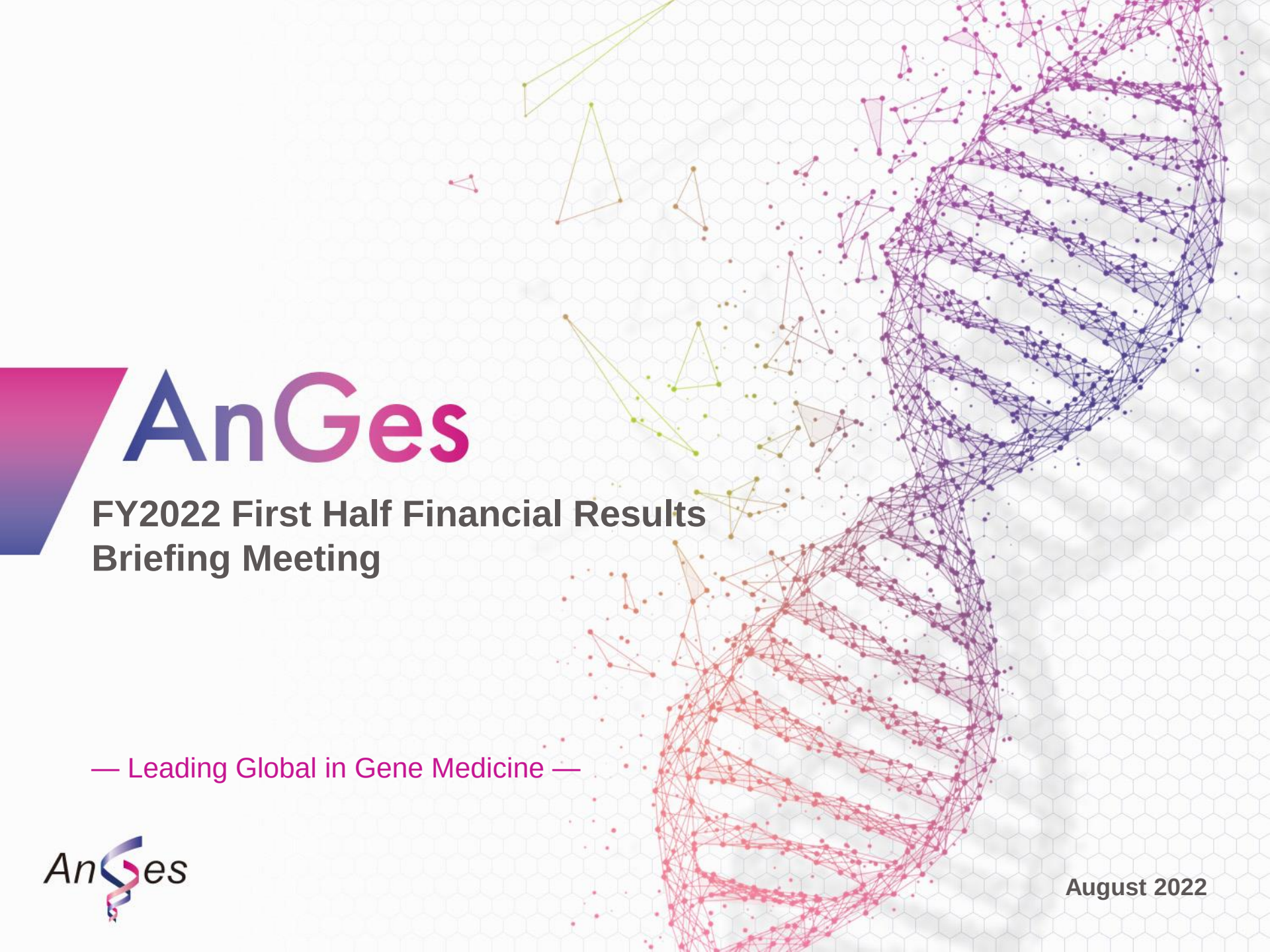


AnGes

# FY2022 First Half Financial Results Briefing Meeting

— Leading Global in Gene Medicine —

AnGes

August 2022

◆ The performance forecasts and forward-looking statements in these materials are based on information currently available to the Company and include potential risks and uncertainties.

◆ These risks and uncertainties include changes in the economic environment surrounding the Company, progress with research and development, the approval of acquisitions by the regulatory authorities, and system changes and revisions to laws and regulations in countries around the world.

◆ Actual business performance and results may differ significantly from the described forecasts due to various factors.

# Agenda

1 About AnGes

2 Summary of Financial Results for the First Half of FY2022

3 Development Pipeline: Topics

\+ Appendix

01

# About AnGes

# VISION & MISSION

## AnGes aims to become a global leader in genetic medicine.

We focus on research and development of the next-generation biopharmaceuticals such as genetic medicines and aim to achieve practical use of innovative drugs.

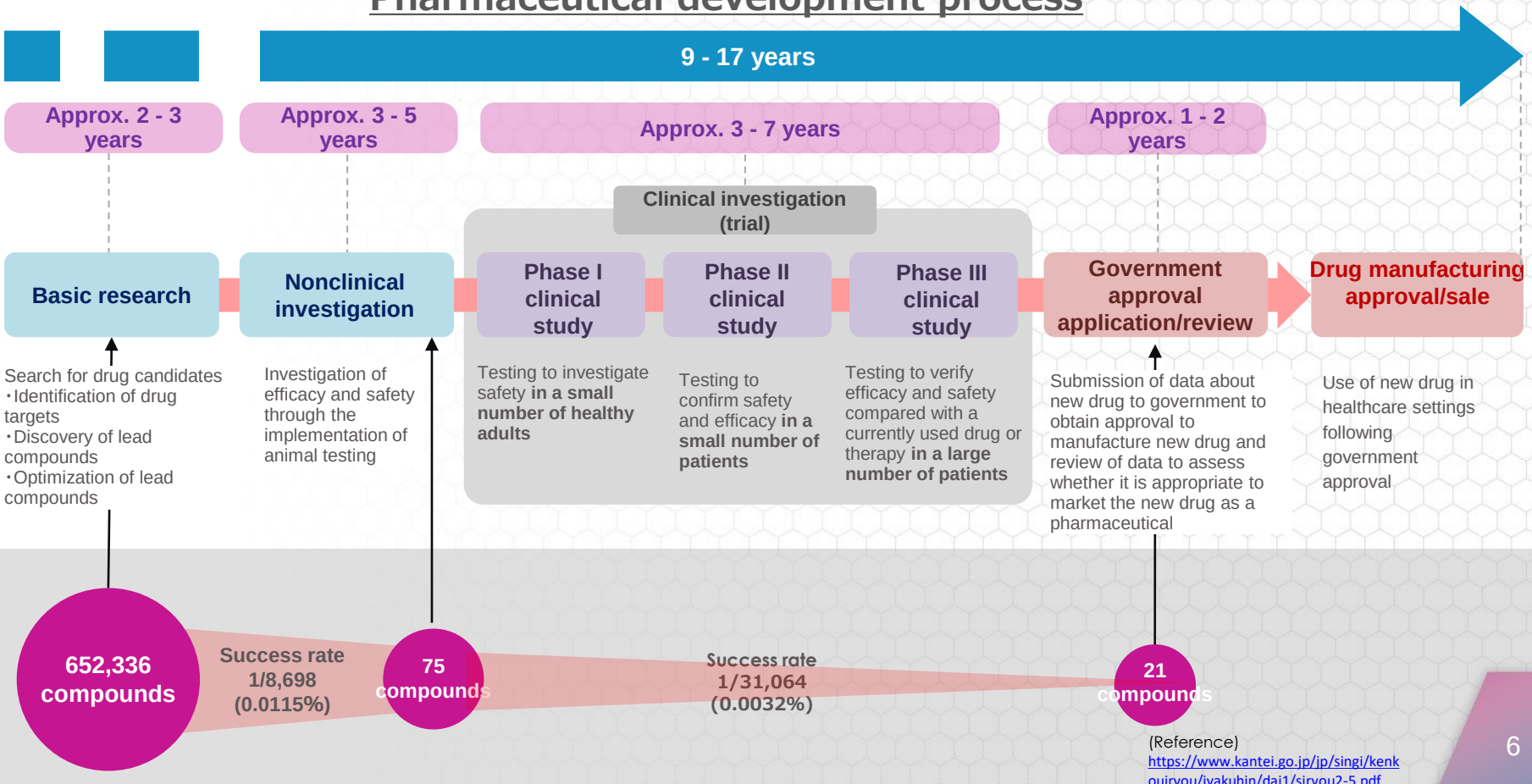
It is our mission to make a contribution to the improvement of people's Quality of Life (QOL) and medical standards through the development of innovative drugs. This is accomplished by utilizing advanced technology for the creation of next-generation biopharmaceuticals such as genetic medicines and therapeutic vaccines for diseases that are intractable or rare, and for which no treatments available. We are dedicated to providing innovative drugs for patients as promptly as possible.

