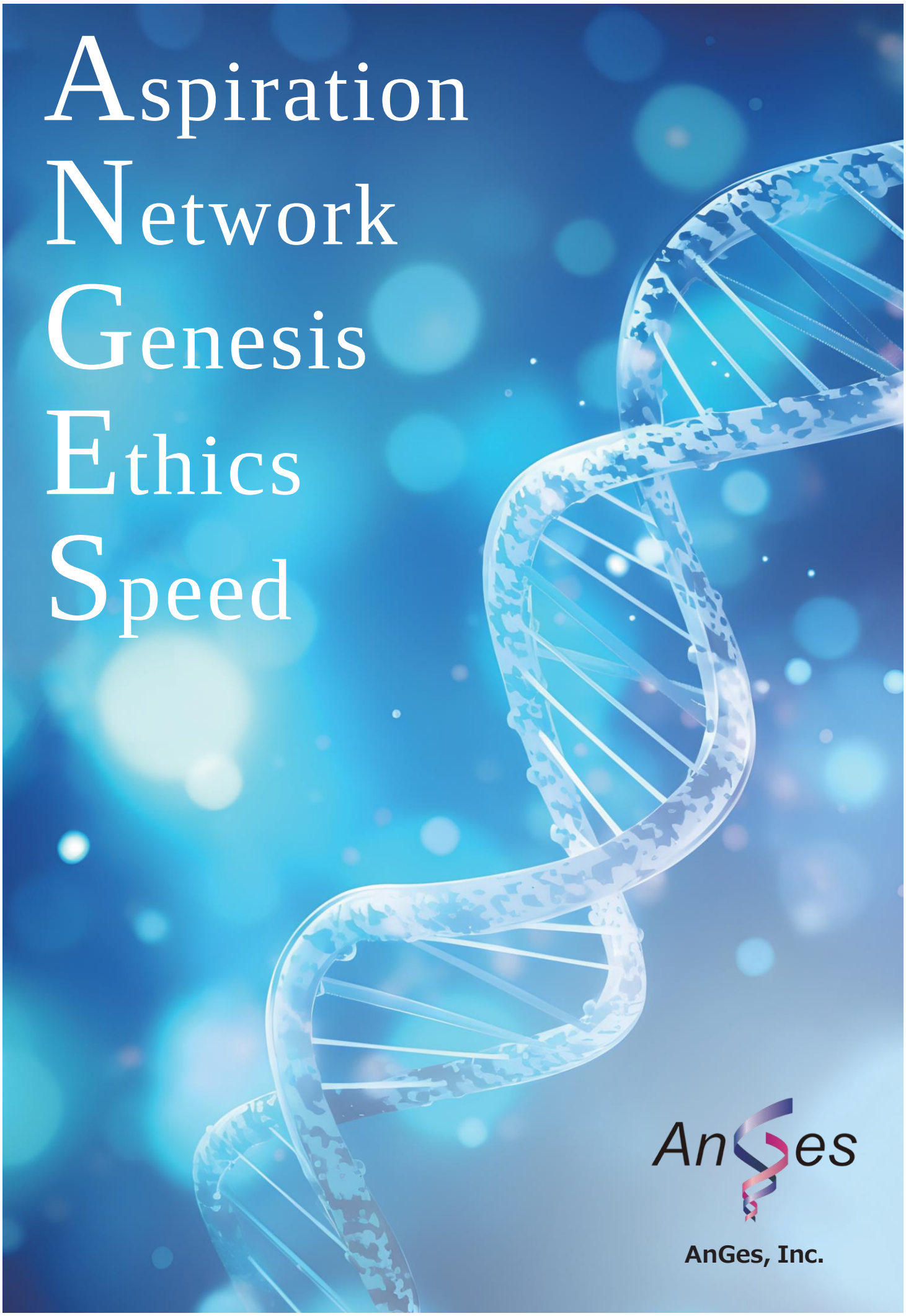

Aspiration
Network
Genesis
Ethics
Speed
AnGes
AnGes, Inc.

Introduction

AnGes is a biopharmaceutical company engaged in the development of innovative pharmaceuticals using gene medicine technology. Aiming to be a global leader in gene medicine, AnGes develops gene medicine, a new type of biopharmaceutical that utilizes the function of genes.

Since its establishment in 1999, based on basic research at Osaka University, the Company has been conducting research and development for the application of Hepatocyte Growth Factor (HGF) to pharmaceuticals, utilizing HGF's ability to “regenerate blood vessels” to develop HGF gene therapy for chronic arterial occlusive disease, a condition in which blood flow in the legs deteriorates to an extremely low level. We are also developing HGF gene therapy products for chronic arterial occlusive disease, a condition in which blood flow in the legs deteriorates to an extreme degree. In addition, we are developing pharmaceuticals with new mechanisms of action that have not yet been commercialized through collaborative research with academia and pharmaceutical development in cooperation with bio-ventures.

