April 9, 2002
AnGes MG, Inc.
Daiichi Pharmaceutical Co., Ltd.

AnGes MG and Daiichi Pharmaceutical Entered into a Distribution Agreement for HGF Gene Medicine in Japan, USA, and Europe

AnGes MG, Inc., Osaka, Japan (former name: MedGene Bioscience, Inc.; President: Masanori Murayama) has agreed on a distribution agreement with Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan (President: Kiyoshi Morita) for a Hepatocyte Growth Factor (HGF) gene medicine, an experimental HGF DNA drug product.

In January 2001, Daiichi Pharmaceutical acquired the exclusive sales and marketing rights in Japan and for peripheral arterial disease (PAD) indications. The new agreement allows Daiichi to acquire the exclusive sales and marketing rights in USA and Europe for PAD, and in Japan, USA, and Europe for coronary arterial disease (CAD) indications.

This experimental drug employs a DNA sequence (HGF gene) that produces HGF protein, having an angiogenic effect, and will be the first gene-based drug for gene therapy being developed in Japan. The HGF DNA injected into the ischemic tissues induces the regeneration of blood vessels that bypass arterial obstructions, thereby improving the blood flow. Through this mechanism, the agent is expected to show an efficacy in the treatment of patients with PAD (including arteriosclerotic obliteration and Buerger's disease) and CAD (including angina pectoris and myocardial infarction). Because the mechanism of action of this DNA therapy differs from that of conventional pharmaceutical agents, it is anticipated that HGF DNA treatment will be effective in patients for whom existing pharmaceutical therapies are insufficient or for whom surgery is not appropriate.

AnGes MG is a bioventure company established in December 1999 aiming to contribute to the human health through R&D of gene-based agents for use in gene therapy, oligodeoxynucleotide drug and a novel vector technology. In cooperation with domestic and international research institutes including Osaka University, AnGes MG strives to seek practical applications for basic technologies that the University has developed in gene medicine. In October 2001, to initiate clinical trials in the international arena, AnGes MG

established a wholly owned subsidiary, AnGes, Inc., in Maryland, USA, and in May this year, the Company plans to establish a subsidiary in Europe.

Daiichi regards the thrombosis and vascular disease area to be of great importance for development of novel therapies and commits itself to contribute to regenerative medicine internationally, through the marketing of HGF gene medicine and support for development of the agent operated by AnGes MG in Japan, USA, and Europe.

Reference

Characteristics and significance of HGF gene medicine for human gene therapy

HGF, first identified in Japan, is a potent angiogenic factor with promise in the treatment of PAD and CAD. The HGF agent will become a first gene therapy agent candidate originating from Japan. Administration of the gene into the ischemic tissue of the legs or heart of patients is expected to result in secretion of HGF protein that will induce localized new blood vessel formation and increase the blood flow in the affected tissue. This agent employs naked DNA technology without using viral vector systems. Thus, this technology avoids the adverse effects and potentially serious events caused by viral vectors. The biological mechanism of this gene transfer technology is distinctly different from that of conventional pharmaceutical therapies. It is expected to be a novel therapy and effective in patients with advanced PAD and CAD who do not respond to currently known therapies.

Glossary

1. Gene medicine

An agent that contains gene(s) or a part of gene that carries the DNA code for protein(s) with therapeutic benefits.

2. Hepatocyte Growth Factor (HGF)

A growth factor identified as the most potent growth factor of hepatocytes, and plays important roles in angiogenesis, organogenesis in embryonic development, and the regeneration of tissues and organs damaged by a various forms of injury.

3. Peripheral arterial disease (PAD)

Narrowing and occlusion of peripheral arteries resulting in ischemia of muscle and skin, manifested by numbness, coldness, difficulty of walking (claudication), rest pain, and

formation of ischemic ulcers. PAD includes arteriosclerotic obliteration and Buerger's disease.

4. Coronary arterial disease (CAD)

Partial or complete blockage of coronary arteries nourishing the heart resulting in reduced supply of blood needed for the blood pumping action of the heart. CAD is manifested as angina pectoris, chest discomfort and chest pain caused by myocardial ischemia, and myocardial infarction caused by complete occlusion of a coronary artery.

5. Naked DNA

For gene expression of its protein, DNA must enter into cells. Expression does not occur with simple adherence to the cell surface. Generally, vector (vehicle) systems including recombinant viruses or liposomes containing therapeutic genes are used in gene transfer technologies. The HGF gene medicine employs a plasmid carrying the HGF gene as naked DNA. Usefulness of the naked DNA (gene) delivery technology is depending upon application routes to the body. Following direct intramuscular administration of the naked DNA into skeletal or heart muscles, the gene enters the cells of the tissue and enables expression of sufficient protein to induce therapeutic effects. This technology is considered safe because it does not result in infection and cell damage as observed with the use of viral vector or liposome gene transfer technologies.