

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

Announcement of UDC Patent Approval (Japan)

HEALIOS K.K. ("Healios") is involved in the research of new therapeutic products using Universal Donor Cells ("UDCs")*, 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. We are pleased to announce that the Japan Patent Office has issued a notification of patent approval for the Healios UDC.

1. Overview of the Approved Patent

- **Title of the Invention:** Hypoimmunogenic Cells
- **Application Number:** JP 2022-526622
- **Patent Holder:** HEALIOS K.K.

2. Key Features of UDC Technology

Healios UDC is a hypoimmunogenic iPS cell developed through genetic editing to remove polymorphic HLA and introduce HLA-G, PD-L1, and PD-L2 genes, thereby granting resistance to both acquired and innate immunity. Furthermore, a "suicide gene" has been incorporated as a safety mechanism. This technology is expected to serve as a next-generation platform for regenerative medical products as a raw material for transplanted cells. In 2020, we successfully established a [clinical-grade UDC line](#) (clinical line), which has since been supplied to research institutions and companies worldwide as a promising raw material for cell-based medicines, enabling the investigation of their potential applications in treating various diseases.

With the approval of this patent, the uniqueness and novelty of our technology have been officially recognized in Japan. Additionally, this patent has been filed in other regions, including the United States, Europe and China, where the patent examination processes are advancing successfully. This achievement enhances our competitive edge both domestically and globally. We aim to position our UDC as an industry-standard product, facilitating joint research and licensing agreements, and driving forward the field of regenerative medicine on a global scale.

* 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 and the introduction of certain genes to improve immune evasion and safety 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.

About Healios:

HEALIOS K.K. is Japan's leading clinical stage biotechnology company harnessing the potential of stem cells for regenerative medicine. It aims to offer new therapies for patients suffering from diseases without effective treatment options. Healios is a pioneer in the development of regenerative medicines in Japan and owns proprietary, global platforms utilizing both somatic stem cells and iPS cells.

In the somatic stem cell field, Healios is developing invimestrocel (HLCM051), a proprietary cell product comprised of multipotent adult progenitor cells (“MAPCs”) derived from the bone marrow of healthy adult donors. Invimestrocel has been shown to exhibit powerful anti-inflammatory and immunomodulatory properties with applicability in a range of disease states, has been tested in hundreds of patients in late stage clinical trials, is manufactured consistently at scale in 3D bioreactors, and has demonstrated both safety and suggested efficacy in hundreds of patients across multiple indications. Healios is seeking to advance invimestrocel on a global basis for ischemic stroke, ARDS, and trauma.

In the iPSC regenerative medicine field, Healios is developing HLCN061, a next generation NK cell treatment for solid tumors that has been functionally enhanced through gene-editing. These cells have demonstrated robust anti-tumor efficacy in animal models, benefit from a scalable 3D bioreactor manufacturing process, and are currently being prepared for initial human testing in collaboration with Akatsuki Therapeutics. The company has also established a proprietary, gene-edited “universal donor” induced pluripotent stem cell line to develop next generation regenerative treatments in immuno-oncology, ophthalmology, liver diseases, and other areas of severe unmet medical need.

Healios was established in 2011 and has been listed on the Tokyo Stock Exchange since 2015 (TSE Growth: 4593). <https://www.healios.co.jp/en>

Contact:

IR & Finance and Accounting Division

HEALIOS K.K.

E-mail: ir@healios.jp