



**Leading Global  
in Gene Medicine**



**October 2022**

# Executive Summary

## Business Expansion

- **Genetic Medicine Pioneer** : Founded in 1999, AnGes is one of the first biotech players in Japan
- **Global Vision:** Focus on treating genetic diseases on a global scale (R&D with partners in US, EU, Israel, and Turkey)
- **Strategic Acquisition & Expansion:** In Dec 2020, AnGes acquired EmendoBio, a cutting-edge gene editing company in Israel to accelerate its focus on innovative medicines and global reach. Newly opened Clinical Research Lab to expand its R&D and screening capabilities

## Subsidiary Progress

- **Next Generation CRISPR Technology:** Emendo is pioneering its OMNI™ technology that leverages AI and machine learning to enable precise targeting and treatment of virtually any and all genes
- **Business Inflection Point:** With a wide variety of clinical applications, the next 18 months are expected to be a pivotal period for Emendo as it transitions from a pre-clinical to clinical stage biotech company

## Financing Overview

- Equity Warrants Issuance** Announced on September 26, 2022
- 380,000 units (38,000,000 shares) to be allotted to Cantor Fitzgerald on October 12<sup>th</sup>, 2022
  - Expected Notional Raise of JPY9.42 Bn (JPY8.51 Bn excluding issuance fees)
  - **Roughly 60~70% of funds to be used for expanding Emendo's research and pipelines**



# OVERVIEW

# Corporate Overview



Established  
**December, 1999**

Founder  
**Prof. Morishita, Osaka Univ**

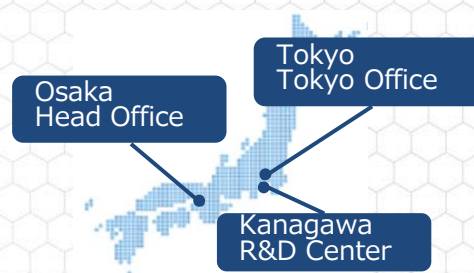
IPO  
**September, 2002**

President & CEO  
**Ei Yamada**

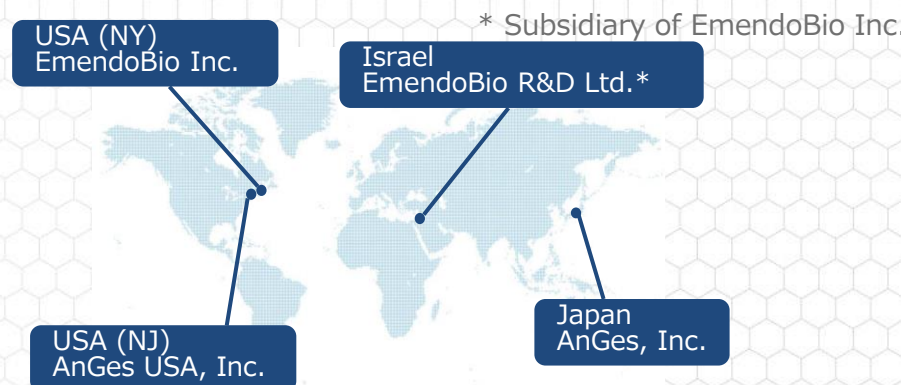
Market Cap (June 30, 2022) 135.73JPY  
**US\$380M**

Employees (Consolidated, December, 2021)  
**131**

## Japan



## Global



**Contribute to the improvement of  
human health and quality of life  
through the development of  
innovative medicines, by harnessing  
the potential of genes**

- *Develop innovative drugs for better Quality of Life and therapeutic options.*
  - **For diseases** with no treatment available, including intractable diseases and rare diseases
  - **With Gene-based medicines** defined as gene therapy, nucleic acid, DNA vaccine and genome editing.
  - **By cutting-edge technology/platform** of plasmid DNA, decoy and genome editing.