We are also in the process of in-licensing drugs for rare diseases that have not been approved in Japan, and have in-licensed drugs for Mucopolysaccharidosis Type VI and Hutchinson-Gilford-Progeria Syndrome, a premature aging disorder, and progeroid laminopathies with defective processing.

Meanwhile, the AnGes Clinical Research Laboratory (ACRL), which opened in April 2021, is a health laboratory whose main purpose is to test for rare genetic diseases and is currently contracted to perform expanded newborn screening, supporting early detection and treatment of genetic diseases in newborns.

In the world, new medicines and treatment methods are being developed one after another, and the technology of genome editing is currently at the forefront of research and development. In 2020, we acquired EmendoBio as a subsidiary and entered into the development of genome editing.

By promoting the development of genetic medicine and genome editing and contributing to the early detection and treatment of rare genetic diseases, we will strive to meet the expectations of patients and their families who are waiting for therapeutic drugs, as well as society that is waiting for new treatment methods.

Management Philosophy

Vision

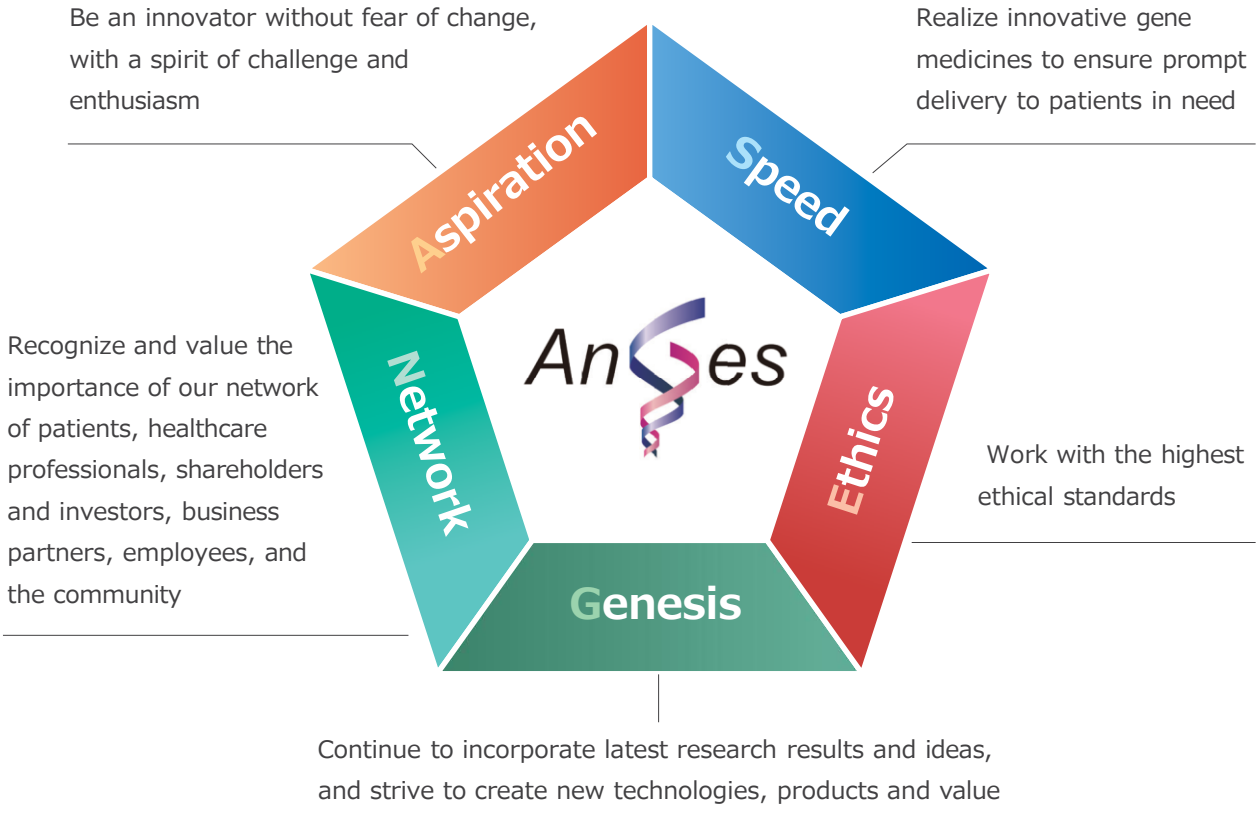
AnGes aims to be a global leader in genetic medicine