# New Drug Development Pathway

**The success rate of new drug development is low and the degree of difficulty is extremely high!**

**The odds of a compound being launched as a new drug is approximately one in every 30000 shots (0.003%)**

## Pharmaceutical development process




(Reference)
https://www.kantei.go.jp/jp/singi/kenkouiryou/iyakuhin/dai1/siryou2-5.pdf

02

# Summary of Financial Results for the First Half of FY2022

# Highlights of Consolidated Results for the First Half of FY2022

| Item (Million yen) | First half of FY2021 | **First half of FY2022** | Increase/decrease |
|---|---|---|---|
| **Business Profit** | 23 | **31** | +8 |
| **Business Expenses** | 7,563 | **9,156** | +1,592 |
| **Operating loss** | -7,540 | **-9,124** | -1,583 |
| **Non-operating income/expenses** | +210 | **+1,704** | +1,494 |
| **Ordinary loss** | -7,330 | **-7,420** | -89 |
| **Extraordinary income/losses** | -105 | **–** | +105 |
| **Loss** | -7,450 | **-7,425** | +24 |

**Business revenues (+38.1% YoY)**

Collategene sales 3 million (compared with 23 million the previous year)
ACRL testing services 28 million (compared with - million the previous year)

**Business expenses (+21.1% YoY)**

Cost of sales 36 million (compared with 13 million the previous year)
Research and development expenses 6,617 million (compared with 4,961 the previous year)
・Increase in outsourcing expenses associated with manufacturing related services for the development of COVID-19 vaccines
・Decrease in research material expenses due to completion of administration in COVID-19 vaccine clinical trials
SG&A expenses 2,502 million (compared with 2,588 million the previous year)
・Goodwill amortization 1,348 million )(compared with 1,180 million the previous year)
Impact of depreciation of yen despite amortization expense in dollar terms being unchanged from the previous year
Average USD JPY exchange rate: Current year: 123.15 JPY Previous year 107.82 JPY

**Non-operating income/expenses**

・AMED and Vasomune government subsidies +202 million
・Foreign exchange gains on the revaluation of foreign denominated assets associated with a weaker yen +1,489 million
(compared with 266 million the previous year)
End of June 2022: 1 USD = 136.69 JPY
End of December 2021: 1 USD = 115.02 JPY

**Extraordinary income/Extraordinary losses**

・No income or losses during the current period

(Previous year: Loss on valuation of investment securities -138 million, etc.)

# Details of Business Expenses


**Cost of sales: ¥36 million**

(+22 million, +165.9% YoY)
Includes cost of optional screening service in addition to Collategene
Optional screening service is testing service at AnGes Clinical Research Laboratory and the cost structure is different from that of Collategene.

**R&D expenses: ¥6,617 million**

(+1,655 million, +133.4% YoY)
(i) Research material expenses 884 million (-621 million YoY)
Decrease in research material expenses due to completion of administration for COVID-19 clinical trials
(ii) Outsourcing expenses 4,170 million (+2,125 million YoY)
Increase in outsourcing expenses associated with manufacturing related services for COVID-19 vaccine development
(iii) Payroll and allowances 501 million (+138 million YoY)
Increase in personnel (researchers) at Emendo

**Selling, general and administrative expenses: ¥2,502 million**

(-85 million, -3.3% YoY)
(i) Commission expenses 958 million (+119 million YoY)
Decrease in Emendo-related consulting expenses
(iii) Goodwill amortization 1,348 million (+167 million YoY)
Increase in amortization expense associated with a weaker yen (because goodwill denominated in dollars is translated into yen)

# Consolidated Balance Sheet Highlights

| Item (Million yen) | Dec. 31, 2021 | June 30, 2022 | Increase/decrease |
|---|---|---|---|
| **Current assets** | 21,426 | **15,771** | -5,654 |
| **Cash and deposits** | 17,899 | **13,211** | -4,687 |
| **Non-current assets** | 24,029 | **26,821** | +2,791 |
| **Goodwill** | 22,675 | **25,450** | +2,775 |
| **Total assets** | 45,455 | **42,592** | -2,862 |
| **Liabilities** | 6,821 | **8,079** | +1,258 |
| **Net assets** | 38,634 | **34,513** | -4,121 |

**Current assets**

■ Year-on-year decrease associated with business expenditures
No new funds were raised.
Cash and deposits 13,211 million
■ Decrease associated with the transfer of COVID-19 vaccine manufacturing-related expenses
Advance payments to suppliers 552 million (-1,161 million YoY)

**Non-current assets**

■ Balance increase due to revaluation of 4,123 million associated with a weaker yen, which offset depreciation and amortization of -1,348 million due to 10 years amortization
(accounted for as translation adjustment under net assets)
Balance of goodwill due to the acquisition of Emendo
25,450 million (+2,775 million YoY)

**Liabilities**

■ Increase in AMED and MHLW subsidies for COVID-19 vaccine development
Advances received 5,764 million (+644 million YoY)
■ Increase associated with recording of COVID-19 manufacturing-related expenses
Accounts payable - trade 1,524 million (+804 million YoY)

**Net assets**

■ Decrease in retained earnings due to loss in the current period
-19,861 million (-7,425 million YoY)
■ Increase as a result of revaluation of goodwill associated with a weaker yen
Translation adjustment 5,220 million (+3,316 million YoY)

03

# Development Pipeline: Topics

# Status of Projects in the Clinical Development Stage

## ■ Products under development

| Project | Area | Licensee/partner | Dosage form | Indications | Basic research | Preclinical study | Clinical investigation (trial) | | Approval/review | Conditional/time-limited approval | Sale | Post-marketing surveillance | Formal approval |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Phase I | Phase II | | | | | |
| HGF gene therapy product | Japan | Mitsubishi Tanabe Pharma | Injectable | Chronic arterial occlusive disease with lower limb ulcer | | | | | | Approved | On Sales | On going | |

| Project | Area | Licensee/partner | Dosage form | Indications | Basic research | Preclinical study | Clinical investigation (trial) | | | Approval/review | Approval |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Phase I | Phase II | Phase III | | |
| HGF gene therapy product | Japan | Mitsubishi Tanabe Pharma | Injectable | Chronic arterial occlusive disease with rest pain | | | | | Underway | | |
| | United States | Mitsubishi Tanabe Pharma | Injectable | Arteriosclerosis obliterans with lower limb ulcer | | | | P2b (on going) | | | |
| | Israel | Kamada | Injectable | Chronic arterial occlusive disease with lower limb ulcer | | | | | | Preparig for application | |
| | Turkey | Er-Kim | Injectable | Chronic arterial occlusive disease with lower limb ulcer | | | | | | Preparig for application | |
| NF-kB decoy oligonucleotide DNA | United States | – | Injectable | Chronic discogenic lumber back pain | | | Completed | | | | |
| DNA vaccine | Australia | – | Injectable | Hypertension | | | Completed | | | | |
| DNA vaccine | Inside and outside Japan | – | Injectable | COVID-19 / ADRS | | | Underway | | | | |
| Tie-2 receptor agonists | United States | Vasomune | Injectable | | | | Completed | P2b (on going) | | | |