# STRATEGY



# Strategy for the Future



**Product**

**Collategene's Product Value to the Max**

**Platform**

**Evolving Plasmid DNA/Nucleic Acid Platform**

**Technology**

**Gene Therapy Expanding to Genome Editing**

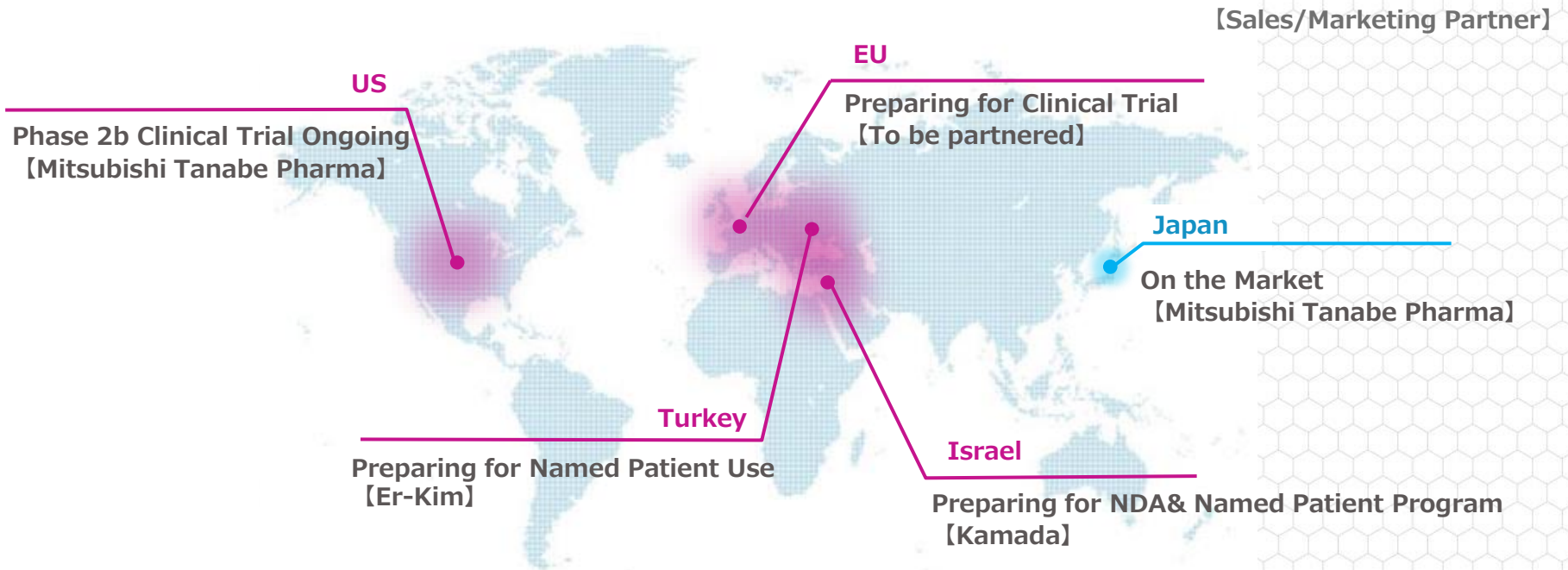
**Testing**

**Genetic Disease Testing for R&D and Business**

# Maximize Collategene's Product Value

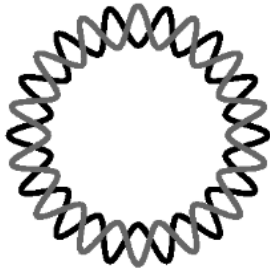


## GLOBAL STRATEGY



# Evolve Plasmid DNA Platform

## Current Platform



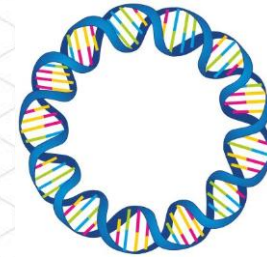
### Product/Projects

- HGF gene therapy product
- DNA vaccine for hypertension
- DNA vaccine for COVID-19

Structural Modification and Optimization

DDS Suitable to Organ/Tissue/Cell

## Next Generation Platform



More efficient expression and transfer

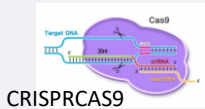
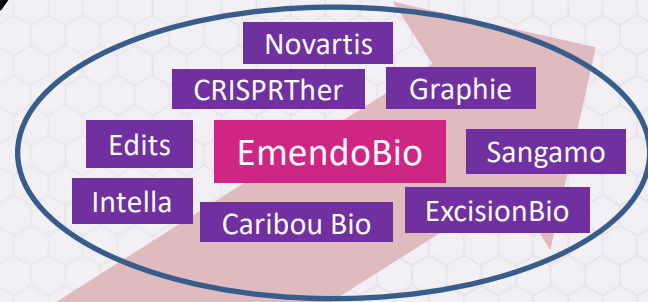
**Original proprietary platform under development  
Applicable to gene therapy and DNA vaccines**