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

Guidelines for action

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



Pipeline

As of June 2024

Origin Project

Project	Code/ Dosage Form	Indication	Area	Development Stage
HGF gene therapy product (Collategene)	AMG0001 Injection	Arteriosclerosis obliterans with lower limb ulcer	Japan	Preparing for a new application for approval
			U.S.	Completed phase 2B clinical trials
NF-κB Decoy Oligonucleotide	AMG0103 Injection	Chronic discogenic lumber back pain	Japan	Phase 2 clinical trials underway
DNA Vaccine	AMG0201 Injection	Hypertension	Australia	Completed phase 1 clinical trials
DNA Vaccine	Intranasal formulation	Covid-19	U.S.	Pre-Clinical Collaborative Research and Development

Joint Development Project

Project	Code/ Dosage Form	Indication	Area	Development Stage
Tie2 Agonists	AV-001 Injection	ARDS	U.S.	Phase 2 A clinical trials underway Vasomune Therapeutics (Canada)

Products on sale

As of June 2024

Installed Products

Product Name	Dosage Form	Indication	Area	Note
Zokinvy	Capsule	HGPS/PDPL	Japan	Launched in May 2024 Purchased from Sentynl Therapeutics (U.S.)

Group companies and partners

As of June 2024

Group Companies

Company	Business
EmendoBio Inc. (U.S.)	Development of genome editing technology
AnGes USA, Inc. (U.S.)	Gene and Drug Development in U.S.

Strategic Alliance Partner

Company	Business
MyBiotics Pharma (Israel)	Microbiome - cultivation and formulation of indigenous bacteria

Drug Development

Project

HGF gene therapy product

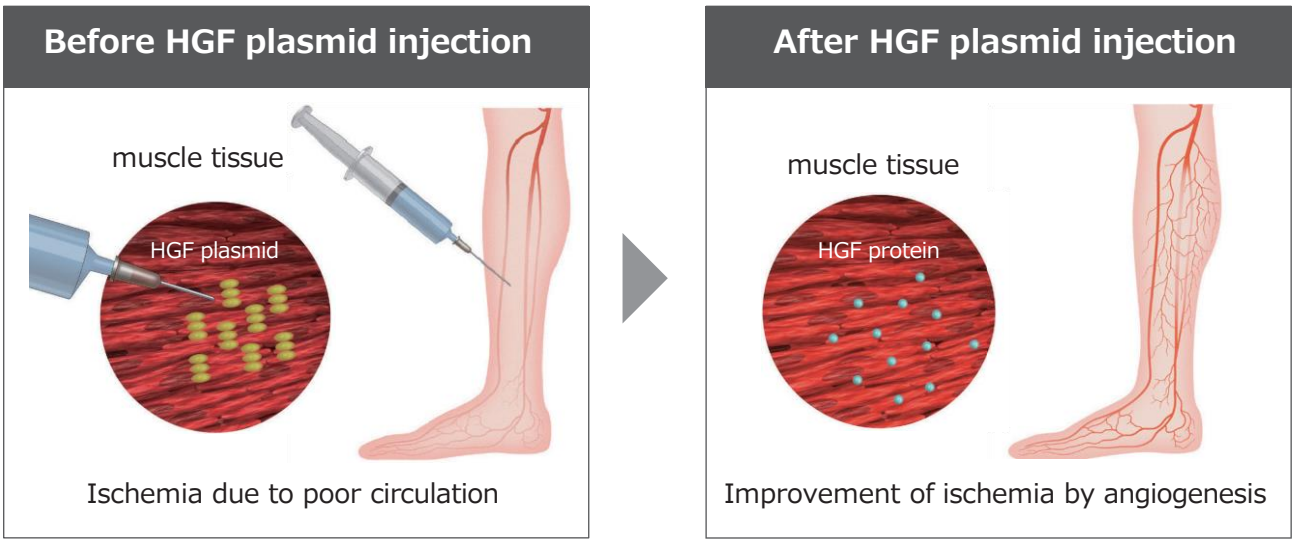
Gene therapy products for chronic arterial occlusive disease

Hepatocyte growth factor HGF was discovered in Japan in 1984 as a factor that increases liver cells. HGF gene therapeutic products treat ischemic diseases in which blood vessels are clogged and blood flow is impaired by its unprecedented action of “vascularization”. This is an unprecedented action to treat ischemic diseases in which blood vessels are clogged and blood flow is impaired.

Diseases in which blood vessels become clogged include, for example, chronic arterial occlusive disease (arteriosclerosis obliterans or Buerger's disease), in which arteries in the legs become blocked due to arteriosclerosis caused by diabetes and other factors, and blood cannot reach them properly, leading to necrosis and eventually necessitating leg amputation. Currently, the most common treatment for these diseases is endovascular therapy using balloon catheters (a method of recanalization of arteries through blood vessels using catheters) or surgical bypass surgery, in addition to drug therapy for severe cases. However, there are no effective treatment options for patients who do not respond to drug therapy and for whom catheters and surgery are not feasible.

