(TSE Growth : 4599)

StemRIM

Presentation Material

Financial Results for the the Fiscal Year Ended July 31, 2024

September 13, 2024

StemRIM

Stem cell Regeneration-Inducing Medicine

Overcoming Refractory Diseases by "Regeneration-Inducing Medicine™"

StemRIM is a biotech company aiming to develop
"Regeneration-Inducing Medicine™"
a next generation of regenerative medicine.

"Regeneration-Inducing Medicine™" is new class of medicine that induces functional regeneration of damaged tissues or organs by maximizing the patient's innate ability of tissue repairing.

We aim for a future in which "Regeneration-Inducing Medicine™" helps patients all over the world suffering from refractory diseases.

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Mode of Action of “Regeneration-Inducing Medicine™”

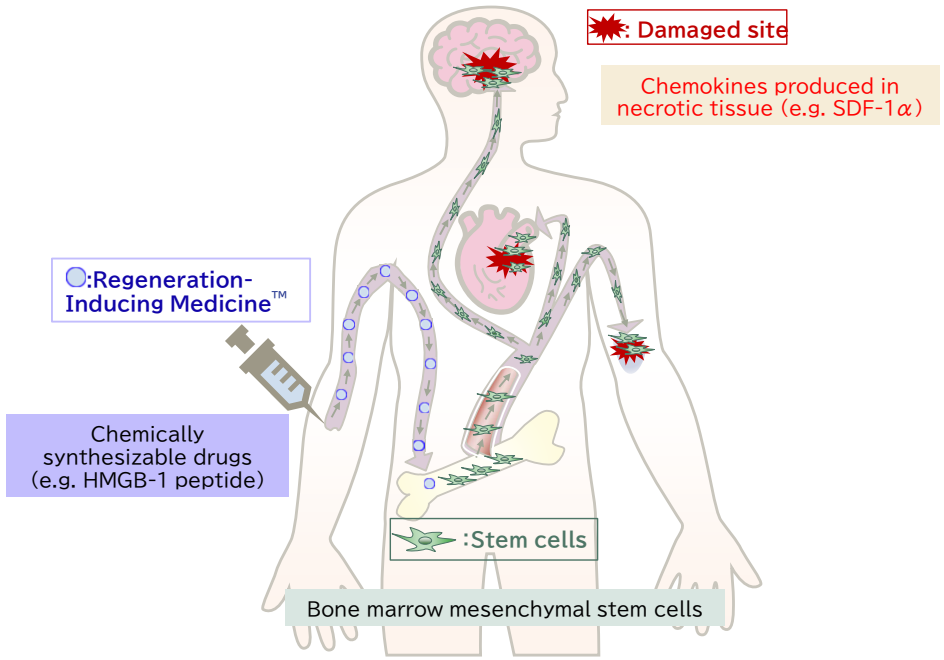
Bone marrow mesenchymal stem cells mobilized into the peripheral blood stream induce the tissue regeneration.

Administration of “Regeneration-Inducing Medicine™”

Mobilizing Stem cells from bone marrow into the blood stream

Stem cells accumulation in the damaged tissues

Functional tissue regeneration



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Agenda

1. Summary of Financial Results for FY 2024
2. Summary of Business Activities for FY 2024
3. Business Development Activities of TRIM3 and TRIM4 Projects
4. Activities of “StemRIM Institute of Regeneration-Inducing Medicine, Osaka University”
5. Activities for Sustainability Goals

Appendix

1. Summary of Financial Results for FY 2024

Summary of Financial Results

・For FY 2024, there were no recognition of milestone revenues related to research progress or upfront payments from contracts. As a result, **operating revenue was none.** Since we are a drug discovery bio-venture, we have an unstable revenue structure considering our business model.

・As of the end of FY 2024, we hold **8,410 million yen** in cash and deposits.
The estimated annual expenditure for the FY 2025 is between 1,430 million yen and 1,910 million yen (cash outflows related to R&D: 1,200 million yen to 1,600 million yen, cash outflows for general administrative expenses: 230 million to 310 million yen). At present, **we have secured sufficient funds to sustain stable R&D activities until 2028.**

(Millions of yen)

	FY2020.7	FY2021.7	FY2022.7	FY2023.7	FY2024.7	Function (FY on FY)
Operating revenue	2,100	1,400	22	2,350	—	—
R&D expenses	1,356	1,523	1,421	1,567	**1,453**	-113
Total operating expenses	1,684	1,993	2,003	2,207	**2,076**	-131
Operating Income (loss)	415	(593)	(1,980)	142	**(2,076)**	-2,218
Ordinary Income (loss)	361	(583)	(1,972)	145	**(2,077)**	-2,223
Net Income (loss)	347	(582)	(1,948)	168	**(2,022)**	-2,190

Cash and deposit	10,675	10,172	8,880	10,217	**8,410**	

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2. Summary of Business Activities for FY 2024

Summary of Business Activities for FY2024

Phase 2 clinical trial targeting Ischemic Cardiomyopathy for Redasemtide has begun in June 2024.
Additionally, multiple patents have been granted in various countries.