## ■ Licensed product

| Project | Area | Licensor | Dosage form | Indications | Basic research | Nonclinical investigation | Clinical investigation (trial) | | | Approval/review | Approval |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Phase I | Phase II | Phase III | | |
| Zokinvy (lonafarnib) | Japan | Eiger | Capsule | Progeria (HGPS・PL) | | | | | | Application being prepared | NEW |

# Development Status of HGF Gene Therapy Product

# What is HGF Gene Therapy Product?

## What is **gene therapy**?

**The therapy involves the injection of a specific gene into a patient's body. The gene will produce a protein that will work to treat a disease.**

## What is **HGF**?

**HGF stimulates the growth of hepatic cells.**
**In Japan in 1984, a growth factor was discovered in the liver, the organ with the highest regeneration capacity.**
**The factor was named Hepatocyte Growth Factor (HGF). Subsequently, it was revealed that HGF plays a major role in the formation and regeneration of the body's organs and tissues, including blood vessels, lymph vessels, and nerves, in addition to the liver.**

## Discovery of HGF's ability to regenerate blood vessels

**In 1995, a research team led by Osaka University's Ryuichi Morishita, M.D., Ph.D., discovered that HGF had angiogenic potential, which triggered the development of an HGF gene therapy drug. The drug is a therapeutic agent with an unprecedented angiogenesis* ability for the treatment of ischemic disease that causes vessel clogging leading to poor blood circulation.**

*Angiogenesis means the new formation of blood vessels. Blood vessels regenerate through angiogenesis, the formation of new blood vessels.

## Gene therapy drug for angiogenesis

# Collategene®, HGF Gene Therapy Product

**AnGes successfully commercialized an HGF gene therapy Product based on plasmid DNA for the first time in the world in 2019.**


### Collategene® Intramuscular Injection 4 mg

**[Drug price]**

611,478 yen/vial

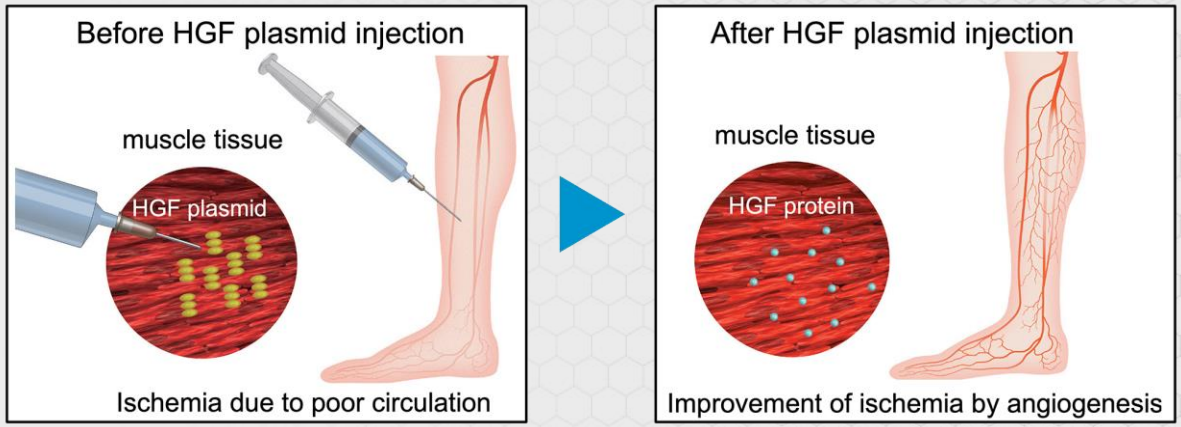
**[Indication or performance]**

Improvement of ulcers in chronic arterial occlusive diseases (obstructive arteriosclerosis and Buerger's disease)

**[Dosage and administration or usage]**

In usual cases, administer the drug at 0.5 mg per site by intramuscularly injecting it at eight sites of the ischemic parts of the affected limb of an adult patient at intervals of four week twice (2 sets of 4 mg per time).

## Angiogenesis by an HGF Gene Therapy Product



# Our HGF Gene Therapy Product is the First Product of Its Kind in Japan in One Way and the First Product of Its Kind in the World in Four Ways

1) Japan's first gene therapy product

Approval criteria of the following three organizations:
- Food and Drug Agency (FDA), USA
- European Medicines Agency (EMA)
- Ministry of Health, Labour and Welfare (MHLW), Japan

2) The world's first plasmid (DNA molecule) product

3) The world's first practical application of HGF

4) The world's first therapeutic product forming new peripheral vessels

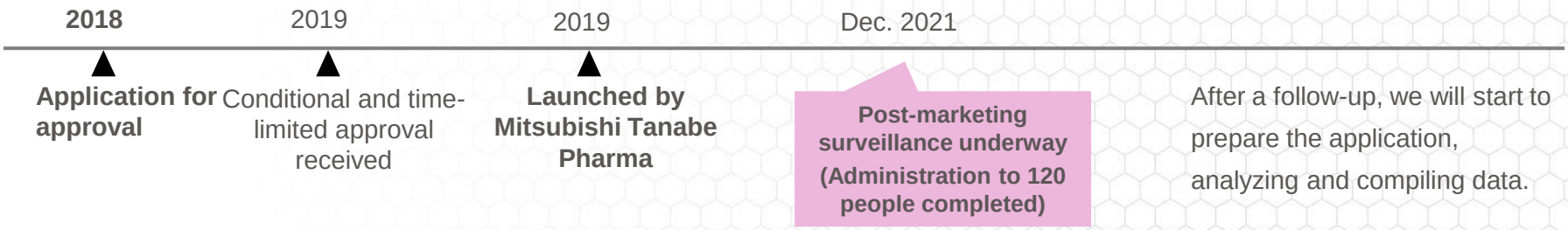
5) The world's first therapeutic product in the field of cardiovascular medicine

The information above is as of March 2019 when we obtained a conditional and time-limited manufacture and sales approval.

