



Press release  
1 February 2023

## **Publication of Combined Treatment for Chronic Complete 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 the publication of a peer-reviewed article in the scientific journal *Biomaterials* online edition issued on January 26, 2023, presenting preclinical results generated from the collaborative research between KRINGLE and Keio University (Located in Tokyo, Japan; President, Kohei Itoh) regarding the combined treatment for chronic complete spinal cord injury.

KRINGLE is currently conducting a Phase III clinical trial of recombinant human hepatocyte growth factor (“HGF”) in subjects with acute spinal cord injury. In parallel, KRINGLE launched a collaborative research program with Professors Hideyuki Okano and Masaya Nakamura at Keio University School of Medicine in 2021, aiming to create next-generation therapies for spinal cord injury. In this research, transplantation of human iPS cell-derived neural stem/progenitor cells owned by Keio University, combined with scaffold-mediated delivery of HGF developed by KRINGLE demonstrated the restoration of locomotor and urinary functions for the first time in the world in the rodent model of chronic complete spinal cord transection. Based on this innovation, KRINGLE and Keio University jointly filed a patent application (Please see the news release dated March 11, 2022). The publication in *Biomaterials* details the results of this study. It is no doubt that these results mark an important milestone toward delivering a novel combination therapy to combat chronic complete spinal cord injury, in which the functional recovery has been considered extremely difficult.

[Publication]

- Title: Microenvironmental modulation in tandem with human stem cell transplantation enhances functional recovery after chronic complete spinal cord injury
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### ***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.



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***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, focused on development of 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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