Month/Year	History
Sep. 2023	Patent Registration (China) for the Use of the HMGB1 Fragment Peptide, Redasemtide, as an Additional Therapeutic Indication for **Cardiomyopathy** and **Old Myocardial Infarction**
Sep.	Patent Registration (US) for the Use of the HMGB1 Fragment Peptide, Redasemtide, as an Additional Therapeutic Indication for Cardiomyopathy (**Dilated Cardiomyopathy**, **Ischemic Cardiomyopathy**, and **Hypertensive Cardiomyopathy**)
Nov.	Extension of the Tripartite Collaborative Research Agreement Updated on January 24, 2023
Dec.	Conclusion of Agreement for the Initiation of a Phase2 Clinical Trial for Redasemtide in **Ischemic Cardiomyopathy**
Jan. 2024	Patent Registration (Russia) for the Use of the HMGB1 Fragment Peptide, Redasemtide, as an Additional Therapeutic Indication of **Cartilage Disorders** (**Traumatic Cartilage Deficiency Syndrome**, **Osteoarthritis**, **Disseverance Osteochondritis**, etc.)
Feb.	Patent Registration (Japan) for the Use of the HMGB1 Fragment Peptide, Redasemtide, as an Additional Therapeutic Indication of **Traumatic Cartilage Deficiency Syndrome**, **Osteoarthritis**, and **Disseverance Osteochondritis**
March	Initiation of Phase 2 Clinical Trial for Redasemtide in **Ischemic Cardiomyopathy**
June	Patent Registration (Australia) for the Use of the HMGB1 Fragment Peptide, Redasemtide, as an Additional Therapeutic Indication for **Cardiomyopathy** and **Old Myocardial Infarction**
July	Patent Registration (Japan) for the Application of Curative Treatment Technology for **Dystrophic Epidermolysis Bullosa**

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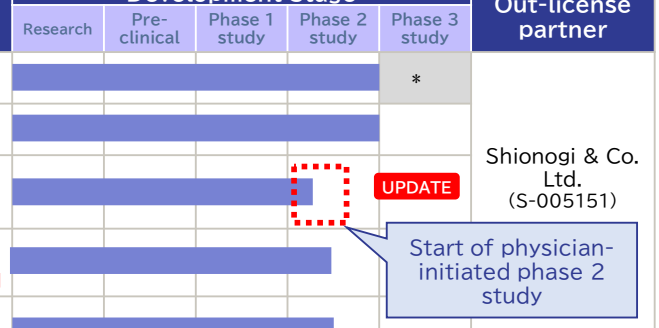
Overview of Development Pipeline

Project code	Development candidate	Indication	Investigator	Status	Out-license partner
PJ1-01	Redasemtide (HMGB1 cell mobilization domain peptides)	Epidermolysis bullosa	Shionogi & Co., Ltd.	Additional P2 Study Ongoing	Shionogi & Co. Ltd. (S-005151)
PJ1-02		Acute Ischemic Stroke	Shionogi & Co., Ltd.	Global P2b Study Ongoing	
PJ1-03		Ischemic Cardiomyopathy	Osaka University	Physician-Initiated P2 Study Ongoing	
PJ1-04		Osteoarthritis of the knee	Hirosaki University	Physician-Initiated P2 Study Primary endpoint achieved	
PJ1-05		Chronic liver disease	Niigata University	Physician-Initiated P2 Study Primary endpoint achieved	
PJ2-01	TRIM3 (Novel Regeneration-Inducing peptide for Systemic administration)	Multiple tissue damage diseases	In-house (partnership is planned)	Pre-clinical	-
PJ2-02	TRIM4 (Novel Regeneration-Inducing peptide for Systemic administration)	Multiple tissue damage diseases	In-house (partnership is planned)	Pre-clinical	-
PJ3	TRIM5 (Novel Regeneration-Inducing peptide for Local administration)	Multiple tissue damage diseases	In-house (partnership is planned)	Pre-clinical	-
PJ4	Autologous cell collection device for treatment	Multiple tissue damage diseases	In-house (partnership is planned)	Pre-clinical	-
PJ5	SR-GT1 (Stem cell gene therapy)	Epidermolysis bullosa	In-house (partnership is planned)	Under preparation for clinical trial	-



* Application for approval is planed after Additional Phase2.