The HGF gene therapy product will be the first gene therapy product in Japan with the indication, efficacy, or performance of improving ulcers in patients with chronic arterial occlusive disease who have difficulty undergoing revascularization surgery due to inadequate response to such standard drug therapy.

Angiogenesis with HGF gene therapy products



Drug Development

Project

NF-κB Decoy Oligonucleotide

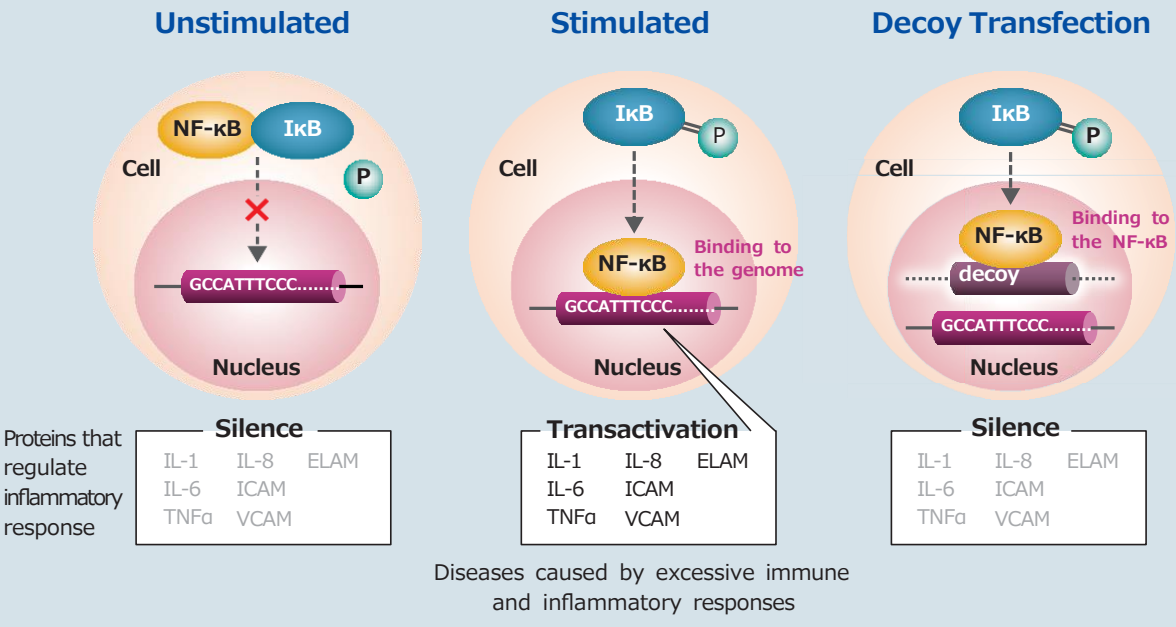
In addition to those that utilize the gene itself, such as HGF gene therapy products, some gene-targeted drugs use artificially created, relatively short nucleic acids to control the function of genes. This type of drug is called nucleic acid medicine and includes decoy oligonucleic acid, antisense, siRNA, and aptamers.

The NF-κB decoy oligonucleotide that we are developing is a type of nucleic acid medicine. When a protein is expressed by the action of a gene, a protein called a transcription factor binds to a specific sequence region of the genome to turn on the transcription factor. Decoy oligonucleic acids bind to specific transcription factors as genomic ‘ decoys’ in the cell, thus preventing the transcription factors from binding to the genome and consequently suppressing the expression of specific proteins.

We have designed “NF-κB decoy oligo”, a specific inhibitor of the transcription factor NF-κB, which is a switch for a group of genes responsible for immune and inflammatory responses in vivo, and are conducting research and development as a new therapeutic agent for diseases caused by excessive immune and inflammatory responses due to activation of NF-κB.

We are currently conducting Phase II clinical trials in Japan.

Principle of action of NF-κB decoy oligos



Drug Development

Project

DNA Vaccine

Hypertension DNA Vaccine

The hypertension DNA vaccine targets angiotensin II and is expected to have features not found in existing hypertension drugs, such as suppressing excessive diurnal fluctuations in blood pressure and being indicated for patients who have difficulty taking daily doses, because of its long-term stable antihypertensive effect.

Intranasal DNA Vaccine

In order to prevent novel coronavirus infection, we have been developing a DNA vaccine using plasmid DNA technology together with Osaka University from March 2020 to September 2022. Based on the findings, we are collaborating with Stanford University in the U.S. on a DNA vaccine using an intranasal formulation.

Joint Development Projects

Tie2 Agonists

We are co-developing a Tie2 receptor agonist (AV-001) for the treatment of ARDS with Canadian biopharmaceutical company Vasomune Therapeutics, Inc.
AV-001 activates the tyrosine kinase receptor Tie2 and promotes barrier defense against vascular leakage, thereby preventing bacterial and viral infections from causing uncontrolled vascular responses, impaired lung function, and edema of vital organs.
Phase II clinical trials are currently underway in the U.S. and other countries.

