Press release
17 January 2023

First Patient Enrollment in Phase III Clinical Study for the Treatment of Vocal Fold Scar

Kringle Pharma, Inc. (Head office located in Osaka, Japan; President & CEO, Kiichi Adachi; "KRINGLE"), a late clinical-stage biopharmaceutical company, today announced that the first patient was enrolled in a placebo-controlled, double-blind Phase III study to evaluate the efficacy and safety of KP-100LI, the intracordal formulation containing recombinant human HGF, administered in patients with vocal fold scar. The first patient was screened and successfully enrolled for the study at University Hospital, Kyoto Prefectural University of Medicine. As announced in the KRINGLE news release dated November 24, 2022, the study will be conducted at the five clinical trial sites across Japan including University Hospital, Kyoto Prefectural University of Medicine. Patient enrollment will subsequently start at the other four clinical sites as soon as the contracts and all preparations are completed.

For additional information about the Phase III study, please visit the following websites:
- jRCT (Japan Registry of Clinical Trials) ID: jRCT2051220132
  https://jrct.niph.go.jp/en-latest-detail/jRCT2051220132
- ClinicalTrials.gov ID: NCT05627648
  https://clinicaltrials.gov/ct2/show/NCT05627648

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. Vocal fold scar is a rare disease, and it is estimated that there are approximately 10,000 patients with vocal fold scar in Japan[1)].

KRINGLE has been a leading company to develop a pharmaceutical treatment for vocal fold scar. At present, we are the only company in the world who completed an early clinical development and has advanced to the Phase III stage in the indication. (Please refer to the attachment.)

1) 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.

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 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.

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

Attachment : Clinical Studies in Vocal Fold Scar

As of December 2022

Company	Stage	Location	Program	Modality	Indication, Route of Administration
Kringle Pharma	Phase III	Japan	KP-100LI (rhHGF)	Recombinant human protein	Vocal fold scar (including vocal fold sulcus), Intracordal injection
Assistance Publique Hopitaux De Marseille	Phase II	France	Autologous adipose-derived stromal vascular fraction	Cell therapy	Vocal fold scar, local injection
Karolinska University Hospital	Phase I/II	Sweden	MSC-KI-PL-204 Autologous mesenchymal stromal cell	Cell therapy	Vocal fold scar, local injection
Mayo Clinic	Phase I	US	Autologous adipose-derived stromal vascular fraction	Cell therapy	Vocal fold scar, local injection

KP-100LI is the only drug candidate which is:

- **at the Phase III stage,**
- **developed in a company-sponsored clinical trial, and**
- **not a cell therapy.**

* Source : ClinicalTrials.gov