# Gene Therapy Expanding to Genome Editing

## Genome Editing "Ultimate Gene Therapy"

- Supplement or add genes
- Destroy abnormal or unwanted genes
- Repair mutations in abnormal genes
- Gene incorporation at safe sites



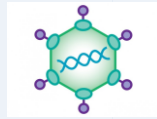
CRISPRCAS9

Approval  
(In vivo/Ex vivo)

2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
------	------	------	------	------	------	------	------	------	------	------



Plasmid DNA



Viral Vector

Glybera (UniQure)

Imlygic (Amgen)

Zalmonix (MolMed)  
Strimvelis (GSK)

Luxterna (Sperk/Novartis)  
Kymlyahq (Novartis)  
Yescarta (Kite Pharma)

Collategene (AnGes)  
Zolgensma (Novartis)  
Zynteglo (Bluebird)

Tecartus (Kite Pharma)  
Libmeldy (Orchard Ther)  
Deligtact (Daiichi-Sankyo)  
Breyanzi (Juno)  
Abecma (Celgene)  
Skysona (Bluebird)

Upstazal (PTC Ther)  
Roctavian (Biomarin)  
Caryktil (Janssen)

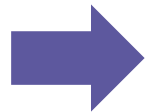
NO PRODTCT  
(As of August 31)

## Gene Therapy

- Supplement or add genes
- Gene incorporation site is random

- **Intranasal DNA Vaccine**

- Collaborative R&D with *Stanford University*
- Application to BARDA funding in view
- Gold-Nanostar-Chitosan-Mediated intranasal delivery of DNA vaccine



***Pursue the most powerful vaccine ever***

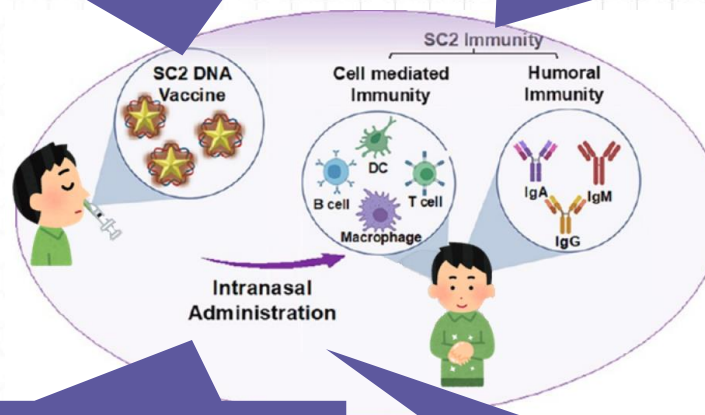
# Intranasal SARS-CoV-2 DNA vaccine

## High Expression of Antigen

Delivery system  
Optimization of plasmid

## Wide immune responses

Humoral (IgG, IgA, IgM) and cellular (T cell)



## Defense at Pathogen Entrance

Immune cells abundant in respiratory tract  
Local mucosal immunity in the nasal cavity

## Higher Compliance and Tolerance

Applicable to future pandemic, new variants and other respiratory diseases



# SARS-CoV-2 DNA vaccine



September 7, 2022

Company Name: AnGes Inc.

Representative: Ei Yamada, President & CEO

## **AnGes Inc. Enters into a Sponsored Research Agreement for Vaccine Development Collaboration with the Stanford School of Medicine in the United States for an Intranasal Formulation of an Improved DNA Vaccine**

AnGes Inc. announces that it has signed a Sponsored Research Agreement for “Vaccine Development Collaboration with the Stanford School of Medicine in the United States (“Stanford Medicine”)” regarding an intranasal formulation of an improved DNA vaccine, as described below.

# Genetic Disease Testing

## Rare Genetic Disease

- Genetic disease with very few patients (Phenyl ketonuria, mucopolysaccharidosis, etc)
- Important to start treatment early

## Tests for Newborns in Japan



### Mass Screening

- Free test for all newborns in Japan  
Phenyl ketonuria, Congenital hypothyroidism, etc.