Installed Products

Our goal is to contribute to the improvement of people's lives and the standard of medical care through the development of innovative drugs for disease areas for which there is no cure, intractable diseases, and rare diseases, and to this end we aim to deliver innovative, internationally recognized drugs to patients as quickly as possible.
As an example, in 2007, we obtained the rights to develop and market a drug for the treatment of Mucopolysaccharidosis VI, a rare genetic disorder, in Japan, and in 2008, we obtained manufacturing and marketing approval for the drug, which we marketed until 2019.
In 2022, we also acquired the rights to market in Japan for the treatment of Hutchinson-Gilford-Progeria Syndrome and Processing-Deficient Progeroid Laminopathy, which is a form of premature aging, and we will begin marketing these drugs in 2024.
We will continue to contribute to the elimination of drug loss and drug lag in Japan by leveraging our experience and working to make available drugs for the treatment of mainly rare diseases that are not sold in Japan.

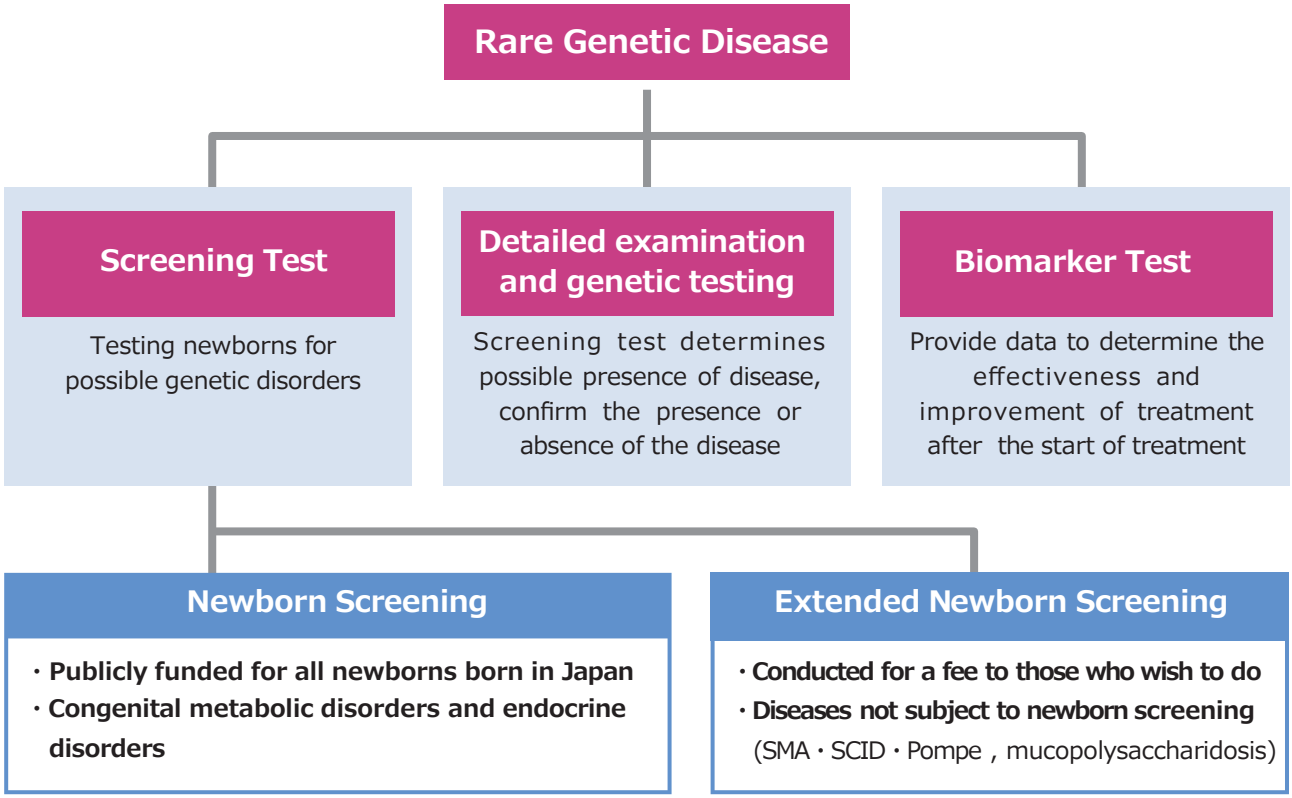
Zokinvy

Sentynl Therapeutics Inc. has acquired the exclusive rights to market Zokinvy in Japan for the treatment of Hutchinson-Gilford Progeria Syndrome (HGPS) and Processing Deficient Progeroid Laminopathy (PDPL), a so-called Progeria Syndrome, which is marketed in the United States and Europe by Sentynl Therapeutics Inc.(The contract was with Eiger BioPharmaceuticals Inc. and later the business was transferred) In March 2023, the drug was designated as an orphan drug, and in May 2023, an application was filed for manufacturing and marketing approval in Japan, which was granted in January 2024. Sales of the product began in May 2024.

