

October 20, 2020

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Chairman & CEO
(TSE Mothers Code: 4593)

Successful Establishment of Healios' Proprietary Clinical Grade Universal Donor iPS Cell Line

HEALIOS K.K. ('Healios') has been developing Universal Donor Cells (UDCs), which are next-generation iPS cells created with gene-editing technology to engineer a low risk of immune rejection*¹ regardless of HLA type.*² We are pleased to announce that we have successfully established a clinical grade proprietary UDC iPS cell line.

As announced on [June 3, 2020](#), Healios previously established a research grade UDC iPSC line. We have now succeeded in establishing a clinical grade line that can be clinically applied to humans in each of Japan, the United States and Europe. Going forward, Healios will proceed with preparation in relation to various clinical applications.

Healios plans to combine its UDC technology with its existing efforts in next generation cancer-targeting immune cells, ophthalmology, organ buds and various other areas to create a pipeline of innovative regenerative medicine therapies with the highest possible safety and efficacy profile.

Typically, transplanted cells trigger an immune rejection response in patients whose HLA type does not match that of the cells. Therefore, doctors must administer an immunosuppressant drug during transplantation, which increases the burden on the patient's body. To avoid the administration of immunosuppressants, it is preferable to utilize autologous iPS cells produced by the patient's own cells, but the production process both takes a long time and is very expensive.

UDCs are iPS cells created using gene-editing technology that allows them to avoid and / or reduce the body's immune rejection response. The production of Healios' UDCs involves the removal of certain HLA genes that elicit a rejection response, the introduction of an immunosuppression gene to improve immune evasion, and the addition of a suicide gene serving as a safety mechanism, each in an allogeneic iPS cell. This next-generation technology platform allows for the creation of regenerative medical products with enhanced safety and a lower risk of immune rejection, while preserving the inherent ability of iPS cells to replicate themselves continuously and their pluripotency in differentiating into various other kinds of cells.

Plans are underway at Healios to promote the internal development of regenerative pharmaceutical products that utilize UDCs. At the same time, the company is considering the use of its proprietary UDCs in relation to certain potential external collaborations.

Healios will promptly announce if any matter occurs that must be disclosed.

*1 Immune rejection

This is a response involving the immune cells during the transplantation of cells or an organ derived

from a different individual which results in the transplanted cells or organ (implant) being recognized as a foreign entity and attacked/rejected by the immune cells.

***2 HLA Type**

HLA (Human Leukocyte Antigen) is an important molecule expressed in all human cells that is involved in how our immune system functions. Any substance in an individual's body with HLA type that differs from the individual's own is recognized as a foreign substance, which triggers an immune response that rejects and attacks that substance. Therefore, ensuring a match of HLA type is extremely important in organ transplantation.

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