# HGF Gene Therapy Product 1
## (Ulcers Associated with Chronic Arterial Occlusive Diseases, Japan)

## Post-marketing surveillance underway for formal approval
## (administration to 120 patients completed as of December 2021)

Based on the results of post-marketing surveillance of 120 patients, we aim to acquire formal approval within five years (by 2024).




| | |
|---|---|
| Applicable disease | **Ulcers associated with chronic arterial occlusive diseases (The condition is that blood vessels are completely obstructed and blood flow is blocked, causing a shortage of nutrients and oxygen hindering the healing of even minor scars, and ischemic ulcers and necrosis occurs.)** |
| Number of patients | 800,000 patients with chronic arterial occlusive disease in Japan (source: IMS Health, survey materials) |
| Development status | Launched by Mitsubishi Tanabe Pharma on September 10, 2019.<br>The goal is to receive formal approval within five years (by 2024) based on results of the post-marketing surveillance of 120 patients.<br>(Administration to 120 patients completed as of December 2021) |

**September 2019: Launched by Mitsubishi Tanabe Pharma**

**February 2019: Conditional and time-limited approval of the Working Group's Meeting on Regenerative Medicine and Biological Technology under the Pharmaceutical Affairs and Food Sanitation Council, Ministry of Health, Labour and Welfare**

**January 2018: Application for approval to manufacture and sell the drug submitted to the Ministry of Health, Labour and Welfare**

**2015: An exclusive domestic distribution rights licensing agreement for the product with the indication for peripheral vascular disease signed with Mitsubishi Tanabe Pharma.**

# HGF Gene Therapy Product 2
## (Rest Pain Associated with Chronic Arterial Occlusive Disease, Japan)

# Administration to patients in the Phase Ⅲ clinical study completed for additional indication

**2018** — Application for approval

**2019** — Launched by Mitsubishi Tanabe Pharma

**2019** — Conditional and time-limited approval obtained

*Ulcers associated with chronic arterial occlusive disease

**From 2019** — Phase Ⅲ clinical study started

*Rest pain associated with chronic arterial occlusive disease

**Dec. 2021** — Administration to patients in Phase Ⅲ clinical study completed

The conventional approval system


Conditional and time-limited approval system


Addition of indication for the product linked with the conditional and time-limited approval system

We aim to get approval for the rest pain indication, an additional indication for the HGF gene therapy drug.

In the approval acquisition process, we will apply for the additional indication using the results of the Phase III clinical study when conditions are removed regarding the improvement of ulcers under the new system in the figure on the left ("the formal approval").

| | |
|---|---|
| **Applicable disease** | **Rest pain associated with chronic arterial occlusive disease** |
| Number of patients | 800,000 patients with chronic arterial occlusive disease in Japan (source: IMS Health, survey materials) |
| Development status | Administration to patients in the Phase Ⅲ clinical study completed (December 2021) |

**December 2021: Administration to patients in the Phase Ⅲ clinical study completed**

**October 2019: Phase III clinical study involving around 40 patients over about two years commenced for formal approval.**

**2015: An exclusive domestic distribution rights licensing agreement for the product with the indication for peripheral vessel diseases signed with Mitsubishi Tanabe Pharma.**

# HGF Gene Therapy Product 3
## (Ulcers Associated with Chronic Arterial Occlusive Disease, Overseas)

## Late Phase II clinical study underway in the USA.


| | |
|---|---|
| Applicable disease | **Ulcers associated with chronic arterial occlusive diseases** |
| Number of patients | Obstructive arteriosclerosis: 7,780,000 (USA) (Source: Foster Rosenblatt, survey materials) |
| Development status | Late Phase II clinical study underway in the USA (from February 2020) |

**2020: A basic agreement on the licensing-out (of exclusive distribution rights) for Turkey signed with Er-Kim.**

**Late Phase II study underway in the USA under the new guidelines (Global Vascular Guideline).**

**2019: A basic agreement on the licensing-out (of exclusive distribution rights) for Israel signed withKamada**

**2012: An exclusive distribution rights licensing agreement in the USA for the product with the indication for peripheral vascular disease signed with Mitsubishi Tanabe Pharma.**

# Development Status of NF-κB decoy oligonucleotide DNA

# What is NF-κB Decoy Oligonucleotide?

**We are developing NF-κB decoy oligonucleotide DNA for the treatment of intervertebral lumbago.**

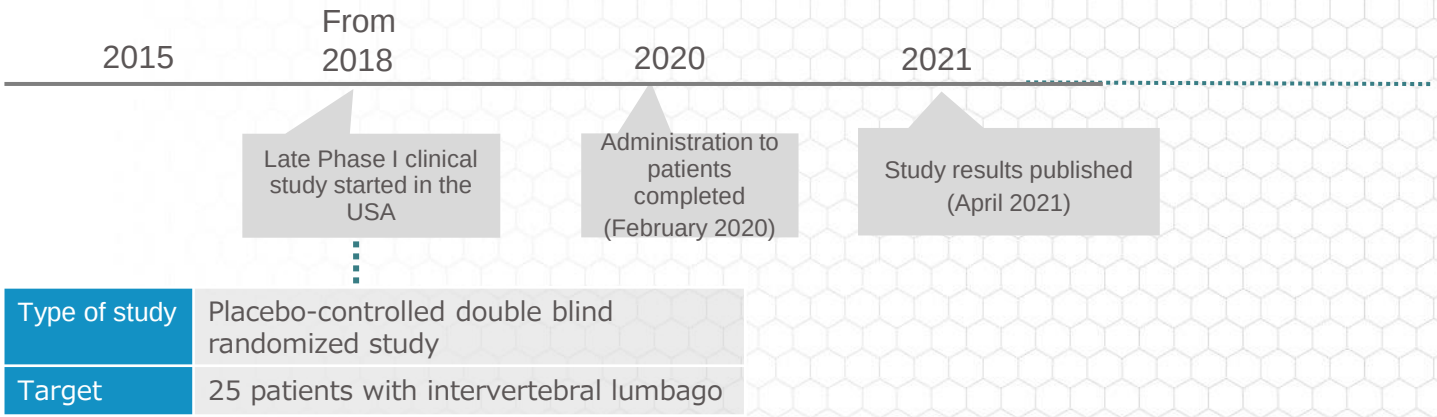
NF-κB is the major transcription factor that is activated due to inflammatory and immune reactions in cells when external stimuli are present, such as oxidative stress from active oxygen, in the case of the activation of inflammation or immunity.

It has been pointed out that it will exacerbate allergic/immunological diseases such as atopic dermatitis and asthma if NF-κB over-activates an inflammation-causing gene.

When a large amount of NF-κB decoy is put in the body as a decoy, **it will inhibit binding between NF-κB and the genetic transcriptional regulatory sequence that causes inflammation.**

# NF-κB decoy oligonucleotide DNA
## (drug for treating Chronic discogenic lumber back pain)

## Administration to patients in a Late Phase I clinical study completed in the USA
## Study results after follow-up published (safety and efficacy confirmed)




| | |
|---|---|
| Type of study | Placebo-controlled double blind randomized study |
| Target | 25 patients with intervertebral lumbago |

| | |
|---|---|
| **Applicable disease** | **Chronic discogenic lumber back pain** |
| Number of patients | 5,770,000 (USA) (Source: https://hpi.georgetown.edu/backpain and Pain Med. 2015,16(8):1490-9) |
| Development status | Administration to 25 patients in the late Phase I clinical study completed in the USA (February 2020).<br>Study results published (safety and efficacy confirmed). |