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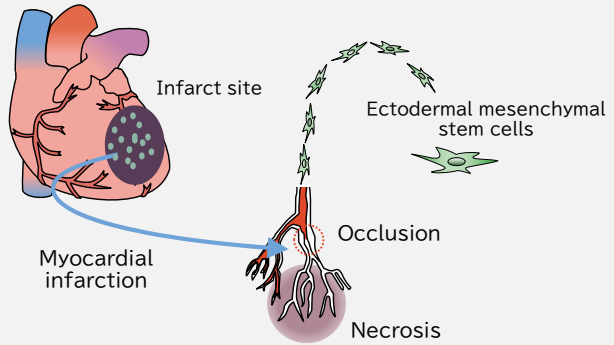
PJ1-03:Phase 2 Clinical Trial in Ischemic Cardiomyopathy

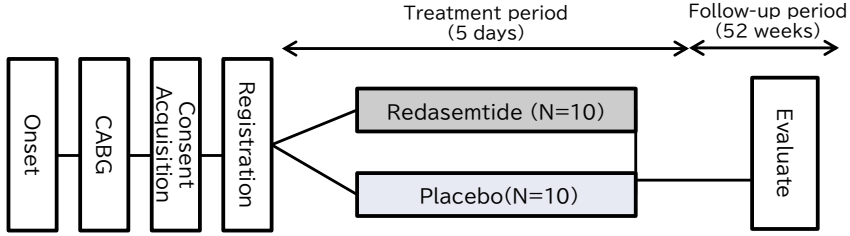
Ischemic Cardiomyopathy



Mechanism of action

- ✓ Confirmed the inhibitory effect of myocardial fibrosis.
- ✓ VEGF[*1] is secreted, promoting neovascularization at the infarct site and improving prognosis.
- ✓ Regeneration of myocardial cells by activation of residual stem cells.
- ✓ Inhibition of ventricular remodeling after myocardial infarction.

Phase 2 Protocol	
Study objectives	Evaluation of the efficacy and safety of Redasemtide in patients with ischemic cardiomyopathy
Study design	Multicenter, Randomized, Double-blind, Placebo-controlled
Subject population	Patients with ischemic cardiomyopathy who have undergone coronary artery bypass grafting (CBAG[*2])
Intervention	Redasemtide : 10 cases Placebo : 10 cases total 20 cases
Regimen	Intravenous administration, 5 days
Efficacy endpoint	**Various cardiac function tests such as echocardiography at 52 weeks after treatment**



Status

March 2024:
Phase 2 Clinical Trial started in Japan

*1 VEGF(vascular endothelial growth factor); A protein that promotes angiogenesis; when VEGF acts on vascular endothelial cells, it induces cell division, migration, and differentiation, resulting in the formation of new blood vessels that branch off from existing vessels.
*2 CABG(coronary artery bypass grafting); Surgery to bypass a blockage in a coronary artery and install a new blood vessel (bypass).

