Press release
17 November 2023

Completion of Pre-IND Meeting with the FDA for KP-100IT

Kringle Pharma, Inc. (Head office located in Osaka, Japan; President & CEO, Kiichi Adachi; "KRINGLE"), a late clinical-stage biopharmaceutical company, today announced that it has completed its pre-IND (Investigation New Drug) meeting with the U.S. Food and Drug Administration (FDA) regarding the development plan of KP-100IT, a lyophilized formulation of recombinant human HGF, for the potential treatment of acute spinal cord injury.

In Japan, KRINGLE completed the Phase 1/2 clinical trial of KP-100IT in patients with the acute phase of spinal cord injury, obtaining positive results confirming safety and suggesting efficacy. In 2019, KP-100IT was designated as an Orphan Drug by the Ministry of Health, Labor and Welfare of Japan. Since 2020, KRINGLE has been conducting the Phase 3 clinical study. To date, the follow-up of the last patient was completed in this study and KRINGLE plans to announce the top-line results from the study in the first half of 2024.

To maximize the value of recombinant human HGF and make the promising treatment broadly available outside Japan, KRINGLE has initiated preparation for the development of KP-100IT in the United States, the largest pharmaceutical market in the world. The engagement with the FDA for the pre-IND meeting is an important milestone that provides regulatory clarity for KP-100IT on key aspects to advance clinical development in the US.

In written responses, the agency provided guidance and addressed KRINGLE's questions related to the FDA's requirements for submitting an acceptable IND, paving the way for the clinical development of KP-100IT. The FDA's direction will allow KRINGLE to be efficient towards utilizing the preclinical and clinical data accumulated in Japan and formulating an effective development strategy in the US up to the BLA (Biologic License Application).

KRINGLE plans to proceed with the development in the US in partnership with a pharmaceutical company with specialized expertise. KRINGLE is currently in business development discussions with potential partners and the feedback from the FDA will accelerate the negotiations.

There are currently no effective options to treat spinal cord injury and the medical need is significant for patients not only in Japan but also in the US and other countries. KEINGLE is committed to developing an innovative medicine based on HGF originating in Japan and bringing it to patients around the world as quickly as possible.

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.
A group led by Professor Shigeru Hirano of the Department of Otolaryngology and Head and Neck Surgery, Kyoto Prefectural University of Medicine, focused on the anti-fibrotic effects of HGF and demonstrated its pharmacological effects on vocal cord scar. HGF is also expected to have the potential to be an effective therapeutic agent for various fibrotic diseases including vocal fold scar.

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*[1] chronic spinal cord injury patients with an incidence of about 6,000 new cases per year*[1]. Worldwide*[2], approximately 60,000 people*[3] are injured annually, and the number of patients, including those in the chronic phase, is estimated to be approximately 1.1 million*[3]. By appropriate early treatment after the injury and specialized rehabilitation, some degree of functional recovery can be expected, but complex severe symptoms, 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:
*[1] Miyakoshi N et al. Spinal Cord 2021 Jun;59(6):626-634., Sakai H et al. J Spine Res. 2010 1(1):41-51.
*[2] Developed countries where advanced treatment is available
*[3] Internal estimates based Spinal Cord Injury Facts and Figures at a Glance (2021), The International Spinal Cord Injury Society web site, World Population Trends by Statistics Bureau, Ministry of Internal Affairs and Communications, etc.

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 3 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.

For more information, please contact:
Daichika Hayata
Director of Pharmaceutical Development, Member of the Board
Kringle Pharma, Inc.
☎ +81-72-641-8739
✉ kpinfo@kringle-pharma.com