AnGes, Inc.

https://www.anges.co.jp/en/

Introduction

About AnGes

AnGes , Inc. is a biopharmaceutical company with the mission of providing patients suffering from diseases for which no effective therapy has been available to date, with innovative drugs. AnGes focuses on the development of gene-based medicines, a next-generation biopharmaceutical.

AnGes , Inc. was founded in December 1999 based on an innovative discovery by researchers at Osaka University. AnGes has already undergone the first stage of research and development, and is now in the second stage of realizing clinical application. For our lead product, HGF Plasmid (gene therapy) for the treatment of Chronic arterial occlusive disease, the company got the conditional and time-limited approval in March 2019. And its practicalizing started in September 2019 in Japan. This is the world's first commercialization using the Plasmid DNA method.
Then, in May 2023, we filed an application for manufacturing and marketing approval to lift the condition.

Development of NF-κB decoy oligonucleotide, a nucleic acid medicine that suppresses inflammation for diseases including, low back pain, and DNA vaccines for high blood pressure is also under way.

AnGes is also developing NF-κB decoy oligonucleotide, a nucleic acid medicine that suppresses various types of inflammation, and COVID-19 prophylactic DNA vaccine and hypertension DNA vaccine in intranasal formulation.

AnGes is also in the process of in-licensing drugs for rare diseases that have not been approved in Japan, and we received approval to manufacture and market Zokinvy, a drug for the treatment of premature aging in January 2024.

Having started from research and development and now embarking on a new stage of realizing clinical application in, AnGes strives to fulfill the expectations of patients, their families, shareholders, investors and the general public who are waiting for new drugs to become available, and aims to be a "global leader in the field of gene medicines."

Our Vision & Mission

Vision

AnGes aims to be a Global Leader in gene medicines

- **Global Leader in Gene Medicines** — Become a globally recognized specialist in Gene Therapies and Nucleic Acid Medicines
- **Creating New Markets** — Develop and deliver new medicines for unmet medical needs

Corporate Mission

Contribute to the improvement of human health and quality of life through the development of innovative medicines, by harnessing the potential of genes, acquired over the long course of the humankind.

Values

Achieve the Corporate Mission by acting along the principles incorporated in the company name "A-N-G-E-S":

Aspiration — Be an innovator without fear of change, with a spirit of challenge and enthusiasm.

Network — AnGes believes that every network is a key to creating new value. Patients, shareholders, alliance partners, employees and local communities are vital partners forming the foundation of its networks

Genesis — Continue to incorporate latest research results and ideas, and strive to create new technologies, products and value

Ethics — Work with the highest ethical standards

Speed — Realize innovative gene medicines to ensure prompt delivery to patients in need

Pipeline

AnGes-Origin Project

As of March 31, 2024

Project	Code / Dosage Form	Indication	Area	Development Stage
HGF Plasmid (Beperminogene Perplasmid)	AMG0001 Injection	Chronic arterial occlusive disease	JP	For Ischemic Ulcer Conditional and time-limited Approval. Launched in Sep. 2019 Filed for manufacturing and marketing approval for removal of conditions in May 2023.
		Arteriosclerosis Obliterans	US	For Ischemic Ulcer P2b (on going)
NF-kB Decoy Oligonucleotide	AMG0103 Injection	Chronic Discogenic Lumbar Back Pain	JP	P2 (on going)
DNA Vaccine	AGMG0201 Injection	Hypertension	AU	P1/2a (completed)
DNA Vaccine	Nasal Dosage Form	COVID-19	US	Joint research with Stanford University
Tie 2 Agonists	AV-001 Injection	COVID-19 / ARDS	US	P2a (on going)

●In-Licensed Project

・Rare Disease Therapeutics “Zokinvy” (lonafarnib)

[Licernsed in the regulatory approval, marketing, and distribution rights for Japan, from Eiger BioPharmaceuticals Inc. (United States)]

January, 2024 Received manufacturing and marketing approval in Japan

May, 2024 Scheduled to be released

Group/Alliance

As of March 31, 2024

Group Company

Company	Business
EmendoBio Inc. (U.S.)	Genome Editing
AnGes USA, Inc. (U.S.)	U.S. based development of Gene Medicine

Licensee of sales rights

Project	Indication	Area	Partner
HGF Plasmid (Beperminogene perplasmid)	Chronic arterial occlusive disease with lower limb ulcer	JP	Mitsubishi Tanabe Pharma
		Israel	Kamada
		Turkey	Er-Kim
	Arteriosclerosis Obliterans with Lower Limb Ulcer	US	Mitsubishi Tanabe Pharma
NF-κB Decoy Oligonucleotide	Dermal Diseases	Worldwide	Shionogi

Strategic Alliance

Parter	Project
MyBiotics Pharma (Israel)	Microbiome-cultivation and formulation of indigenous bacteria
Vasomune Therapeutics (Canada)	Co-development for ARDS