Testing Services

AnGes Clinical Research Laboratory

AnGes Clinical Research Laboratory (ACRL) is a sanitary laboratory whose main purpose is to test for rare genetic diseases and was opened in April 2021.
Since its establishment, the Company has been engaged in the research and development of pharmaceuticals for intractable and rare diseases. An increasing number of rare genetic diseases are also treatable, but even if treatment is possible, there are some diseases for which the desired therapeutic effect cannot be achieved unless treatment is started before symptoms appear.
There are also diseases that have few characteristic symptoms and are difficult to detect with normal diagnosis. It is important to start treatment of rare genetic diseases early, preferably before the onset of disease. Since the establishment of ACRL, we have been contracted by the "Association for the Promotion of Medical Care and Research of Rare Diseases (CReARID)" to provide expanded newborn screening "Optional Screening" services, and since August 2024, we have been contracted directly by local governments to provide expanded newborn screening services. Since August 2024, the company has been directly commissioned to conduct expanded newborn screening tests on a municipal basis. In addition, in conjunction with the launch of Zokinvy in May 2024, we have established a system of "genetic testing" as a definitive test for Hutchinson-Gilford-Progeria Syndrome (HGPS) and Processing-Deficient Progeroid Laminopathy (PDPL), which are the diseases covered by this system, and have begun accepting orders. In the future, in addition to "screening tests," we will work on "precision genetic tests" and "biomarker tests," aiming to provide a comprehensive testing system from screening to diagnosis and treatment of rare genetic diseases.



Testing Services

Features of ACRL

01 The largest number of test items (9 diseases) in Japan in the expanded newborn screening test

The following 9 diseases are tested

Lysosomal diseases (Mucopolysaccharidosis type I/II/IVA/VI, Fabry's disease, Pompe disease) and Adrenoleukodystrophy, Spinal Muscular Atrophy, Severe Combined Immunodeficiency Syndrome

These diseases must be detected early, before symptoms appear, and treatment must begin at the appropriate time to be fully effective.

In addition, because these diseases are rare, many of them are difficult to detect in routine medical care, and by the time they are found, symptoms may have progressed.

In the United States, a country with advanced medical care, the Recommended Uniform Screening Panel (RUSP) is a system for recommending and prioritizing diseases for newborn screening.

Disease	Method of Testing	Treatment Methods
Mucopolysaccharidosis (MPS) Type I	filter paper blood enzyme activity	Enzyme replacement, hematopoietic stem cell transplantation
Mucopolysaccharidosis (MPS) Type II	filter paper blood enzyme activity	Enzyme replacement, hematopoietic stem cell transplantation
Mucopolysaccharidosis (MPS) Type IV A	filter paper blood enzyme activity	Enzyme replacement
Mucopolysaccharidosis (MPS) Type IV	filter paper blood enzyme activity	Enzyme replacement
Fabry's disease	filter paper blood enzyme activity	Enzyme replacement, Chemical chaperone
Pompe disease	filter paper blood enzyme activity	Enzyme replacement
adrenoleukodystrophy (ALD)	C26 : 0-lyso-phosphatidylcholine	Cerebral type: hematopoietic stem cell transplant
spinal muscular atrophy (SMA)	SMN1 gene quantitative PCR	Antisense nucleic acid drugs, gene therapy
severe combined immunodeficiency syndrome (SCID)	TREC Quantitative PCR	Hematopoietic stem cell transplantation (before infection)

In addition to the above 9 diseases, we are working on development for contract screening of new diseases such as Mucopolysaccharidosis VII, Gaucher disease, Niemann-Pick disease type A/B, Krabbe disease, B cell deficiency, and adenosine deaminase deficiency.

Testing Services

Features of ACRL

02 Flexible contracting arrangements are available, including inspection package proposals that meet your needs

While some laboratories offer specific packages of test items, ACRL can be flexible to meet your needs.