**April 2021:Results of the late Phase I clinical study (observation period: 12 months) published.**

**February 2021:Results of the late Phase I clinical study (observation period: 6 months) published.**

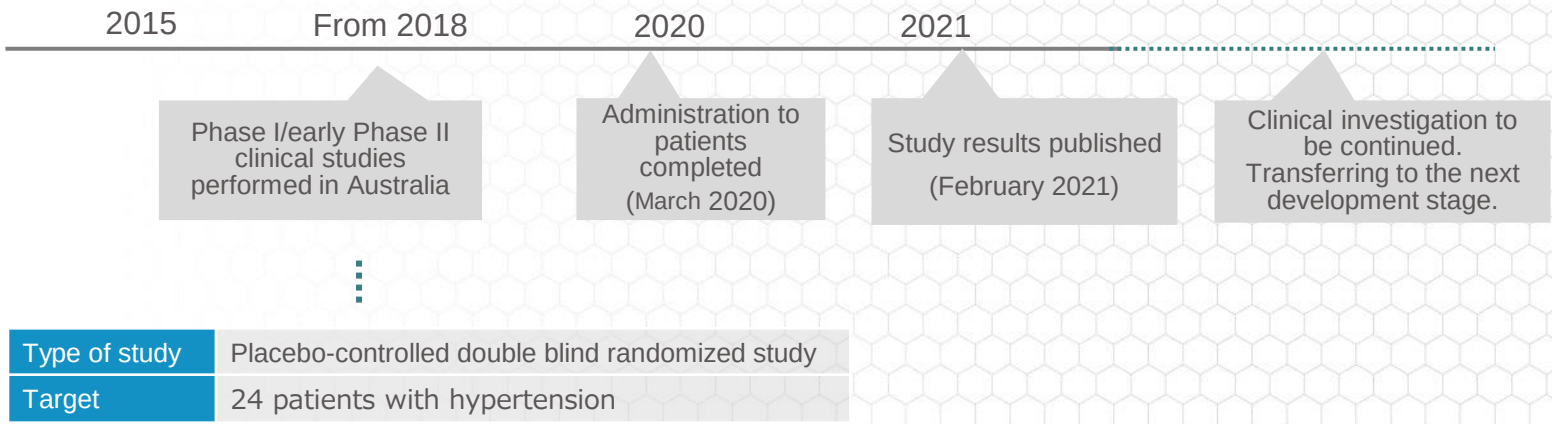
**February 2020:Administration to 25 patients completed.**

**February 2018: Late Phase I clinical study started in the USA**

**Note: The global market size is large, including the USA**

# Development Status of DNA Vaccine for Hypertension

# Administration to patients in Phase I/early Phase II clinical studies completed. Study results after follow-up published (no problem with safety).




| | |
|---|---|
| Type of study | Placebo-controlled double blind randomized study |
| Target | 24 patients with hypertension |

| | |
|---|---|
| **Applicable disease** | **Hypertension** |
| Number of patients | 61,460,000 (USA) (Source: AHA (https://www.ahajournals.org/doi/epub/10.1161/CIR.0000000000000757) |
| Development status | Administration to patients in Phase I/early Phase II clinical studies completed (March 2020)<br>Study results published (no serious adverse events, no problem with safety) Under preparation for the start of the next stage of clinical investigation. |

**February 2021: Results of Phase I/early Phase II clinical studies published.**

**March 2020: Administration to patients in Phase I/early Phase II clinical studies completed.**

**Safety and efficacy to be evaluated in a double-blind setting for about 6 months.**

**Then, long-term safety and efficacy in an open-label setting for about 6 months.**

**April 2018: Phase I/early Phase II clinical studies started in Australia.**

# Development Status of Covid-19 Coronavirus DNA Vaccine

# Data from Phase I/II clinical studies under analysis with higher doses using high-dose preparations

Investigation (analysis) underway at overseas organizations since it is important to judge clinical trial results in accordance with international standards.

**From Mar. 2020** — Vaccine development project published

**Aug. 2020** — Adopted for the Vaccine Production System Urgent Development Project implemented by the Ministry of Health, Labour and Welfare.

**Oct. 2020** — Vaccination of all subjects in Phase I/II clinical studies completed

**Mar. 2021** — Vaccination in Phase II/III clinical studies completed

**Nov. 2021** — Vaccination of all subjects in Phase I/II clinical studies completed with high-dose preparations

| | |
|---|---|
| **Applicable disease** | **COVID-19 Coronavirus** |
| Development status | Vaccination of all subjects in Phase I/II clinical studies completed with high-dose preparations. Data under analysis. |

**November 2021:Vaccination of all subjects in Phase I/II clinical studies completed with high-dose preparations.**

**August 2021:Vaccination of all subjects in Phase I/II clinical studies started with high-dose preparations.**

**March 2021:Vaccination of all subjects in Phase II/III clinical studies completed**

**October 2020:Vaccination of all subjects in Phase I/II clinical studies completed**

**March 2020: Joint development of a prophylactic SARS-CoV-2 DNA vaccine with Osaka University commenced.**

**Development of the active pharmaceutical ingredient finished. Nonclinical investigation started.**

# Review Flow for Vaccines to Protect Against Covid-19 Variants

## Guidelines published by the PMDA

**The review process for vaccines to protect against Covid-19 variants follows the guidelines for the evaluation of vaccines against Covid-19 variants published by the PMDA.**

**Review flow for vaccines to protect against Covid-19 variants**


1) Obtain approval in Japan for a vaccine that protects against Covid-19(parent vaccine).

2) Prepare to apply for approval of vaccines for Covid-19 variants after the parent vaccine is approved.

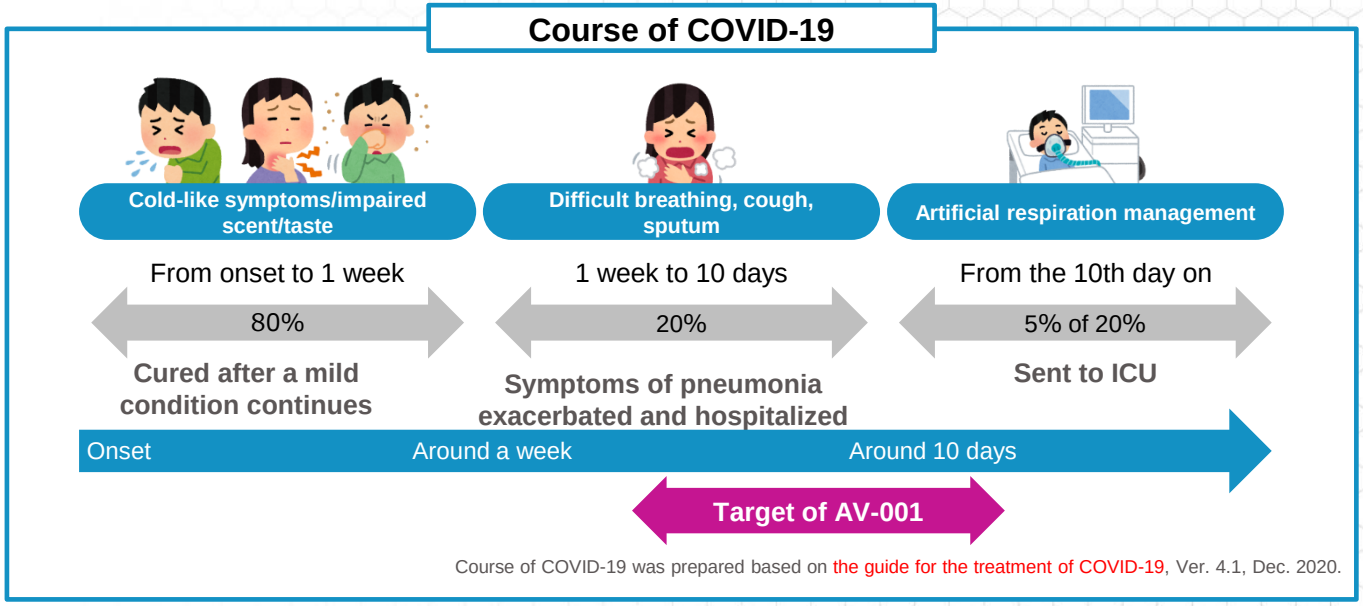
For more information, see the materials prepared by the PMDA.
Supplement 1 to the perspective regarding the evaluation of vaccines to protect against Covid-19 coronavirus : Evaluation of vaccines that protect against variants
https://www.pmda.go.jp/files/000240283.pdf

# Tie-2 (Tyrosine Kinase) Receptor Agonist(AV-001)

# What is Tie-2 (Tyrosine Kinase) Receptor agonist?

We are **jointly developing** AV-001 with **Vasomune**, a Canadian bio-pharmaceutical company. Originally, the joint development commenced globally in 2018 as a pharmaceutical for acute respiratory failure arising from the insufficiency of blood vessels.

