Company Name: HEALIOS K.K. Representative: Hardy TS Kagimoto, Chairman & CEO (TSE Mothers Code: 4593)

## Successful differentiation of Healios Universal Donor Cells into pancreatic β-cells in our joint research with the National Center for Global Health and Medicine

HEALIOS K.K. ("Healios") is involved in the research of new therapeutic products using Universal Donor Cells ("UDCs")<sup>\*1</sup>, which are next-generation iPS cells created with gene-editing technology that have a reduced risk of immune rejection regardless of a patient's HLA type. <u>As announced on October 20<sup>th</sup>, 2020</u>, Healios established its proprietary clinical-grade UDC line, and we are currently conducting research both internally and through joint collaborations with several institutions on new treatments for diseases for which there is no existing cure.

In our joint research with the Department of Regenerative Medicine at the National Center for Global Health and Medicine in Tokyo, we have been aiming to establish a method for inducing differentiation of human iPS cells into pancreatic  $\beta$ -cells<sup>\*2</sup> for use in clinical applications, and we are pleased to announce that we have successfully confirmed the differentiation of UDCs into pancreatic  $\beta$ -cells.

Moving forward, our joint research will work on optimizing the process and verifying the efficacy and safety of these cells in animal models of diabetes. Through this achievement, we hope to develop a new more effective therapeutic approach for diabetes<sup>\*3</sup> and further expand the value and impact of our company's iPSC platform.



UDC-derived pancreatic  $\beta$  cells (HE staining)



(Photo provided by the National Center for Global Health and Medicine)

This action has no impact on our company's consolidated financial results for the current fiscal year. We will promptly make the necessary announcements if any matter requiring disclosure arises in the future.

## \*1 UDC

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 involve 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 medicine 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.

## \*2 Pancreatic β-cells

Pancreatic  $\beta$ -cells are a type of cells present in the islets of Langerhans within the pancreas. They produce and secrete insulin in response to blood glucose levels and serve to regulate the amount of glucose in the bloodstream.

## \*3 Diabetes

Diabetes is a disease in which the patient's blood glucose levels are chronically high because their pancreatic  $\beta$ -cells produce insufficient or no insulin, or because of the reduced action of insulin due to insulin resistance. The inability to control blood glucose levels cause various complications in the nerves, eyes, kidneys, and other organs, which can affect the patient's healthy lifespan. Current treatment of diabetes requires the use of oral drugs or the injection of insulin or GLP-1 agonists, depending on the type of diabetes and the patient's lifestyle.

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