・Contract screening tests for all nine diseases

・Entrusted with testing only for certain diseases

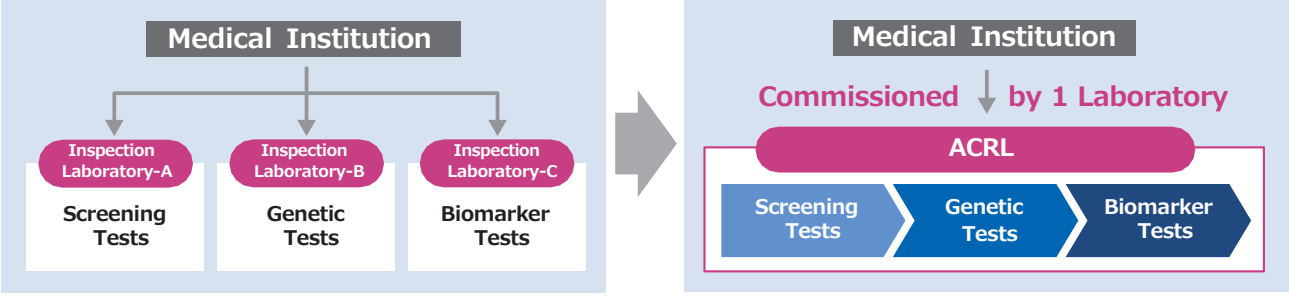
	Municipality①	Municipality②	Municipality③
Number of diseases tested	9 diseases	7 diseases	4 diseases
Mucopolysaccharidosis (MPS) Type I	ACRL	ACRL	ACRL
Mucopolysaccharidosis (MPS) Type II	ACRL	ACRL	ACRL
Mucopolysaccharidosis (MPS) Type IV A	ACRL	ACRL	ACRL
Mucopolysaccharidosis (MPS) Type IV	ACRL	ACRL	ACRL
Fabry's disease	ACRL	ACRL	–
Pompe disease	ACRL	ACRL	–
adrenoleukodystrophy (ALD)	ACRL	ACRL	–
spinal muscular atrophy (SMA)	ACRL	Labo A	Labo B
severe combined immunodeficiency syndrome (SCID)	ACRL	Labo A	Labo B

※ACRL can contract out inspections to meet local government requirements.

Features of ACRL

03 The only one-stop service in Japan for testing for rare genetic disorders

While there are few laboratories that perform all the tests for rare genetic diseases due to lack of profitability, ACRL has the systems and functions necessary for rare genetic disease testing, including “screening tests,” “genetic tests,” and “biomarker tests,” without physicians and local governments having to request multiple laboratories to perform the tests, allowing local governments and medical institutions to have a single point of contact. ACRL is equipped with the systems and functions necessary for rare genetic disease testing, including “screening tests,” “genetic tests,” and “biomarker tests,” without the need for physicians and medical institutions to request multiple testing organizations.



Genome editing technology platform and product development for gene therapy

In 2020, we entered the development of gene therapy through genome editing by making EmendoBio Inc. a subsidiary in the United States.

Genome editing is a technology that modifies genes by cutting only specific base sequences.

For genome editing to be used in medicine, it is important to prevent off-target effects, in which nucleotide sequences other than the targeted ones are accidentally cut.

EmendoBio is developing platform technology (OMNI Platform) for searching and optimizing novel CRISPR nucleases and developing novel nucleases with new characteristics (OMNI nucleases) with the aim of safe medical applications of genome editing.

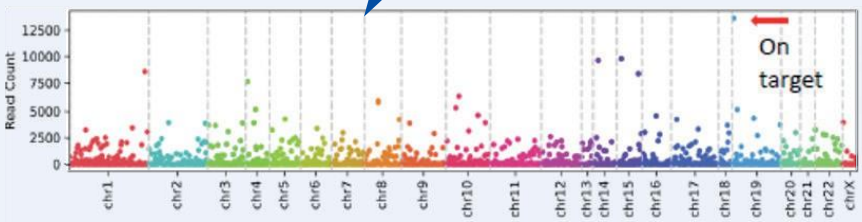
By optimizing OMNI nuclease, the occurrence of off-target effects can be suppressed and highly institutionalized genome editing becomes possible.

CRISPR/Cas9

In addition to on-target sites, a significant number of off-target sites are seen quite frequently

SpCas9

Colored dots in the data are the number of disconnected sections.

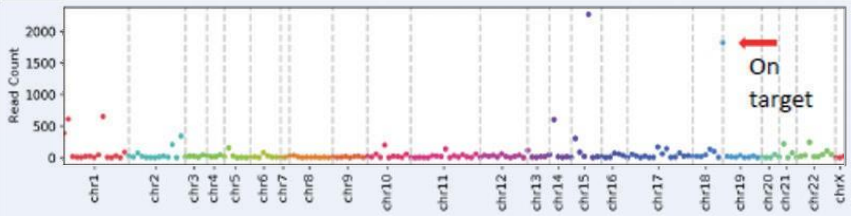


EmendoBio's genome editing technology

Wild type OMNI-A1

Off-target sites are fairly scarce, but there are scattered disconnect points other than on-target

