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# Heartseed Announces the Presentation of HS-001, an Investigational Stem Cell-Derived Therapy for the Treatment of Advanced Heart Failure at the 71st Annual Meeting of the Japanese College of Cardiology

**TOKYO, JAPAN, September 11, 2023** – Heartseed (Heartseed Inc.), a Tokyo-based biotechnology company developing iPSC-derived cardiomyocytes for heart failure, today announced that the case reports of two patients in the Phase 1/2 clinical trial (LAPiS Study) of HS-001, a lead pipeline of Heartseed, in combination with coronary artery bypass grafting surgery for advanced heart failure, was presented by the investigator at the 71st Annual Meeting of the Japanese College of Cardiology on September 9, 2023.

A special session on cardiac replacement therapy was held at the 71st Annual Meeting of the Japanese College of Cardiology (September 8-10, 2023, Chair: Professor. Minoru Ono, Department of Cardiac Surgery, The University of Tokyo) and Dr. Yuki Ichihara, Department of Cardiovascular Surgery, Tokyo Women's Medical University, presented his experience of two patients in the LAPiS study on September 9. According to the presentation, the cell transplantation went smoothly, and the immunosuppressants management proceeded without major complications, and improvement in cardiac function was observed.

Dr. Ichihara stated, "Among ischaemic heart failure patients with reduced left ventricular ejection fraction (LVEF), we have experienced that LVEF does not improve after coronary artery bypass surgery, especially in severe cases with little remaining myocardium. In this clinical trial, the initial results suggest that the transplanted cardiomyocytes have engrafted, and I believe that this can be a new treatment method that aims to improve cardiac function by transplanting and replacing cardiomyocytes mainly in areas where there is little viable myocardium."

The efficacy results of the two cases presented at the congress (pre-transplant baseline and 26-week post-transplant) are shown in the table below.

| | | First Patient | Second Patient |
|---|---|---|---|
| LVEF (%) | Echo | 26 → 28 | 17 → 38 |
| | MRI | 15 → 19 | 10.8 → 18.0 |
| LVEDV (mL) | Echo | 345 → 252 (-27%) | 196 → 164 (-16%) |
| | MRI | 431 → 389 (-10%) | 265 → 197 (-26%) |
| Cardiothoracic ratio (%) | | 63.1 → 60.0 | 61.6 → 48.3 |
| NT-proBNP (pg/mL) | | 11,471 → 5,733 (-50%) | 5,225 → 817 (-84%) |
| NYHA functional classification | | III → II | III → I |

(All data are from the hospital)

The first patient had severe heart failure with an enlarged Left Ventricular End Diastolic Volume (LVEDV) of more than 400mL measured by MRI. Although there was no change in the first week after the procedure, there were signs of "reverse remodeling" with a decrease in LVEDV at 26-week by 27% in echocardiogram and 10% in MRI, respectively. Left ventricular ejection fraction (LVEF) improved from the baseline to 26-week by 2% points in echocardiogram and 4% points in MRI, and New York Heart Association (NYHA) functional classification also improved from III at baseline to II. NT-proBNP, a marker of heart failure also decreased by 50% from the baseline to 26-week and by 63% at 34-week.

The second patient had severe heart failure with a baseline LVEF of less than 20%. Although no specific changes were observed 1 week after the treatment, a sign of "reverse remodeling" was observed at week 4. LVEF improved significantly by 21% in echocardiogram and 7% points in MRI from baseline to week 26. NT-proBNP also improved significantly by 84% and NYHA functional classification improved from III to I at 26-week.

*Heartseed's press release dated July 6, 2023 published 13-week data for this patient as the third one in the LAPiS study.

Currently, four patients were dosed in the LAPiS study. Regarding safety, there have been no events that would be problematic for the continuation of the clinical trial. Heartseed continues patient enrollment in the LAPiS study and plans to conduct an evaluation by the Safety Monitoring Committee once the data are compiled.

### About the main indices and terms

- **Left Ventricular End Diastolic Volume (LVEDV)**: The volume of the left ventricle when it is mostly dilated, and 102-235 mL is considered normal, depending on body weight and other factors.
- **Reverse remodeling**: In heart failure, various factors are known to cause the change of myocardial shape (ventricular remodeling), resulting in cardiac enlargement. Reverse remodeling, on the other hand, refers to the structural and functional improvement of ventricular remodeling, resulting in the reduction of left ventricular size. Reverse remodeling is associated with improved prognoses.
- **Left Ventricular Ejection Fraction (LVEF)**: a measure of how efficiently the heart pumps blood; normal is 55-73%; the LAPiS study used an LVEF of 15-40% as inclusion criteria.
- **Cardiothoracic ratio**: the ratio of the width of the thorax to the width of the heart on an x-ray image. Normal values are less than 50%.
- **NT-proBNP**: A type of hormone secreted by the heart; the lower the heart function and the greater the burden on the heart, the more it is secreted into the blood and the higher the number.
- **New York Heart Association (NYHA) functional classification**: The severity of heart failure, rated on a 4-point scale from I to IV according to subjective symptoms, with I being the mildest (no limitation of physical activity) and IV being the most severe (any physical activity is restricted).

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## About HS-001 and LAPiS Study

HS-001, is allogeneic iPSC-derived, highly purified ventricular cardiomyocyte spheroids. By forming micro-tissue-like spheroids, retention rate and viability of cell transplant are improved. The spheroids are transplanted using a special administration needle (SEEDPLANTER®) and guide adapter developed for safe and efficient administration of the spheroids into the myocardial layer of the heart. The expected mechanism of action is that the transplanted cardiomyocytes electrically couple with the patient's myocardium to improve cardiac output by remuscularization, and secretion of angiogenic factors to form new blood vessels around the transplant site (neovascularization).

LAPiS Study, a 52-week, phase 1/2, open-label, dose-escalation study in patients with advanced heart failure caused by ischaemic heart disease, is being conducted at various study sites in Japan. HS-001 will be transplanted into the diseased tissue of the heart during open-heart surgery in conjunction with a planned coronary artery bypass graft procedure. The study will enrol 10 patients in two dose cohorts of 50 million and 150 million cardiomyocytes. The primary endpoint of the study is safety at 26-week post-transplantation, and secondary efficacy endpoints include LVEF and myocardial wall motion.

## About Heartseed

Heartseed Inc. was founded in 2015 to develop and commercialize cardiac remuscularization therapy developed by Professor Keiichi Fukuda and his group at the Department of Cardiology, Keio University, Tokyo, Japan. 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. Heartseed received "Minister of Science and Technology Policy Award" at Japan Venture Awards 2021 and "Ministry of Education, Culture, Sports, Science and Technology Award" at Academic Startups 2021, and "Most Promising Pipelines Awards (iPSC)" at Asia Pacific Cell & Gene Therapy Excellence Awards 2022. For more information, visit heartseed.jp, LinkedIn and YouTube.

Source: Heartseed Inc.

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