### Optional Screening

- Optional, fee-based test
- Diseases not covered by mass screening  
Congenital hypothyroidism, Mucopolysaccharidosis, etc.

## ACRL



- Established April 2021
- Start optional screening in coordination with CReARID\* (July 2021)

\* Clinical and Research Association for Rare, Intractable Disease

**Wider Testing Items, Screening to Definitive Diagnosis**

# Testing for R&D/Prescription of Drugs



**AnGes**  
Clinical Research  
Lab



**Emendo's  
Genome Editing  
Therapy**

**New Products  
Under Negotiation for In-  
licensing**



**Zokinvy®**  
Hutchinson-Gilford progeria  
syndrome  
Agreement with Eiger in 2022

2021

2022

Testing Capabilities Enhance In-licensing Opportunities



# PIPELINE & PROJECTS

# Pipeline

## ■ Conditional and time-limited approval system

Project	Area	Partner	Dosage Form	Indication	Basic research	Preclinical study	Clinical trial		Application for Approval	Conditional and time-limited approval	Launch – Distribution	Post Marketing Surveillance	Approval
							Phase 1	Phase 2					
HGF gene therapy product	JP	Mitsubishi Tanabe Pharma	Injection	Chronic arterial occlusive disease with lower limb ulcer	▶	▶	▶	▶	▶	Approved	On sale	On going	

## ■ Approval Process

Project	Area	Partner	Dosage Form	Indication	Basic research	Preclinical study	Clinical trial			Application for Approval	Approval
							Phase 1	Phase 2	Phase 3		
HGF gene therapy product	USA	Mitsubishi Tanabe Pharma	Injection	Arteriosclerosis obliterans with lower limb ulcer	▶	▶	▶	P2b (on going)			
	Israel	Kamada	Injection	Chronic arterial occlusive disease with lower limb ulcer	▶					Preparing for application	
	Turkey	Er-Kim	Injection	Chronic arterial occlusive disease with lower limb ulcer	▶					Preparing for application	
NF-κB Decoy Oligonucleotide	USA	–	Injection	Chronic discogenic lumbar back pain	▶	▶	Completed				
DNA Vaccine	Australia	–	Injection	Hypertension	▶	▶	Completed				
DNA Vaccine	USA/JP	–	Intranasal formulation	COVID-19	on going						
Tie2 agonists	USA/EU/JP	Vasomune	Injection	COVID-19 / ARDS	▶	▶	Completed	P2a (on going)			
Lonafarnib	JP	Eiger	Oral capsule	Premature aging diseases (HGPS·PL) *	▶					Preparing for application	

※In addition to the above projects, the development pipeline includes drugs for chronic hepatitis B in the exploratory, basic research and pre-clinical stages.

\*「HGPS」: Hutchinson-Gilford progeria syndrome / 「PL」: Progeroid laminopathies

## ■ EmendoBio's Pipeline

Project	Area	Indication	LEAD OPTIMIZATION	PRE-CLINICAL	IND-ENABLING	PHASE 1-3
Development of genome editing	USA	Severe Congenital Neutropenia	▶			
		Diseases in hematology, ophthalmology, immuno-oncology, etc.	▶			

# HGF Gene Therapy Product (Collategene®)

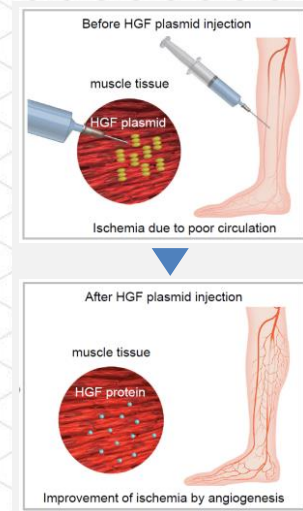
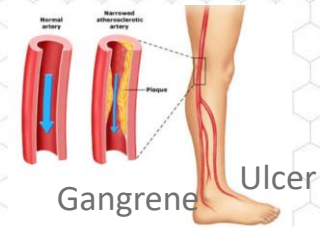


- **Critical Limb Ischemia**

- Serious form of Peripheral Artery Disease

- **Collategene**

- Plasmid DNA encoding human hepatocyte growth factor (hHGF)
- Angiogenesis, anti-apoptosis, anti-fibrosis and anti-inflammation