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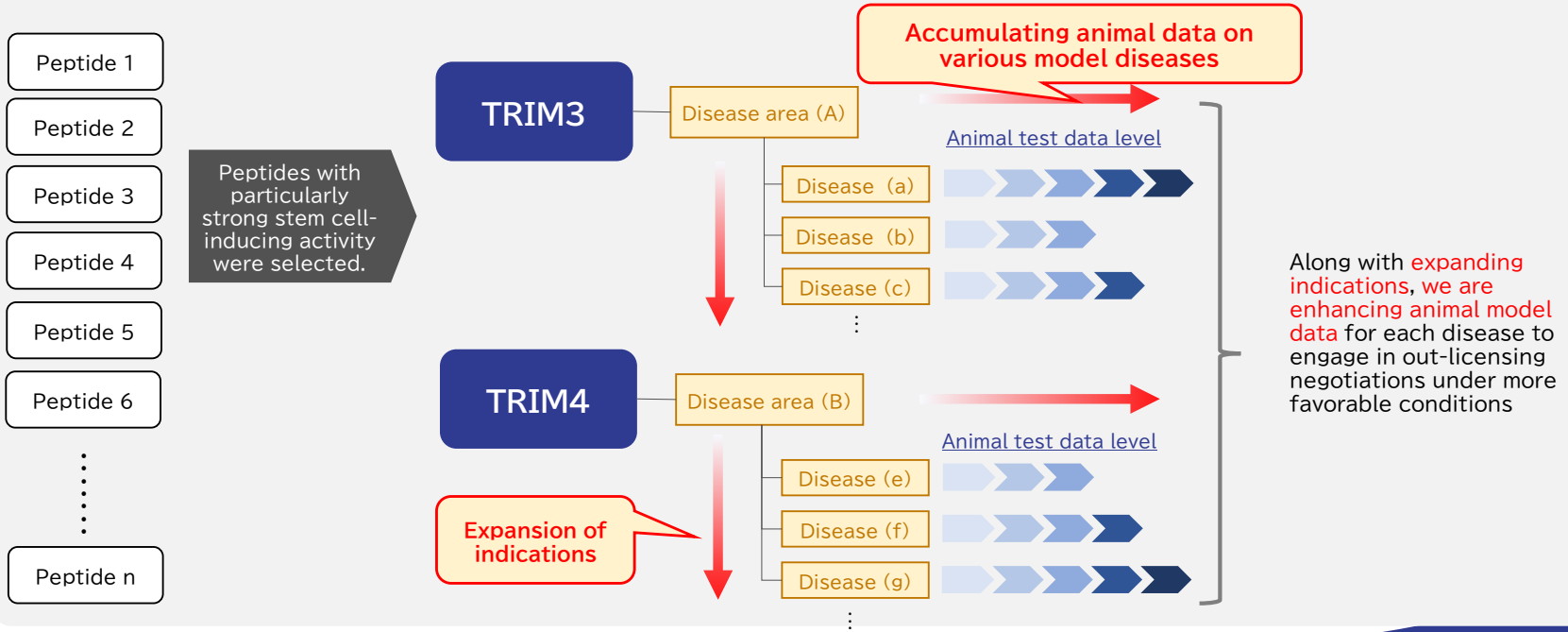
3. Business Development Activities of TRIM3 and TRIM4 Projects

Next-generation “Regeneration-Inducing Medicine™” TRIM3, TRIM4

We have identified several peptides that mobilize mesenchymal stem cells from the bone marrow into the bloodstream, accumulate in damaged tissues, and induce functional regeneration. Among them, two peptides with particularly prominent activity have been selected as candidates for the next-generation “Regeneration-Inducing Medicine™” : TRIM3 and TRIM4, and out-licensing activities have been initiated.



*TRIM: Tissue Regeneration-Inducing Medicine

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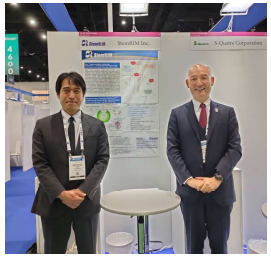
Out-licensing activities for new “Regeneration-Inducing Medicine™”

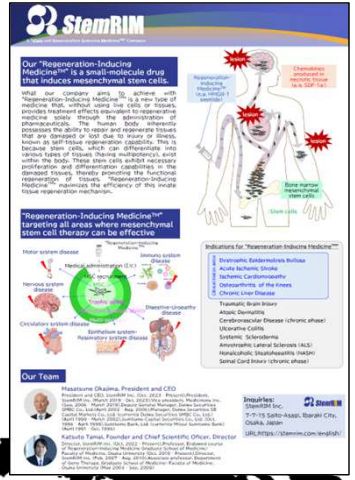
FY 2024.7
Conference Participation

BioJapan 2023
2023.10.11~13 @Yokohama

42nd Annual J.P. Morgan Healthcare Conference
2024.1.8~11 @San Francisco, CA

BIO International Convention 2024
2024.6.3~6 @San Diego, CA





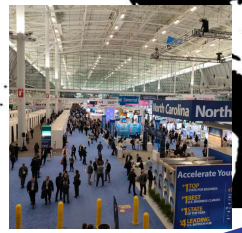
FY 2023.7
Conference Participation

BioJapan 2022
2022.10.11~13 @Yokohama

EU-Japan Biotech & Pharma Partnering Conference 2022
2022.10.11 @Osaka

41st Annual J.P. Morgan Healthcare Conference
2023.1.9~12 @San Francisco, CA

BIO International Convention 2023
2023.6.5~8 @Boston, MA



Conducted out-licensing negotiations with several domestic and foreign pharmaceutical companies

