July 14, 2021

To whom it may concern,

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Announcement on Initiation of Clinical Trial for Jointly Developed Product

Japan Lifeline Co., Ltd. is pleased to announce that an investigator-initiated Phase I clinical trial of MTC001 has initiated at the University of Tsukuba Hospital in June 2021. The MTC001 is a regenerative medicine product that the Company has been developing in collaboration with the University of Tsukuba Hospital and Metcela Inc. for treatment of patients with chronic ischemic heart failure.

The impact of this matter on the consolidated business results of the Company is not significant. For details, please refer to the attached document.

July 14th, 2021
Metcela Inc.
Japan Lifeline Co., Ltd.

Initiation of a Phase I Clinical Trial of MTC001 in Patients with Chronic Ischemic Heart Failure

Metcela Inc. and Japan Lifeline Co., Ltd. (JLL) announced the start of an investigator-initiated Phase I clinical trial of MTC001 for treatment of patients with chronic ischemic heart failure. The clinical trial is conducted at the University of Tsukuba Hospital, and Metcela will be supplying MTC001. Metcela and JLL have been collaborating on multiple research projects with the University of Tsukuba Hospital in preparation for this clinical trial.

Background on Heart Failure

Heart failure is a condition in which the heart is unable to pump enough blood due to cardiac dysfunction. While there is no cure for heart failure, the number of patients is increasing globally due to the aging population. There is an urgent need to develop therapies to restore cardiac function. It is estimated that there are 1.2 million patients living with heart failure in Japan and 26 million patients worldwide.

Background on MTC001

Metcela is collaborating with JLL and the University of Tsukuba to bring MTC001 to the clinic. MTC001 is a combination product consisting of an autologous cell therapy and a dedicated administration catheter.

Metcela has researched and developed VCAM-1-positive cardiac fibroblasts (VCF1). Fibroblasts are known for their role in scar formation and wound healing and have drawn much interest in the recent years for their critical role in heart development and maintenance of cardiac microenvironment. A specific subpopulation of fibroblasts, VCF1, has shown improvements in cardiac function in preclinical models through mechanisms related to lymphangiogenesis and cardiomyocyte proliferation, as previously reported (Ref.1, Ref.2). Patient-derived (autologous) VCF1 will be used in this clinical trial.

To deliver the cell therapy, MTC001 will include a minimally invasive cell administration injection catheter, primarily developed by JLL. The catheter will be connected to the commercially available 3D mapping system to visualize the lesion site for precision cell administration.

Background on the clinical trial

The trial is conducted at the University of Tsukuba Hospital and led by their interventional cardiologists with the funding support of the Japan Agency for Medical Research and Development (AMED).
The clinical trial will evaluate the safety of the autologous VCF1 and the administration method in patients with chronic ischemic heart failure by observation of major cardiovascular events as the primary endpoint, as well as exploratory and preliminary analyses of efficacy. For further information about this trial, please visit:
https://jrct.niph.go.jp/en-latest-detail/jRCT2033210078

References

1. Iwamiya, T., Matsuura, K., Masuda, S., Shimizu, T., & Okano, T. (2016). Cardiac fibroblast-derived VCAM-1 enhances cardiomyocyte proliferation for fabrication of bioengineered cardiac tissue. Regenerative therapy, 4, 92-102.
2. Iwamiya, T., Segard, B. D., Matsuoka, Y., & Imamura, T. (2020). Human cardiac fibroblasts expressing VCAM1 improve heart function in postinfarct heart failure rat models by stimulating lymphangiogenesis. PloS one, 15(9), e0237810.

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