



Kringle
Pharma

Press release
8 September 2023

Patent Application Claiming a Priority for the Treatment of Spinal Cord Injury Using HGF and iPS Cell

Kringle Pharma, Inc. (Head office located in Osaka, Japan; President & CEO, Kiichi Adachi; “KRINGLE”) today announced that KRINGLE and Keio University (Located in Tokyo, Japan; President, Kohei Itoh) jointly filed a patent application regarding the combination use of recombinant human hepatocyte growth factor (“HGF”) with human induced pluripotent stem cell-derived neural stem/progenitor cell (“hiPSC-NS/PC”) as an effective treatment for severe spinal cord injury. The filing is to claim a priority based on the previous patent application* filed with Keio University on September 8, 2022, providing broad and comprehensive patent protection on the therapeutic agents for the acute to sub-acute phase of spinal cord injury.

*News release dated September 9, 2022: https://ssl4.eir-parts.net/doc/4884/ir_material1/199099/00.pdf

Title of the invention: Therapeutic agent for the acute to sub-acute phase of spinal cord injury

Application No.: PCT/JP2023/32768

Filing date: September 8, 2023

KRINGLE has continued collaborative research with Professors Hideyuki Okano and Masaya Nakamura at Keio University School of Medicine since 2021, aiming to create novel therapies for spinal cord injury. In the collaborative research, HGF administration in the acute phase, followed by transplantation of hiPSC-NS/PC in the sub-acute phase, significantly improved motor function in the animal model of severe spinal cord injury compared to each single treatment group, leading to the second** patent application jointly filed by KRINGLE and Keio University on September 8, 2022. Since then, new robust data was accumulated through further research, and a priority claim was filed today in this patent application adding the supplemental data to strengthen the innovation.

** News release dated March 13, 2023 for the first patent application:

https://ssl4.eir-parts.net/doc/4884/ir_material1/202379/00.pdf

“HGF monotherapy in the acute phase of spinal cord injury and hiPSC-NS/PC transplantation in the sub-acute phase are both being tested in separate clinical trials by KRINGLE and Keio University, respectively. Therefore, a next-generation regenerative therapy combining the HGF and iPS cell technologies is expected to be put into clinical use before long for the treatment of acute to sub-acute spinal cord injuries,” said Kiichi Adachi, President & CEO of KRINGLE. “We aim to deliver a new innovative therapy to spinal cord injury patients in the world, as we obtain and utilize global rights for this patent application.”

About Hepatocyte Growth Factor (HGF)

HGF was originally discovered as an endogenous mitogen for mature hepatocytes. Subsequent studies demonstrated that HGF exerts multiple biological functions based on its mitogenic, motogenic, anti-apoptotic, morphogenic, anti-fibrotic, and angiogenic activities, and facilitates regeneration and protection of a wide variety of organs. HGF exerts neurotrophic effects and enhances neurite outgrowth, and the therapeutic effect



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of HGF on spinal cord injury has been demonstrated in animal models by Professors Hideyuki Okano and Masaya Nakamura at Keio University School of Medicine. Expectations for HGF as a novel therapeutic agent are increasing for spinal cord injury.

About Human Induced Pluripotent Stem Cell-derived Neural Stem/Progenitor Cell (hiPSC-NS/PC)

hiPSC-NS/PC is derived from human induced pluripotent stem cells and has the self-renewal capability, enabling proliferation maintaining undifferentiated state, as well as pluripotency, enabling differentiation into cells constituting the central nervous system such as neurons, astrocytes, and oligodendrocytes. The first-inhuman clinical trial of transplantation: regenerative medicine using hiPSC-NS/PC to treat complete subacute spinal cord injury is currently underway at Keio University Hospital.

(For more information, please see the press release dated January 14, 2022, by Keio University.

<https://www.keio.ac.jp/en/press-releases/files/2022/1/14/220114-1.pdf>)

About Spinal Cord Injury

Spinal cord injury is caused by trauma, leading to a variety of paralytic or painful symptoms. In descending order of incidence, tripping over, traffic accidents and falls from height are the main causes of spinal damage. Recently, due to the rise in the elderly population, tripping over is becoming an increasingly common cause. In Japan, there are approximately 100,000 to 200,000 chronic spinal cord injury subjects with an incidence of about 6,000 new cases per year*. By appropriate early treatment after the injury and specialized rehabilitation, some degree of functional recovery can be expected, but complex severe symptom, including motor paralysis, muscular spasticity, sensory paralysis, dysfunction of internal organs (rectal and bladder disorder, thermoregulatory dysfunction, decreased visceral function, decreased respiratory function) may often remain. For these reasons, therefore, there is a strong need for the development of a novel drug.

*Source:

Miyakoshi N et al. Spinal Cord 2021 Jun;59(6):626-634.

Sakai H et al. J Spine Res. 2010 1(1):41-51.

About Kringle Pharma, Inc. <https://www.kringle-pharma.com/en/>

Kringle Pharma is a late clinical-stage biopharmaceutical company established in December 2001 to develop novel biologics based on HGF. Currently, Kringle conducts two Phase III clinical studies, which is the final stage of the drug development, in acute spinal cord injury and vocal fold scar among other target indications. Kringle's mission is to contribute to societal and global healthcare through the continued research, development, and commercialization of HGF drug for patients suffering from incurable diseases.

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