We started clinical investigation with the drug as **a therapy for pneumonia associated with moderate to severe COVID-19** in the USA in 2020.



# Early Phase II clinical study underway

**From Dec. 2020** — Phase I clinical study started in the USA

| | |
|---|---|
| Type of study | Placebo-controlled double blind study |
| Target | Healthy adults |

**Mar. 2021** — Favorable results of Phase I clinical study published in the USA

**Jan. 2022** — Early Phase II clinical study started in the USA

Preparing for the start of the late Phase II clinical study

| | |
|---|---|
| **Applicable disease** | **Acute respiratory distress syndrome associated with COVID-19** |
| Number of patients | Acute respiratory distress syndrome: 260,000 (USA) (Source: Am J Resp Crit Care Med, Volume 195 Number 7) |
| Development status | AV-001, Tie-2 receptor agonist compound (drug for treating COVID-19)<br>Early Phase II clinical study underway in the USA |

**March 2021: Favorable results of the Phase I clinical study with the drug for treating COVID-19 AV-001 published in the USA.**

**Vasomune obtained a subsidy from the Canadian government for development of AV-001, the drug for treating COVID-19**

**December 2020: Phase I clinical study with the drug for treating COVID-19 AV-001 started in the USA.**

**Safety and tolerability of AV-001 confirmed in the Phase I clinical study.**

**July 2018: Joint development of AV-001 with Vasomune Therapeutics (Canada) started.**

**Target diseases: Diseases caused by insufficiency of blood vessels, such as acute respiratory failure**

# Zokinvy®,
# a Drug for Treating Rare Diseases
## (Lonafarnib)

Wednesday, May 11, 2022

# We announced that we concluded a sales agreement for Zokinvy, a drug for treating rare diseases, with Eiger BioPharmaceuticals Inc.

**You can find the news release on our website.**

https://www.anges.co.jp/pdf_news/public/JJMxX06VGzBIyaSSDiXWYZ9eBf3zbz83.pdf

# About Zokinvy®

## Applicable disease

**Indications are Hutchinson-Gilford progeria syndrome (HGPS, a.k.a. progeria) and progeroid laminopathy (PL).**

*Progeria: A generic term for diseases showing signs of aging in the entire body more rapidly than the person's actual age.
The term progeria mainly consists of "pro" meaning early and "gest" meaning aging because aging advances more rapidly than is natural.

## Efficacy and safety of Zokinvy

*Based on data from a survey in the USA

◆ **Efficacy**

**Certain data shows Zokinvy reduced mortality 60% and extended the average survival period 2.5 years in patients with Hutchinson-Gilford progeria syndrome (HGPS).**

◆ **Safety**

**Many progeria patients have continued to use Zokinvy for over ten years. Reported side effects include vomiting, diarrhea and nausea. The severity is mild or moderate in most cases.**

## Why did AnGes launch the Zokinvy initiative?

**Our business aims to contribute to the betterment of people's standard of living and healthcare through the development of innovative pharmaceuticals for diseases for which there are no remedies, intractable diseases and rare diseases, so we deliver world-class innovative medicines to patients as quickly as possible. Zokinvy is the product suitable for our business goals.**

# AnGes Clinical Research Laboratory (ACRL)

# AnGes Clinical Research Laboratory (ACRL)

**They are a health laboratory whose main purpose is to perform testing for rare genetic diseases**

| | |
|---|---|
| **Rare genetic diseases** | **- Ultra-rare diseases with very small number of patients**<br>(e.g., phenylketonuria, mucopolysaccharidosis, duchenne muscular dystrophy)<br>**- <u>It is important to start treatment in the early stages after onset and ideally before onset.</u>** |

## AnGes Clinical Research Laboratory

We have been contracted to provide testing services for optional screening, fee-based testing provided by the Clinical & Research Association for Rare, Intractable Diseases (CReARID) for people who wish to be tested.

- Established in April 2021
- Optional screening started in cooperation with CReARID. (July 2021)

**- Today, about 10,000 tests are performed per year.**

**- We will enhance tests to test for more diseases and increase the number of test labs in the future.**

## Tests for newborns

### Mass screening

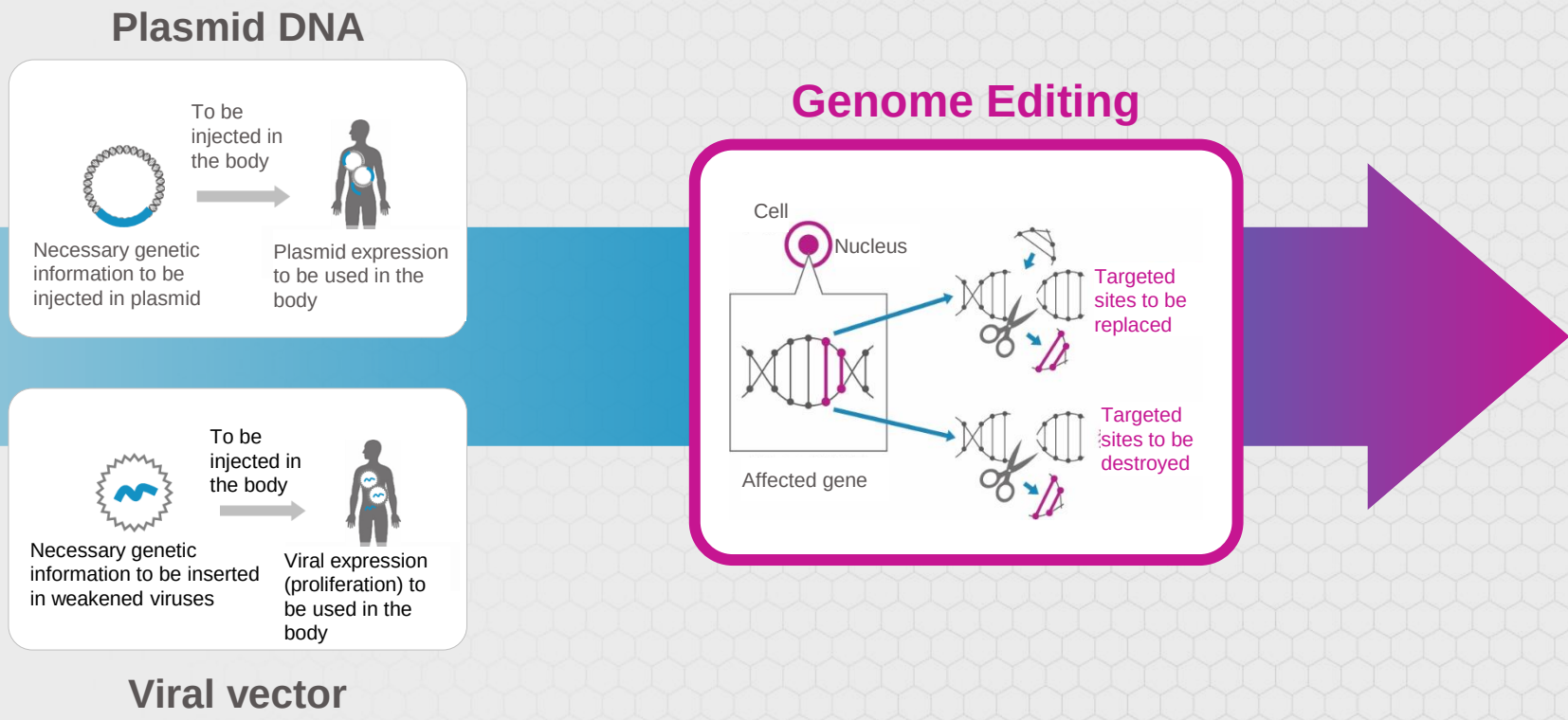
**- Provided free to all babies born in Japan**
(e.g., phenylketonuria, congenital hypothyroidism)

