



Kringle  
Pharma

Press release  
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## **Kringle Pharma to initiate a phase I clinical trial of recombinant human HGF for acute renal failure cooperatively with The Rogosin Institute**

Toyonaka, Osaka, March 27, 2007 – Kunio Iwatani, president and chief executive officer of Kringle Pharma, Inc., announced that Kringle will initiate a phase I clinical trial of recombinant hepatocyte growth factor (HGF) for acute renal failure (ARF) with The Rogosin Institute (Rogosin) of New York City, NY. The phase I studies are scheduled to begin at Rogosin following US Food and Drug Administration review of the clinical program.

ARF is a clinical syndrome characterized by a rapid loss of kidney function due to injury to the tubular epithelial cells, or acute tubular necrosis. The causes of ARF include dehydration, shock, nephrotoxins, operation, ischemia, and acute glomerular or interstitial nephritis. There is no cure for ARF and the mortality rate is as high as 50 percent. In the US, approximately 700,000 patients develop ARF annually, with 20 percent of those patients requiring care in ICU (intensive-care unit) settings.

Commenting on the agreement, Albert Rubin, M.D., director of the Rogosin Institute, said, “ARF is a serious and life-threatening disease that needs improved therapies. We are extremely pleased to work with Kringle to study what role HGF may play in the treatment of ARF by conducting these early studies at Rogosin.”

“Rogosin is a world renowned medical institution, having top ranked clinicians and researchers in the field of kidney disease and a cutting-edge facility located in New York,” said Kunio Iwatani. “It is also worth noting that Rogosin’s affiliate, The New York-Presbyterian Hospital, is ranked 5th among US hospitals in the treatment of kidney diseases (America’s Best Hospitals, U.S. News & World Report®, July, 2006). Rogosin is undeniably an ideal location for Kringle to initiate a clinical trial of recombinant HGF for ARF.”

HGF was discovered, purified and molecularly cloned as a potent mitogen for mature hepatocytes by Professor Toshikazu Nakamura of Osaka University, a founder of Kringle and its Scientific Advisor. Professor Nakamura discovered that HGF possesses a wide variety of physiological activities beyond being a mitogenic factor for liver cells to include activity as a motogenic, anti-apoptotic (prevention of cell death) and morphogenic factor for various other types of cells. HGF is now considered as an intrinsic factor with an organotrophic role in the regeneration and repair of various tissues and organs including the liver, kidneys, nervous system, and skin. Preclinical models have shown recombinant HGF to have a potential therapeutic effect in a variety of diseases.

According to Kringle, clinical studies in ARF will determine whether the effect shown in pre-clinical studies translates into therapeutic effect in humans. Kringle is currently manufacturing clinical batches of recombinant HGF and will be ready for phase I studies in the near future.

### *About Kringle Pharma, Inc.*

Kringle Pharma is a venture biopharmaceutical company spun-off from Osaka University. The company was established in 2001 to develop novel biopharmaceuticals based on HGF and NK4, both discovered by Professor Toshikazu Nakamura and Associate Professor Kunio Matsumoto at Osaka University. HGF is considered an intrinsic factor with an organotrophic role in the repair and regeneration of various tissues and organs, and is thought to have significant potential in becoming a regenerative medicine. NK4 is a molecule which functions as both an HGF-antagonist and an angiogenesis inhibitor that is induced by various growth factors including HGF. NK4 is a bi-functional and multi-target compound developed by Kringle Pharma for the treatment of various kinds of cancer.

*For more details on Kringle's technologies, please refer to the company's website at [www.kringle-pharma.com/en/index.html](http://www.kringle-pharma.com/en/index.html)*

*About The Rogosin Institute*

The Rogosin Institute, affiliated with The New York-Presbyterian Hospital and Weill Medical College of Cornell University, is a not-for-profit institution for medical research and treatment in kidney disease (including dialysis and transplantation) and cardiovascular disease related to cholesterol and other lipid abnormalities. Rogosin also has extensive research programs in diabetes and cancer. Rogosin's treatment programs include the Jack J. Dreyfus Clinic, an outpatient facility for the prevention and treatment of renal (kidney) disease, the David D. Thompson Transplantation Center, the Susan R. Knafel Polycystic Kidney Disease Center and the Maurice R. Greenberg Comprehensive Lipid Control Center.

*For more details on The Rogosin Institute, please refer to the company's website at [www.rogosin.org](http://www.rogosin.org)*

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