Project

HGF Plasmid

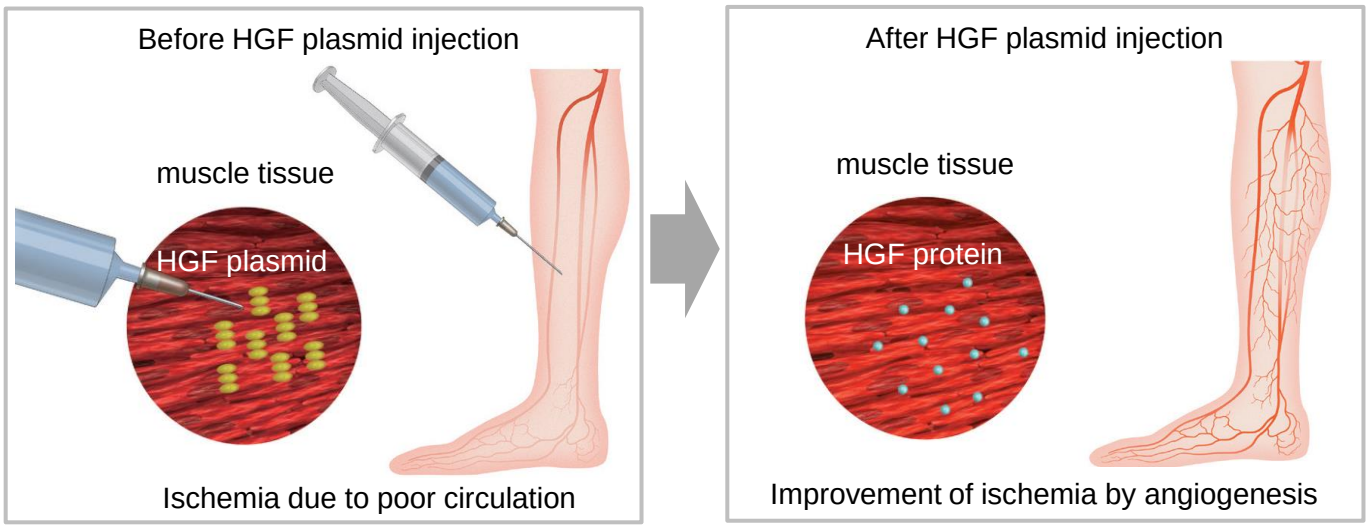
Gene Therapy Targeting Ischemic Diseases

HGF (Hepatocyte Growth Factor) was discovered in 1984 in Japan as a protein to accelerate the growth of hepatocytes. Although research on HGF initially focused on the development of medicines for liver diseases, in 1995 the research team, led by Dr. Ryuichi Morishita at Osaka University, found that HGF has a novel function as an angiogenic growth factor that promotes the growth of blood vessels. The local delivery of HGF Plasmid (Plasmid encoding HGF DNA) developed a new method of regenerating blood vessels and has strong potential to become a curative medicine for ischemic patients who are suffering from deteriorating circulation due to clogged blood vessels.

Examples of diseases caused by the clogging of blood vessels include: Chronic arterial occlusive disease with lower limb ulcer, which may ultimately lead to the amputation of a lower limb due to necrosis caused by poor circulation. For patients with severe ischemic conditions, the current treatment involves balloon-catheter treatment (plasty for cologged arteries by inserting a catheter into blood vessels) as well as bypass surgery in addition to drug administration. These treatments, however, do not always ensure a full recovery.

In March 2019, AnGes,Inc. acquired an application for marketing approval for HGF for critical limb ischemic in Japan. It is the first gene therapy medicine approved in Japan.