### Fee-based additional tests

**- Fee-based tests provided to applicants**
**- Diseases excluded from mass screening**
(e.g., Pompe disease, mucopolysaccharidosis)

# Genome Editing
# Development Status at EmendoBio

# The Stage Following Gene Therapy




**Genome editing is the ultimate gene therapy**

# What is Genome Editing?

**The technology uses nuclease, the enzyme for cleaving DNA that selectively cuts off specific base sequences (target sequences).**

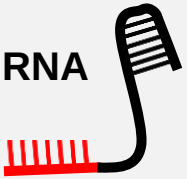
## ★ CRISPR/Cas9

(Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-Associated Proteins 9 )

In 2012, an innovative technology was developed for cleaving target DNA sequences more quickly and easily than the conventional technologies.

1) Read a base sequence.

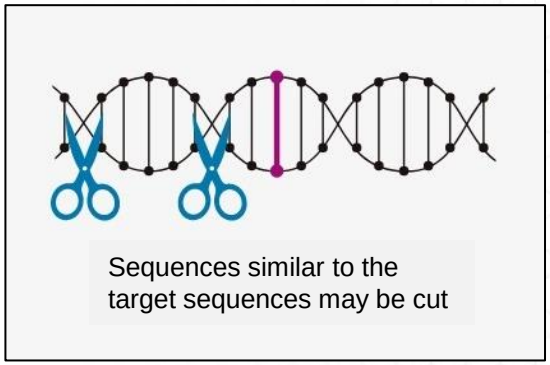

2) Identify a specific site.

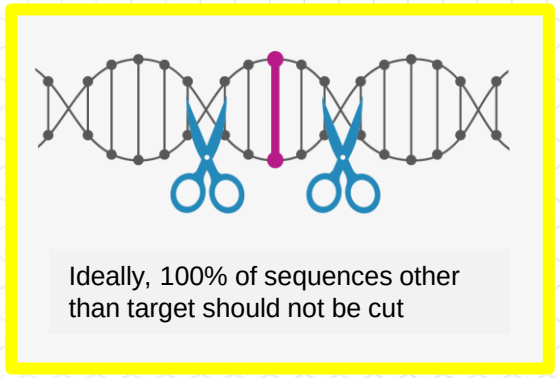



3) Cut off a specific part at a place where nuclease is guided


**Genome editing won the Nobel Prize in Chemistry in 2020.**
**The technology is attracting global attention, and is expected to be applied in humans.**

# For the Avoidance of Off-target Effects




**It is important to avoid off-target effects**

**To mitigate off-target effects:**

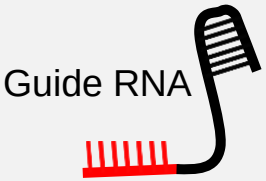
- **Search for any sequences similar to target sequences in genomes.**
- **Avoid target sequences if there are similar ones. Look for other target sequences.**

**"Off-target effects" was a concern for conventional technologies. Emendo, however, aims to establish highly safe genome editing and apply the technology in healthcare using an improved nuclease.**

# OMNI nuclease

1) Read a base sequence.


2) Identify a specific site.




3) Cut off a specific site **with higher precision** at a place the nuclease is guided to.

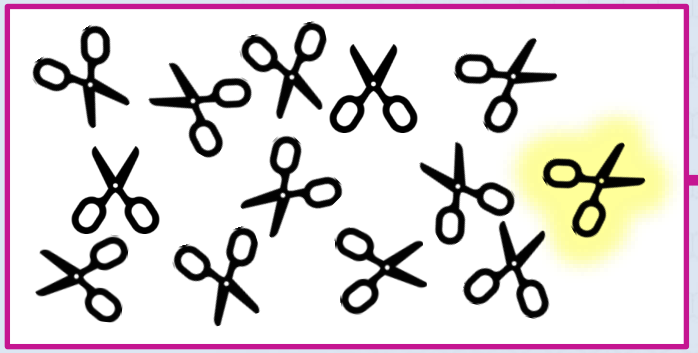
**The original nuclease (enzyme)**

**Original search technology (development platform) established**

## Mitigation of off-target effects enabled

# Development of the Original Platform

A large number of OMNI nucleases created



A treatment strategy suitable for each disease constructed

An appropriate nuclease is selected

Further optimization for a target sequence

Increase precision to mitigate off-target effects and enable the editing of allele-specific genes.

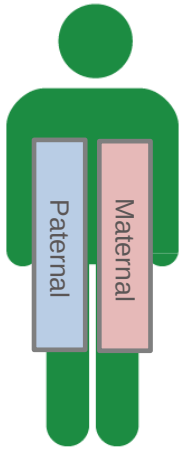
## Establishment of the OMNI Platform

Emendo creates a large number of OMNI nucleases with new characteristics, selects the appropriate nucleases from many OMNI nucleases, and optimizes them for the target sequences. They are developing safe and effective remedies, exploring new nucleases and using optimization technology.

# Materialization of Allele-specific Genome Editing 1)

## Basically, a human has a pair of genes with the same base sequence.

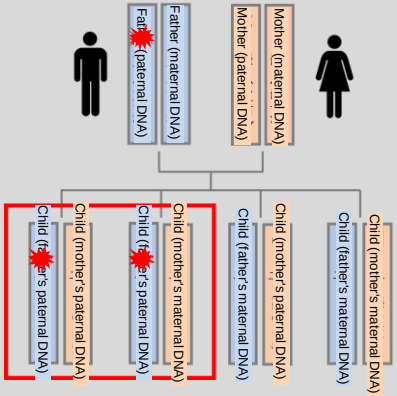
Allele (allelic gene)




Having a pair of genes with the same base sequence

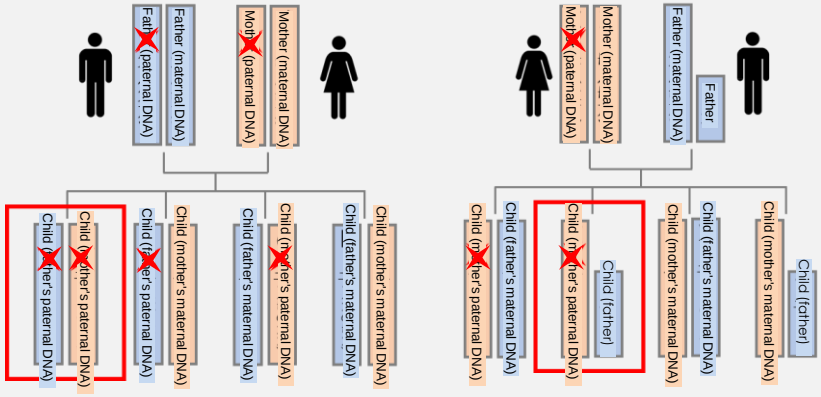
Genetic disease

An abnormal gene acts, developing a disease.




