



Kringle
Pharma

Press release
12 June, 2007

Kringle Pharma has completed the manufacture of the required volume of recombinant HGF to conduct initial clinical studies.

Kringle Pharma, Inc. (Head office located in Toyonaka, Osaka; President & CEO: Kunio Iwatani, “KRINGLE”) is proud to announce that it has completed the manufacture of the required volume of drug substance of recombinant human HGF (Hepatocyte Growth Factor) protein to conduct initial clinical studies.

HGF was initially discovered, purified, and molecularly cloned by Professor Nakamura—one of the founders of KRINGLE and presently KRINGLE’s Scientific Advisor—at Osaka University as a potent mitogen for mature hepatocytes. Through ongoing efforts by Professor Nakamura’s team, it was then discovered that HGF possesses a wide variety of physiological activities beyond being a mitogenic factor for liver cells, 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, as well as skin. KRINGLE has strategically identified skin ulcers and acute renal failure (ARF) as focus areas and is planning to conduct clinical studies on recombinant HGF protein. (*ref.* Press releases published on February 21 and March 28, 2007)

The production of recombinant HGF protein was contracted out to Toyobo Biologics, Inc. (Head office located in Otsu, Shiga; President: Shin Shimizu, “TBI”). TBI is fully equipped with GMP*-compliant recombinant protein manufacturing facilities and is highly experienced in producing drug substances for clinical studies. Kunio Iwatani said: “For the past two years, KRINGLE has been involved in the establishment of a new and innovative manufacturing system of recombinant human HGF protein and has made enormous efforts in building and validating its characteristic methods. Today, I am proud to announce that KRINGLE, in a collaborative relationship with TBI, has successfully completed the manufacture of two batches of HGF drug substance. KRINGLE has now obtained the required volume of HGF to initiate clinical trials in moving forward with its two development projects concerning HGF, wound-healing, and ARF therapy. As the next step, KRINGLE will proceed to develop the most suitable formulation of HGF for each indication and continue negotiations with the relevant authorities. My hope is to commence clinical studies of HGF as soon as possible”.

As for TBI, Shin Shimizu said: “TBI has its pride in production of recombinant protein overall in advanced technology, in which we developed the expression system using Chinese hamster ovary (CHO) cell line. Benefiting from the scientific know-how TBI has accumulated over decades, we have succeeded in manufacturing GMP-compliant recombinant human HGF for KRINGLE to allow it to proceed with its clinical development of the potent compound”.

*GMP: GMP refers to the Good Manufacturing Practice used internationally to describe a set of principles and procedures which, when followed by manufacturers of therapeutic goods, helps ensure that the products manufactured will have the required quality. GMP regulations address issues including recordkeeping, personnel qualifications, sanitation, cleanliness, equipment verification, process validation, and complaint handling.



Kringle Pharma

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 at Osaka University and Professor Kunio Matsumoto at Kanazawa 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

About Toyobo Biologics, Inc.

In November 2001, the biopharmaceutical contract manufacturing section was separated from the pharmaceutical division of Toyobo Co., Ltd. and reorganized as PAC Biologics Inc. ("PBI"). PBI changed its name to Toyobo Biologics, Inc. in April 2007. TBI, as a contract manufacturing organization, owns a multi-purpose 4,000-liter bioreactor, one of the largest in Japan, which is operated under cutting-edge technology compliance with FDA cGMP standards. As a leading contract manufacturing organization in Japan, TBI is capable of serving the international pharmaceutical industry through its provision of the latest development and manufacturing services.

For more details on Toyobo Biologics, Inc., please refer to the company's website at http://www.pacbiologics.com/index_e.html

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