First in Japan

**Gene Therapy Product**

First in the world

**Plasmid DNA Product**

First in the world

**HGF Product**

First in the world

**Product for Peripheral Angiogenesis**

First in the world

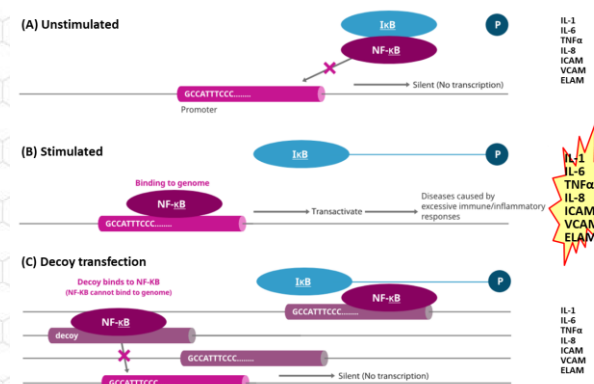
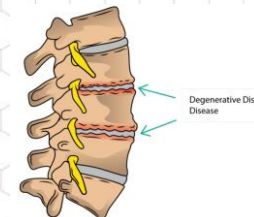
**Product for Cardiovascular Diseases**

	Disease	Status	Partner
Japan	CLI/Ulcer	Conditional approval & launch in 2019	Mitsubishi Tanabe Pharma
US	CLI/Ulcer	P2b Trial ongoing	
Israel	CLI/Ulcer	Preparing for NPP agreement	Kamada
Turkey	CLI/Ulcer	Waiting for approval (NPU)	Er-Kim

CLI: Critical limb ischemia | NPP: Named patient program | NPU: Named patient use

# NF-κB Decoy Oligo DNA

- **Degenerative disc disease**
  - Inflammatory proteins act on nerve to cause pain
- **NF-κB**
  - Key regulator of pro-inflammatory gene induction
- **NF-κB Decoy Oligo DNA**
  - Double-stranded DNA with sequence identical to DNA binding site of NF-κB works as decoy to inhibit inflammation

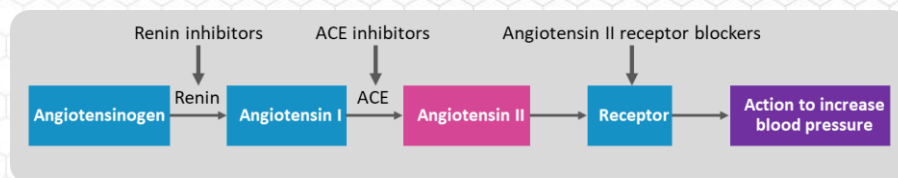


	Disease	Status	Partner
US	Chronic discogenic back pain	P1b Trial Completed (Safe & sustained efficacy) Preparing for P2 Trial	To be partnered
Japan	Chronic discogenic back pain	Preparing for 2 Trial	To be partnered



# DNA Vaccine for Hypertension

- **Angiotensin II (Ang II)**
  - Peptide hormone that causes vasoconstriction and raise blood pressure
- **Current Therapy**
  - Many classes available
  - Low compliance due to daily dosing
- **Ang II DNA Vaccine**
  - Combination of plasmid DNA encoding Ang II and Ang II-KLH peptide conjugate
  - Sustained increase in anti-Ang II antibody titer and reduction in blood pressure for months by a single injection

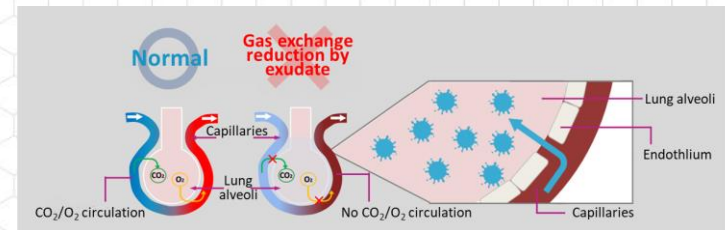


	Disease	Status	Partner
Australia	Hypertension	P1/2a Trial Completed (Safe & antibody against Ang II produced)	To be partnered

# Tie2 Agonist "AV-001"

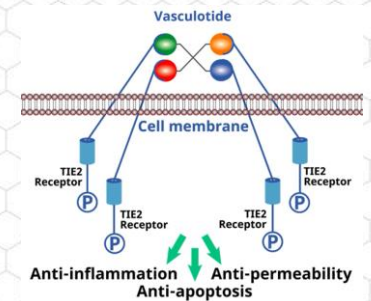
- **Acute Respiratory Distress Syndrome (ARDS)**

- Permeable endothelial cells (EC) allows blood leaks from the capillaries into the alveoli of the lungs, making gas-exchange difficult.