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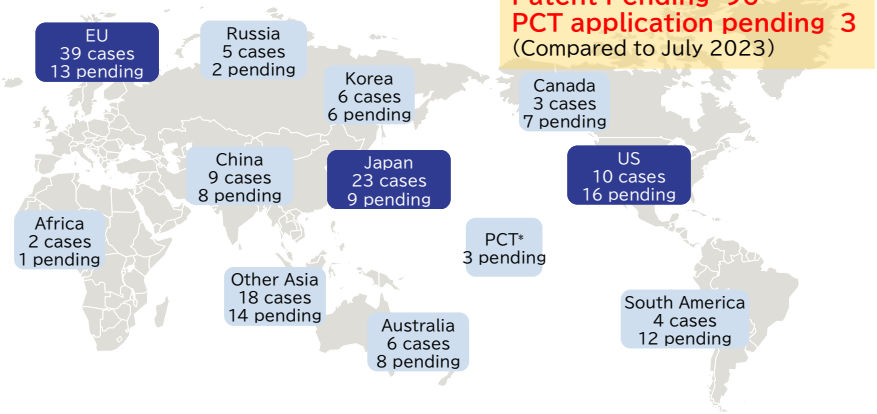
IP Strategy

Patents related to “Regeneration-Inducing Medicine™” have been granted in various countries. We are steadily promoting the intellectual property protection of our research outcomes, paving the way for global expansion.

Patent Grant Status



Total Patents 125(+12)
Patent Pending 96
PCT application pending 3
(Compared to July 2023)

Number of IP

Countries of Grant and Application

JPN USA CHN GER KOR IND ESP POL SWD RUS BEL IDN BRA MEX ZAF

ISR HKG GBR FRA AUS CAN ITA IRL NLD CHE DNK FIN TUR SGP TWN

*PCT: Members of the Patent Cooperation Treaty
** As of July 2024

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4. Activities of “StemRIM Institute of Regeneration-Inducing Medicine, Osaka University”

R&D Structure and Facilities

StemRIM Institute of Regeneration-Inducing Medicine, Osaka University will be established in June 2020 on the Suita Campus of Osaka University as a world-leading research and development center for “Regeneration-Inducing Medicine™” research.

大阪大学 OSAKA UNIVERSITY

・Basic Research in “Regeneration-Inducing Medicine™”.
・Proof of mechanism of action

Other domestic and international university research institutions

Collaboration

Establishment of a robust R&D structure for the realization of “Regeneration-Inducing Medicine™”.

StemRIM

・Identifying candidates
・Proof of mechanism
・Establishing manufacturing method
・POC in animal models
・POC in early-phase clinical studies

StemRIM
StemRIM Institute of Regeneration-Inducing Medicine

・Consistent promotion from basic research to clinical research
・Collaboration with other domestic and international universities and research institutions

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Activities of “StemRIM Institute of Regeneration-Inducing Medicine, Osaka University”

StemRIM

StemRIM Institute of Regeneration-Inducing Medicine

In June 2020, StemRIM Institute of Regeneration-Inducing Medicine, Osaka University (covering an area of 1,540 square meters) was established on the 6th and 7th floors of the Techno Alliance Building at Osaka University’s Suita Campus. Professor Masayuki Endo (Department of Children’s and Women’s Health, Graduate School of medicine and Division of Health Sciences, Osaka University) was appointed as the institute’s director. The team includes distinguished members such as Specially Appointed Professor Shinya Murakami (Department of Periodontology and Regenerative Dentistry, Osaka University, Graduate School of Dentistry.), Professor Masaru Ishii (Department of Immunology and Cell Biology, Graduate School of medicine and Frontier Biosciences, Osaka University), and Professor Manabu Fujimoto (Department of Integrated Medicine, Graduate School of medicine, Osaka University). Together, they aim to explore and advance the multi-faceted development of “Regeneration-Inducing Medicine™”. To date, several collaborative research projects have made significant progress.