WT-OMNI A1

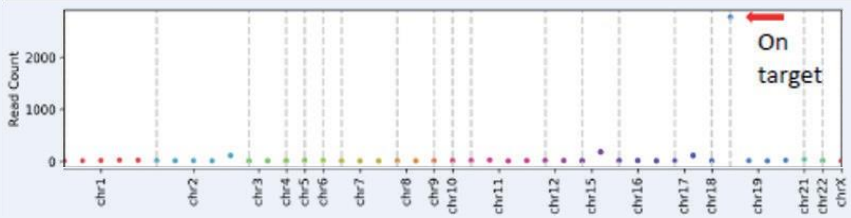


Optimization (AI for further optimization of allele-specific gene editing)

OMNI-A1-V10

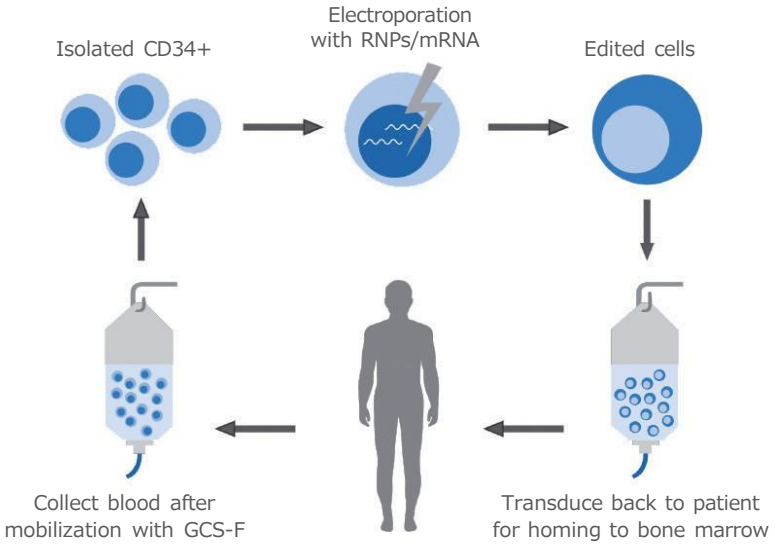
Almost no cutting occurs except for on-target (disease-causing) areas
⇒No extra cutting is done except where it should be done.

OMNI A1 V10



Aiming to treat ELANE-related severe congenital neutropenia requiring avoidance of off-target effects

EmendoBio's OMNI Platform is being used to develop a treatment for ELANE-related severe congenital neutropenia (SCN).
In pre-clinical studies, we have confirmed that only abnormal genes with almost identical sequences can be accurately distinguished and disrupted (allele-specific gene editing) without damaging normal genes, and as a result, HSCs are now able to differentiate into neutrophils.
The company aims to initiate clinical trials for ELANE-related severe congenital neutropenia (SCN) in the future.



EmendoBio pipeline

Disease Area	Program	Target	Indication	Approach	Research	Lead Optimization	IND-Enabling	Phase 1
Hematology	EMD-101	ELANE	Severe Congenital Neutropenia	Allele-specific ex vivo excision				
Cardiovascular	EMD-301	LDLR	**ASCVD not at LDL-C goal** Including Heterozygous Familial Hypercholesterolemia (HeFH)	In vivo excision				
	EMD-302	ANGPTL3	**ASCVD not at LDL-C goal** Including Homozygous Familial Hypercholesterolemia (HoFH)	In vivo KO				
Ocular	EMD-201	SARM1	Glaucoma	In vivo KO				
	EMD-202	RHO	Retinitis Pigmentosa	In vivo excision				
	EMD-203	RPE65	Retinitis Pigmentosa	In vivo excision				

Corporate information

Company Profile

Corporate Name	AnGes , Inc
Head Office	Saito Bio-Incubator, 7-7-15, Saito-asagi, Ibaraki, Osaka, 567-0085
President & CEO	Ei Yamada
Established	December 17, 1999
Capitalization	37,255million yen (As of December 31,2024)
Employees	55 (As of December 31, 2024 : Consolidated)
Business	Research and Development of Gene Medicine・Contract Testing Services

Offices

Head Office

Saito Bio-Incubator, 7-7-15, Saito-asagi, Ibaraki, Osaka, 567-0085

Tokyo Office

9F, PMO TAMACHI Ⅱ, 4-13-3, Shiba, Minato-ku, Tokyo, 108-0014

Tonomachi R&D Center (CMC/ Drug Discovery Research)

Innovation Center of NanoMedicine, 3-25-14, Tonomachi,
Kawasaki-ku, Kawasaki, Kanagawa, 210-0821

AnGes Clinical Research Laboratory (ACRL)

Life Science & Environment research center,
3-25-13 Tonomachi, Kawasaki-ku, Kawasaki, Kanagawa,
210-0821

Group Company

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400 W 61st St, #2330 New York, NY USA

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

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