- **AV-001**

- Peptide that selectively binds to Tie2 receptors on EC
- Inhibit vascular leakage and stabilize vascular function



Supported by:

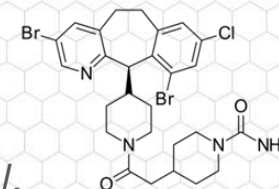
- 1) PRMRP/CTA grant from the U.S. Department of Defense
- 2) Advisory services and R&D funding from NRC/IRAP

PRMRP/CTA: Peer-Reviewed Medical Research Program Clinical Trial Award

NRC/IRAP: National Research Council of Canada Industrial Research Assistance Program

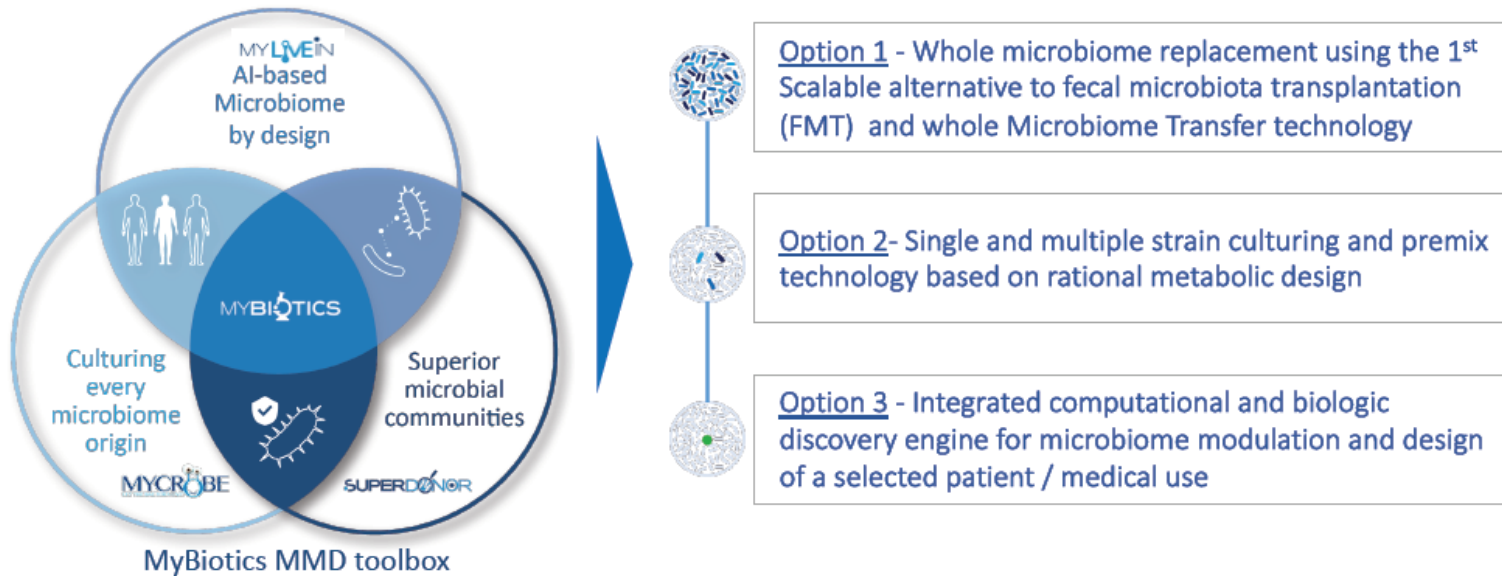
	Disease	Status	Partner
US/EU	ARDS/ COVID-19	P1 Trial Completed (Safe & well tolerated) P2a Trial Ongoing	To be partnered

