this document are based on the information currently available to the Company and certain assumptions considered reasonable by the Company. It is not a guarantee that the forecasts will be achieved, and actual results may differ significantly from such forecasts depending on various factors.

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

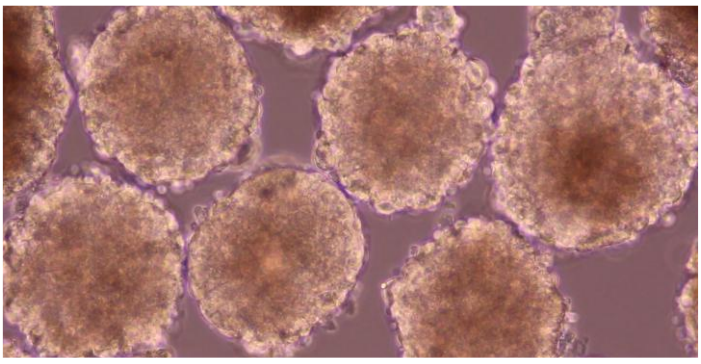
TOKYO, JAPAN, November 4, 2025 - Heartseed Inc. (Headquarters: Minato-ku, Tokyo; CEO: Keiichi Fukuda; hereinafter referred to as "Heartseed") is pleased to announce that the 30-day review of the clinical trial notification (CTN) submitted to the Pharmaceuticals and Medical Devices Agency (PMDA) for its 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】

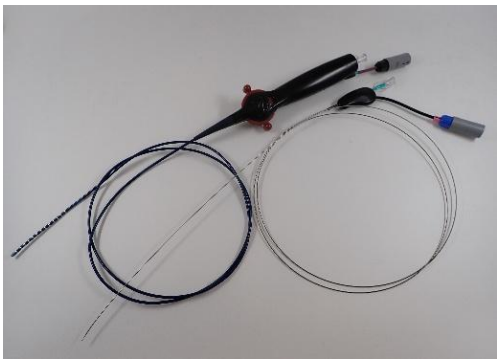
The EMERALD study is the Phase I/II clinical trial to proceed the development of HS-005 program which utilizes a catheter system for endocardial delivery to administer cardiomyocyte spheroids. In the EMERALD study, it aims at treating severe heart failure with reduced ejection fraction (HFrEF) with underlying 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 **E**ndocardial delivery for **M**yocardial R**e**gene**r**ation using **A**llogeneic iPSC-derived Cardiomyocyte Spheroids for Heart Failure with Systolic **D**ysfunction (**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 administrating 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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This press release contains forward-looking statements, including statements regarding intent, belief or the companies' current expectations and/or those involved in its clinical trials and R&D activities as such. These forward-looking statements are based on the information available to the companies as of the date hereof as well as certain assumptions. Accordingly, such forward-looking statements are subject to various risks and uncertainties that may cause the actual results to significantly differ from those expressed or implied in such statements. Therefore, readers are advised not to place undue reliance on these forward-looking statements. The information in this press release is as of the date of this release (or otherwise specified dates), and the companies are under no obligation to regularly update the information herein.