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(TSE Mothers Code: 4593)

## **Successful Establishment of Healios' Proprietary Universal Donor Cell Research Line**

HEALIOS K.K. ('Healios') has been creating Universal Donor Cells (UDCs), which are next-generation iPS cells created with gene-editing technology to engineer a low risk of immune rejection\*<sup>1</sup> regardless of HLA type.<sup>\*2</sup> We are pleased to announce that we have successfully established a proprietary UDC research line and characterized its gene expression and other features.

Healios plans to combine its UDC technology with its existing efforts in next generation cancer-targeting immune cells, ophthalmology, organ buds and so on to create a line of 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 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 pharmaceutical 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 and further reinforce our pipeline. We are committed to working towards the early completion of a clinical-grade UDC line that meets global approvability standards.

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 types is extremely important in organ transplantation.

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