- **Progeria** (Htchinson-Gilford Progeria Sndrome, Progeroid Laminopathies)
  - Ultra-rare, fatal, genetic premature aging diseases
  - Caused by mutation in LMNA (lamin) and/or ZMPSTE24 gene, yielding the farnesylated aberrant proteins leading to cellular instability and premature aging
  - Avg. age 14.5 years, Patient#(ww) HGPS 400/PL 200
- **Zokinvy**
  - A farnesyltransferase inhibitor
  - Blocks accumulation of farnesylated proteins
  - First-in-class agent with survival benefit
  - *Agreement with Eiger Biopharmaceuticals Inc. for the regulatory approval, marketing, and distribution in Japan.*

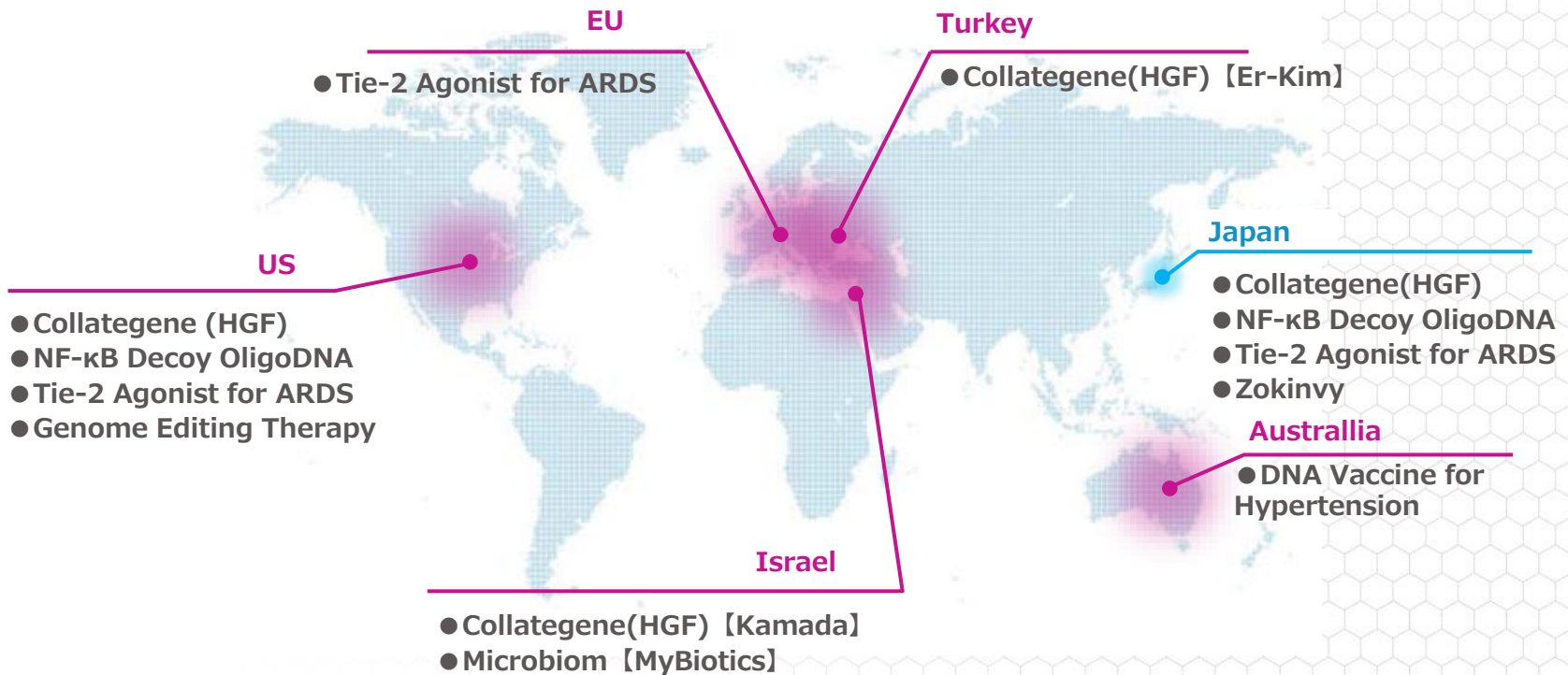


## Microbiome Modulation by Design (MMD)

MyBiotics utilized the capabilities of its integrated platform to translate scientific microbiome evidence to products while choosing the best technological fit to program the patient microbiome







This is a summary translation of the original Japanese Announcement.

