



Press release  
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## **A Phase III Study of HGF in Vocal Fold Scar : Submission of the Clinical Trial Application**

Kringle Pharma, Inc. (Head office located in Osaka, Japan; President & CEO, Kiichi Adachi; “KRINGLE”), a late clinical-stage biopharmaceutical company, today announces that the clinical trial application has successfully submitted to the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan to initiate a Phase III study of recombinant human HGF (KP-100LI) in patients with vocal fold scar.

HGF, hepatocyte growth factor, is an endogenous protein responsible for regeneration and repair of tissues and organs in the human body. Its therapeutic effects have been validated in animal models of various diseases. One of the multiple biological functions of HGF is its potent antifibrotic activity, and HGF is expected to be an effective therapeutic agent for various intractable fibrotic diseases.

KRINGLE is focusing on vocal fold scar as a target indication of drug development for fibrotic diseases. The investigator-initiated Phase I/II study already completed, demonstrating the safety and efficacy of intracordal administration of HGF (Hirano et al. J Tissue Eng Regen Med. 2018). The upcoming pivotal Phase III study is designed as a multicenter, randomized, placebo-controlled, double-blind, parallel-group study to confirm the safety and efficacy of KP-100LI in patients with vocal fold scar. This study will be conducted at five clinical sites in Japan including University Hospital, Kyoto Prefectural University of Medicine.

The Phase III study has been supported by the Japan Agency for Medical Research and Development (AMED) as its CiCLE program (Project title: Clinical development of recombinant HGF protein for the treatment of refractory fibrosis).

### ***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 including not only liver, but also kidneys, heart, lungs, nerve tissues and skin.

### ***About Vocal Fold Scar***

Vocal fold scar is a fibrotic disease which causes severe dysphonia. In patients with vocal fold scar, fibrosis is formed in the vocal fold mucosa due to inflammation or injury, hardening the mucosa and impairing the function of the vocal cords. Dysphonia makes daily communication difficult, leading to a significant deterioration in QOL (Quality of Life). No effective treatment has been established and there are huge unmet medical needs for the patients who suffer greatly. It is estimated that there are approximately 10,000 patients with vocal fold scar in Japan<sup>1)</sup>.

1)Source: Koichi Tsunoda, “Research to formulate guidelines for establishment and standardization of diagnosis and treatment of vocal fold abnormalities” Research paper on epidemiology of intractable diseases, the Ministry of Health, Labour and Welfare of Japan. 2009.



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***About CiCLE (Cyclic Innovation for Clinical Empowerment)***

CiCLE is a funding program operated by AMED to support medical research and development in the field of pharmaceuticals, medical devices, regenerative medicine products and medical technology. It aims to drive the creation of an environment that strongly promotes the fostering of open innovation through efforts of government, academia and the private sector.

***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 promotes clinical development for acute spinal cord injury, ALS and vocal fold scar. 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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