December 2, 2002
AnGes MG, Inc.

Investigational New Drug (IND) application filed with the US FDA for HGF genetic medicine

AnGes Inc., the U.S. subsidiary of AnGes MG Incorporated, submitted the IND application to the FDA to be able to perform second phase of HGF genetic medicine clinical trials with PAD patients (suffering from arteriosclerosis obliterans). This is the first time for a Japanese company to perform clinical trials for a genetic medicine in the U.S.

The HGF genetic medicine regenerates the blood vessels to improve the condition of patients with alveoli clogged due to arteriosclerosis and similar blood circulation disorders. Application of the present medicine is principally different from all conventional drugs, enabling effective treatment in cases when general pharmacological therapy is insufficient, but surgery might not improve a patient's condition. We are developing medication mainly to treat PAD patients with progressing blood circulation disorders of lower limbs (arteriosclerosis obliterans, Buerger's disease), as well as those with progressing arteriosclerosis affecting blood circulation in the heart (ischemic heart disease, myocardial disorders).

The present application to FDA shall enable us to proceed with clinical trials in the U.S., where their second phase will be conducted, since we have already conducted clinical research in this regard at the Osaka University.

Marketing / distribution of the HGF genetic medicine for both PAD and CAD will be handled by Daiichi SeiYaku (Daiichi Pharmaceutical) Co., Ltd.

Reference
Specific therapeutic significance of the HGF genetic medicine
It is known that HGF has a strong vascularization effect; the present pharmacological agent deposits a gene to produce HGF in sites of vascular necrosis, thus the HGF protein is generated locally, resulting in blood vessel regeneration to improve the (arteriosclerotic) condition ? the first genetic medication to be produced in Japan. The agent thus developed

does not employ a virus vector to introduce the genetic sequence to a patient?s DNA ? it is a pure, "naked" DNA sequence, so negative effects that usually accompany a DNA sequence introduction with a virus vector do not appear here. In addition, since the present medicine alters the condition of necrosis by re-generating the blood vessels, as opposed to all conventional pharmacological agents, positive results can be expected in cases when conventional therapy for PAD and CAD fails, or is increasingly complicated.

Explanation of specialized terms

1. Gene medicine

A medicine, wholly, or partially comprising a genetic expression.

2. Hepatocyte Growth Factor (HGF)

A growth factor developed from hepatocytes; in addition to blood vessel regeneration, it initiates various processes necessary for tissue / organ regeneration during organ formation (organogenesis).

3. Peripheral arterial disease (PAD)

Since peripheral blood vessels of the four limbs can become clogged, the supply of blood to muscle and skin tissues is not adversely affected, causing the following symptoms: a feeling of paralysis, coldness, arrest of blood flow (intermittent claudication), ulcer of lower limbs (thrombic disease), pain even when there is no motion. A condition characteristic of arteriosclerosis obliterans (ASO), Buerger's disease.

4. Ischemic heart diseases

Vessels supplying the heart (coronary blood vessels) become contracted (or constricted) to a certain extent resulting in insufficient blood flow after physical activity; characteristic symptoms of stenocardic chest pains and a tightness in the chest, disorders of coronary blood vessels becoming completely clogged - heart muscle tissue becomes ischemic.

5. Pure (or "naked) DNA

For a genetic expression to work properly, genes have to enter a cell; in conventional practice, however, genes may only come as close as to be attached to the cell membrane, unable to penetrate it. A carrier, an agent to introduce the genetic expression to a cell, becomes necessary at this point. An improved virus (i.e., purified not to pose danger to the host cell) is usually used for these purposes, and the method features a genetic expression introduced to a cell through a ribosome. Our methodology of the HGF genetic medication,

by contrast, has genes spiraling in "plasmidic DNA" (a naked DNA technology). Plasmidic DNA alone may not be able to penetrate the cell membrane, it can, however, generate genes if injected intra-muscularly. The technology is extremely safe with no danger of contamination and cytotoxicity due to ribosomes or viruses.