September 26, 2022  
 Company Name: AnGes Inc.  
 Stock Code: 4563, TSE Growth  
 Representative: Ei Yamada, President & CEO

**Notice of Issuance of 42<sup>nd</sup> Series of Stock Acquisition Rights  
 (Third Party Allotment of Moving Strike Warrants)**

AnGes, Inc., a cutting-edge gene therapy and next-generation genome editing company, announces the pricing of its moving strike warrants, which are expected to raise JPY 8,509mn via Overseas Institutional Investors helping secure its position as a Global Leader in gene-based medicines.

The Board of Directors of AnGes, Inc. (hereinafter referred to as the “Company”, “AnGes”, or “we”), approved a resolution on September 26, 2022 to issue the 42<sup>nd</sup> series of stock acquisition rights (Moving Strike Warrants) through a third-party allotment. We believe this transaction provides us with an efficient and flexible source of capital as we continue our efforts to become a Global Leader in gene medicines.

**Outline of Offering**

(1) Issue/Allotment date	October 12, 2022
(2) Number of warrants to be issued	380,000 units
(3) Issue price	JPY 134 per unit (Total: JPY 50,920,000)
(4) Number of dilutive shares after the issuance of warrants	38,000,000 shares (100 shares per unit)
(5) Dilution rate	24.82%
(6) Exercise price and price revision mechanism	Initial exercise price: JPY 224; 90% of the closing price of September 22, 2022 Maximum exercise price: None Minimum (floor) exercise price: JPY 124; 50% of the closing price on September 22, 2022
(7) Estimated Proceeds (excluding Issuance Fees)	JPY 8,509 million
(8) Method of Offering/Allotment	Third-party allotment
(9) Allottee	Cantor Fitzgerald & Co.
(10) Others	Exercise Period: October 13, 2022 to October 15, 2024

**Usage of Funds**

The funds procured from these transactions are intended to be used for the following:

- (1) Research and Development and Working Capital by EmendoBio Inc. (“Emendo”), which we acquired in December 2020;
- (2) Strengthening and Expanding our business foundation, including through (1) R&D to improve production and manufacturing efficiencies relating to our HGF gene therapeutic products, (2) conducting novel research for pipeline expansion, and (3) when appropriate, engage in investments or acquisitions to further our global presence.

**I. Research and Development Expenses and Working Capital for Emendo**

In December 2020, we acquired Emendo, a bioventure company engaged in the development of genome-editing therapies that target and edit genetic information. Emendo is currently preparing for a clinical trial ELANE-related severe congenital neutropenia (SCN) in the United States.

While funds from the previous financing were used to further Emendo’s data collection efforts leading up to the Investigation New Drug (IND) application, a portion of the funds raised from this financing will be used to cover the expenses relating to the submission of its IND application, as well as to promote the study of genome-editing therapies in the field of ophthalmologic diseases. In order for Emendo to continue its research and developments, AnGes intends to allocate funds from this third-party allotment to Emendo’s operations by way of capital injections or loans from the Company to Emendo.

We believe that practical application of Emendo’s next-generation genome-editing technology will benefit from the Company’s deep know-how in preclinical, CMC (Chemistry, Manufacturing, and Control processes that bridge discovery research with commercial production), and clinical development, as well as manufacturing management that has been cultivated over 20+ years of gene therapy product development. Through our support of Emendo, the Company aims to become a world-class developer of genome-editing therapies, utilizing next-generation genome-editing technology.

**II. Funds for Expansion of Our Business Foundations**

We continue our efforts to strengthen our business foundation via our existing pipelines, focused on HGF gene therapy products, which have been the Company’s main development pipeline since inception. Accordingly, we are advancing clinical trials for HGF gene therapy products in the U.S. and other countries, and are aiming to obtain approval in Japan by FY 2024.

Moreover, in view of ensuring the company’s future growth and strengthening the business’s foundation, we believe that that it is necessary to continue to expand our development pipeline. As such, we intend to use a portion of the fundraising proceeds to expand our development pipeline and disease capabilities and capacities at the Anges Clinical Research Laboratory (ACRL) that we opened in April 2021.

In addition to the above, we will continue to consider opportunities to expand our business base through acquisitions and capital participation in overseas companies when appropriate.

# Leading Global in Gene Medicine



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