● Prepotency (dominant inheritance)
Genetic disease occurring either party of a pair
(gain-of-function mutation/haploinsufficiency)

The lack of a necessary gene develops a disease



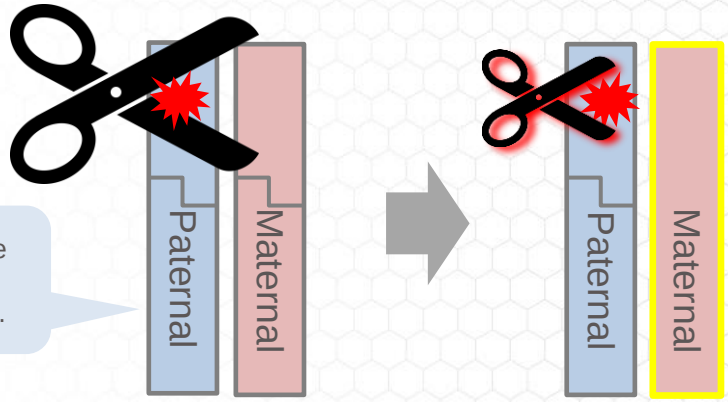

● Recessive inheritance
Genetic disease occurring in a pair
(complex heterozygote/homozygote)

● Sex-linked inheritance
Genetic diseases with pathogenesis that differs by sex

**Genetic diseases can occur if both paternal and maternal genes are abnormal or either the paternal or maternal gene is abnormal.**

# Materialization of Allele-specific Genome Editing 2)

**Allele-specific gene editing means editing selectively targeted abnormal genes without damaging the other allelic genes.**




Genome editing may edit even the other normal gene (allelic gene) when targeting an abnormal gene.

**Emendo has enabled high-precision genome editing that is able to discriminate between even the slightest differences between allele genes.**

**Emendo will first realize the treatment of many different dominantly inherited diseases where there is an abnormality in either of the genes by optimizing their original nuclease to have precision that is high enough to enable safe and effective gene editing. It will expand the scope of application of genome editing in treatments.**

# Operationalization of a Project for ELANE-related Severe Congenital Neutropenia

**We will perform a clinical investigation for ELANE-related severe congenital neutropenia (SCN), using Emendo's technology (OMNI Platform) to create a new genome editing tool.**

[Applicable Disease]

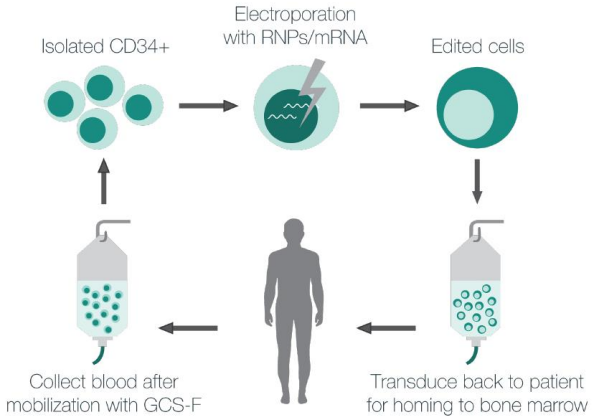
- ELANE (Elastase, Neutrophil Expressed)-related severe congenital neutropenia (SCN)

*Neutropenia stems from a maturation defect of granulocytic series cells in bone marrow. It can result in developing tympanitis, respiratory tract infections, cellulitis, and skin infections repeatedly and occasionally sepsis.

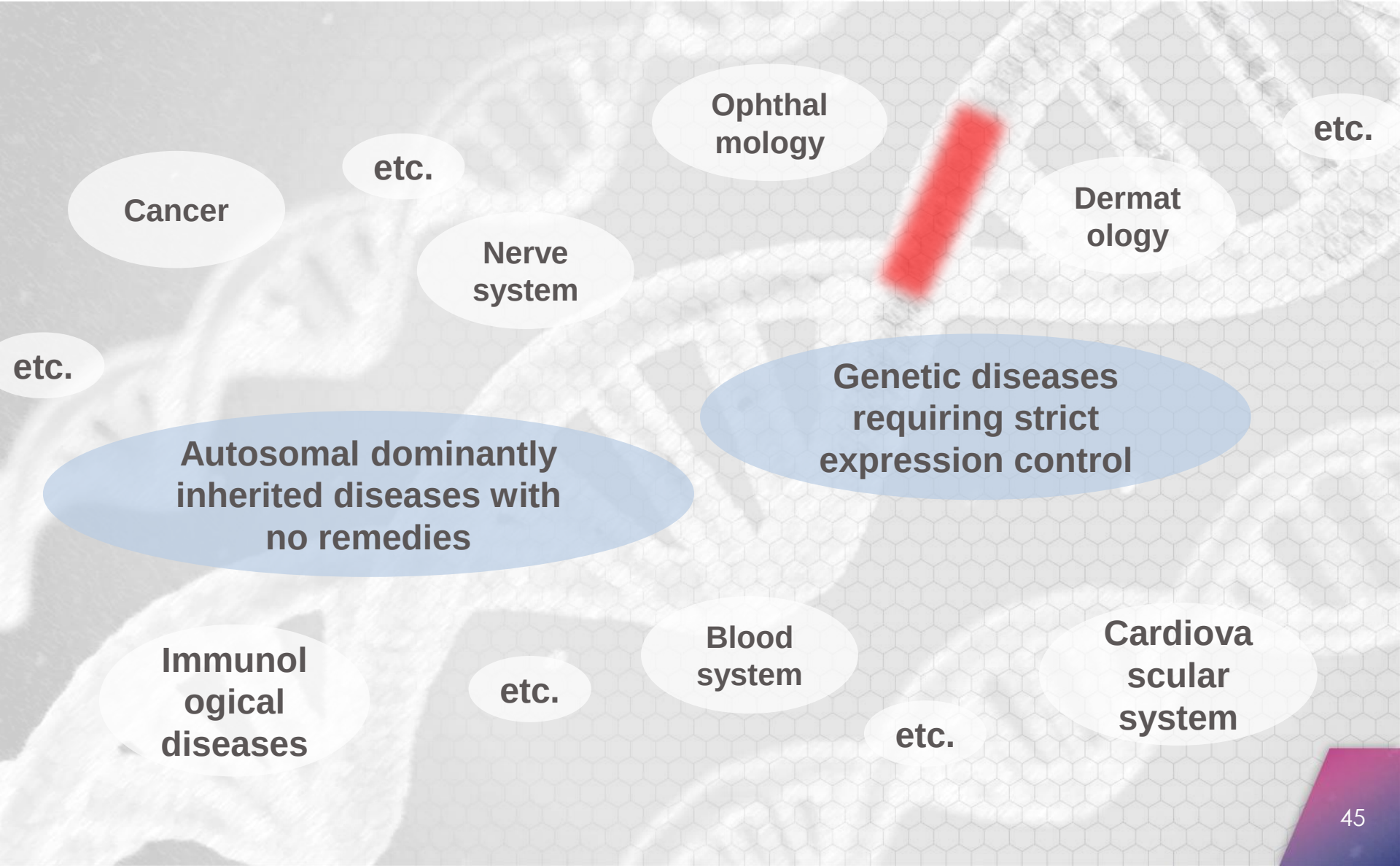
NEW

**In June 2022, they published their thesis that had been published in the journal of the world' largest group of gene and cellular therapy researchers on their website.**

**They have confirmed that they differentiated blood-forming stem cells into neutrophils when they precisely identified abnormal genes with almost the same sequence and destroyed them accurately without damaging normal genes.**



# Future Possible Indications



# Leading Global in Gene Medicine

AnGes's website
https://www.anges.co.jp/en/