Gene Therapy with HGF Plasmid on Peripheral Arterial Diseases



Project

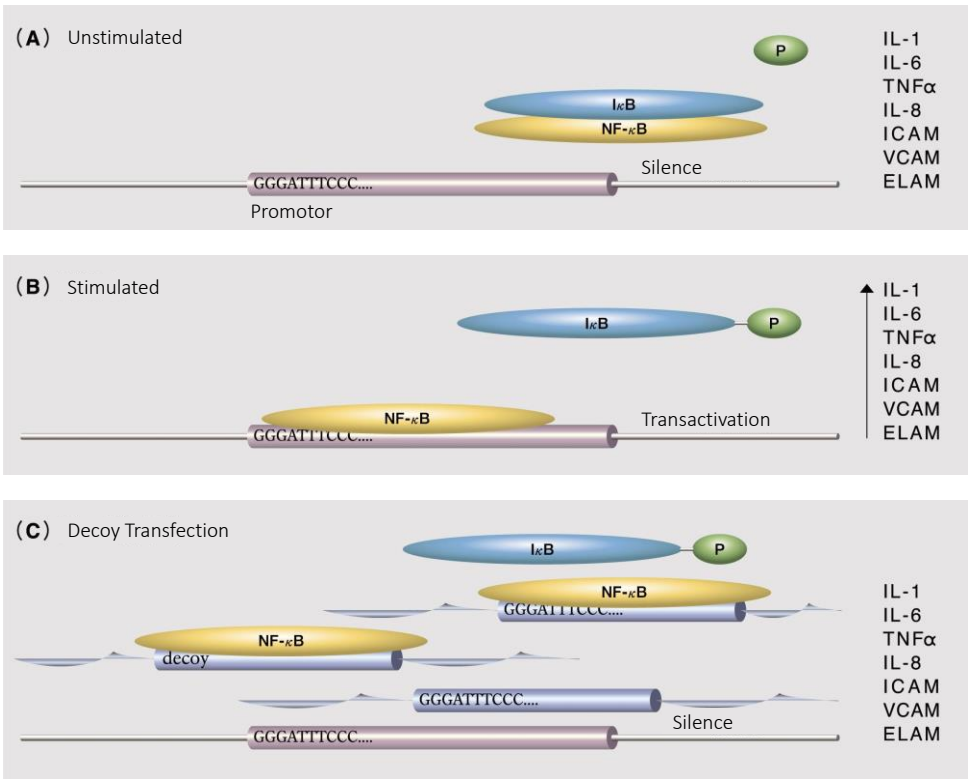
NF-kB Decoy Oligonucleotide

There are two major types of gene-based medicines. The first involves the utilization of the genes themselves, as is the case with HGF non-viral therapy; the other involves the utilization of relatively short artificial nucleic acid to regulate gene expression. The latter is known as nucleic-acid medicines and includes decoy oligodeoxynucleotide (Oligo), antisense, siRNA, aptamer and so on.

NF-κB decoy oligonucleotide is a type of nucleic-acid medicine. A gene is switched on when a protein called the transcription factor binds on the promoter region, which is a part of the genome that regulates gene expression and has a specific sequence. Decoy oligonucleotide is a synthesized short DNA compound, which has the same sequence as that found on the portion of the promoter region where the transcription factor binds. Since decoy literally means “lure,” Decoy oligonucelotide acts as the promoter’s lure and binds with the specific transcription factor in the cell. As a result, the transcription factor cannot bind on the genome, and the gene expression is suppressed.

AnGes has designed NF-κB decoy oligonucleotide as a specific inhibitor for NF-κB that acts as a switch on a gene cluster involved in the immune inflammatory responses in the body. AnGes has been conducting research and development on NF-κB decoy oligonucleotide as a new pharmaceutical product for immune and inflammatory diseases.

Mechanism of Action of NF-κB Decoy Oligonucleotide



Project

DNA Vaccine

AnGes is undertaking the research and development of DNA vaccine projects as a new type of gene-based medicine that utilizes its drug discovery know-how and development technology cultivated through the research and development of gene-based medicines. The injection of DNA vaccine directly introduces a plasmid DNA encoding the target antigen (protein), resulting in the in-situ production of the antigen. DNA vaccine is considered to have a relatively high and long-acting efficacy. It may become a promising treatment approach for cancer and allergy diseases as well as for some chronic diseases, and is expected to create a major market.

Hypertension DNA Vaccine

AnGes is proceeding with the research and development of a hypertension DNA vaccine. The hypertension DNA vaccine, which targets angiotensin II, has a longer blood pressure lowering effect duration compared to existing drugs. It may contribute to the improvement of patient convenience for those who have difficulties with daily administration, such as the elderly.

COVID-19 DNA Vaccine

AnGes has been developing DNA vaccines based on its track record of commercializing HGF gene therapeutic products using plasmid DNA manufacturing method with Osaka University since March 2020 as a vaccine to prevent COVID-19, which has raged worldwide since the end of 2019. Based on this knowledge, we have been collaborating with Stanford University in the U.S. since September 2022 on a DNA vaccine using an intranasal administration formulation.

Corporate information

Company Profile

Corporate Name	AnGes , Inc.
Head Office	Saito Bio-Incubator, 7-7-15, Saito-asagi, Ibaraki, Osaka, 567-0085 Japan
President & CEO	Ei Yamada
Established	December 17, 1999
Capitalization	35,053 million yen (As of December 31, 2023)
Outstanding Shares	198,470,300 shares (As of December 31, 2023)
Number of Employees	145 (As of December 31, 2023, Consolidated)
Scope of Business	Research and Development of Gene Medicine

Offices

Head Office	Saito Bio-Incubator, 7-7-15, Saito-asagi, Ibaraki, Osaka, 567-0085 Japan
Tokyo Office	9F, PMO TAMACHI Ⅱ, 4-13-3, Shiba, Minato-ku, Tokyo, 108-0014 Japan
Tonomachi R&D Center (CMC/ Drug Discovery Research)	Innovation Center of NanoMedicine, 3-25-14, Tonomachi, Kawasaki-ku, Kawasaki, Kanagawa, 210-0821 Japan
AnGes Clinical Research Laboratory	Life Science & Environment research center, 3-25-13 Tonomachi Kawasaki-ku, Kawasaki, Kanagawa, 210-0821 Japan

Group Company

AnGes USA,Inc.	111 Town Square Place, Suite 1140, Jersey City, New Jersey, 07310 USA
EmendoBio Inc.	400 W 61st St, #2330 New York, NY USA

Leading Global in Gene Medicine

AnGes Website

https://www.anges.co.jp/en/

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