



Press release  
11 March, 2022

## **Kringle Pharma Files Patent Application for 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 announces that it has jointly filed a patent application with Keio University (Located in Tokyo, Japan; President, Kohei Itoh) for the treatment of chronic 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 project with Professors Hideyuki Okano and Masaya Nakamura at Keio University School of Medicine in 2021, 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 HGF developed by KRINGLE, demonstrated improvement of functional recovery in the animal model of chronic complete spinal cord injury, leading to the new patent application as follows:

Title of the invention: Therapeutic Agent for Spinal Cord Injuries

Application No.: PCT/JP2022/10976

Filing Date: March 11, 2022

Summary: Spinal cord injury commonly results from a traumatic impact on the spinal cord. In the acute phase, due to severe inflammation, the secondary injury follows and worsens the damage. As the inflammation decreases, the injury progresses from the subacute to the chronic phase. In the chronic phase, the injury involves the formation of a cystic cavity and the development of scar tissue, which disables axonal outgrowth. In this research, the scaffold containing HGF was placed at the injury site in the rat model of thoracic complete spinal cord injury, prior to the hiPSC-NS/PC transplantation. As a result, we confirmed axonal outgrowth at the injury site and motor function recovery with lower limbs. Based on these results, it is suggested that the combination of the transplantation of hiPSC-NS/PC with the scaffold-mediated delivery of HGF could be a novel therapeutic strategy to combat chronic spinal cord injury with no effective treatment option, benefitting even the most severe subjects of complete spinal transection.

### ***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 effects of HGF on spinal cord injury and ALS have been demonstrated in animal models by Professors Hideyuki Okano and Masaya Nakamura at Keio University School of Medicine and Professor Masashi Aoki at Tohoku University School of Medicine, respectively. Expectations for HGF as a novel therapeutic agent are increasing for such intractable neuronal diseases.



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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 to develop novel biologics based on HGF. Currently, Kringle's clinical programs with recombinant human HGF are: 1) Phase 3 ongoing in acute spinal cord injury, 2) investigator-initiated Phase 2 ongoing in ALS, 3) Phase 2/3 in preparation in vocal fold scar, and 4) Phase 1a and 1b completed in acute kidney injury. 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.

**For more information, please contact:**

Daichika Hayata

Director, Pharmaceutical Development

Kringle Pharma, Inc.

☎ +81-72-641-8739

✉ [kpinfo@kringle-pharma.com](mailto:kpinfo@kringle-pharma.com)