



Press release
13 March 2023

Patent Application Claiming a Priority for the Treatment of Chronic Spinal Cord Injury

Kringle Pharma, Inc. (Head office located in Osaka, Japan; President & CEO, Kiichi Adachi; “KRINGLE”), a late clinical-stage biopharmaceutical company, today announced that KRINGLE and Keio University (Located in Tokyo, Japan; President, Kohei Itoh) jointly filed a patent application regarding the treatment of chronic spinal cord injury. The filing is to claim a priority based on the previous patent application* filed with Keio University on March 11, 2022, providing broad and comprehensive patent protection on therapeutic agents for chronic spinal cord injury.

*News release dated March 11, 2022 : https://ssl4.eir-parts.net/doc/4884/ir_material1/199091/00.pdf

Title of the invention: Therapeutic Agent for Spinal Cord Injuries
Application No.: PCT/JP2023/9421
Filing date: March 10, 2023

As announced in the news release dated February 20, 2021, KRINGLE launched a collaborative research project with Professors Hideyuki Okano and Masaya Nakamura at Keio University School of Medicine, aiming to create novel therapies for spinal cord injury. In this research, the transplantation of human induced pluripotent stem cell-derived neural stem/progenitor cell (“hiPSC-NS/PC”) owned by Keio University, combined with the scaffold-mediated delivery of recombinant human hepatocyte growth factor (“HGF”) developed by KRINGLE demonstrated the formation of neural circuits, resulting in the world's first successful restoration of locomotor and urinary functions in the rodent model of chronic complete spinal cord transection. The results were published* in the scientific journal *Biomaterials* online edition issued on January 26, 2023.

*Please see the press release dated February 2, 2023 issued by Keio University for further information:
<https://www.keio.ac.jp/en/press-releases/2023/Feb/2/49-135220/>

“This innovative research opens the door to a novel treatment for chronic spinal cord injury for which there exists no effective treatment,” said Kiichi Adachi, President & CEO of KRINGLE. “These patients are suffering from the disease for a longer time since injury. The treatment will greatly improve quality of life with patients and reduce the burden on families and caregivers, which will bring significant medical and social values to the world. We are currently conducting a Phase III clinical trial of recombinant human HGF in patients with spinal cord injury in the acute phase. We aim to expand our target indication to the chronic phase of spinal cord injury as well, as we obtain and utilize global rights for this patent application as the basis for commercialization.”

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



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-in-human 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 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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