Joint Research Projects

(number of events)

	FY 2021	FY 2022	FY 2023	FY 2024	Notes
Division of Health Sciences	1	2	3	2	Neonatal-Associated Diseases
Division of Biofunctional Research	—	—	—	—	
Division of Medical Research	—	1	2	2	Nervous System Diseases, Orthopedic-Related Diseases
Division of Dentistry	3	5	5	5	Periodontitis-Related Diseases
Total	4	8	10	9	

Website (Japanese): https://stemrim-osaka-u.jp/

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5. Activities for Sustainability Goals

Approach to Sustainability

Under the corporate philosophy of ‘**Overcoming Refractory Diseases by “Regeneration-Inducing Medicine™”**,’ we are actively engaged in the development of next-generation pharmaceuticals, “Regeneration-Inducing Medicine™” , which overcome the challenges of conventional regenerative medicine and cell therapy. This effort leverages the collaborative research with universities, including Osaka University, as well as the research outcomes from the Collaborative Research Institute for “Regeneration-Inducing Medicine™” . Our mission, **’Delivering smiles to patients worldwide suffering from intractable diseases through the development of Regeneration-Inducing Medicine™,**’ is something we believe will make a positive impact on society. Moving forward, we will continue contributing to societal progress through the development of “Regeneration-Inducing Medicine™” and addressing key societal issues related to our business.

Target

Our SDGs Target*;
3.4, 3.8

Health and Well-Being for All

StemRIM is dedicated to achieving a sustainable future by providing therapeutic solutions to people worldwide suffering from refractory diseases through the realization of “Regeneration-Inducing Medicine™”.
We aim to support healthy and prosperous lives for all.

We aim to bring smiles to patients suffering from rare diseases worldwide in the future.

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1 Fostering a workplace culture where diverse talent can thrive

We recognize that securing and continuously developing diverse talent with advanced expertise, skills, and experience, as well as fostering a workplace culture where employees can thrive, are critical to achieving our mission. To maintain and enhance this, we implement fundamental human resource policies.

Specific initiatives

Introduction of a flextime system and expansion of core working hours aimed at achieving work-life balance
Allowing individuals to freely choose their start and finish times, as well as the length of their working hours according to their lifestyle, has led to improved productivity.

Implementation of various online training programs, including compliance training, information security training, and harassment prevention training
Enhancing talent development

Stock option system
It contributes to securing talented personnel and enhancing employee retention.

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2 Creating a Safe and Comfortable Working Environment

We believe that supporting our employees' growth to help them thrive leads to sustainable and stable organizational development. With the aim of creating a more comfortable working environment, we regularly review and update various initiatives.

Specific initiatives

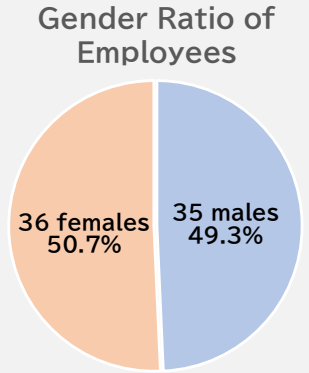
Development of Various Systems, Including the Promotion of Paternity Leave for Men, Maternity and Childcare Leave, Leave of Absence, and Shortened Working Hours Programs
This contributes to the promotion of women's empowerment and the strengthening of organizational capabilities.

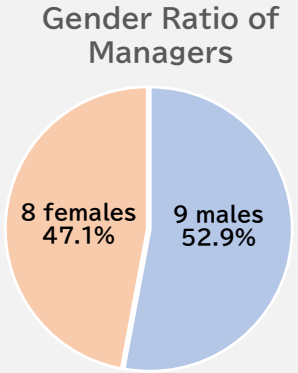
Introduction of Online Mental Health Counseling
This contributes to the early detection and prevention of employees' mental health issues.

Parental Leave Utilization (As of September 2024, Data for the Past Two Years)

Male	100%
Female	100%

Ratio of male to female (as of July 2024)





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Sustainability Initiatives

3 Initiatives related to intellectual property

Our company operates a business model in which we license out the development and sales rights of the pharmaceuticals we develop to pharmaceutical companies, generating revenue through upfront payments, milestone payments, and royalties. Therefore, we believe that appropriately managing and utilizing the intellectual property we hold is essential for enhancing corporate value.To that end, we strive to secure strategic intellectual property that supports our business and to maintain and manage the intellectual property we have acquired.In our Intellectual Property Department, not only do we have personnel with patent attorney qualifications, but we also employ specialists with advanced knowledge inRegeneration-Inducing Medicine™ who are actively engaged in promoting patent applications and protecting intellectual property, both in the domestic and international markets.

4 Promotion of Resource Recycling

At our company, we are committed to promoting activities aimed at realizing a globally sustainable society by making the most effective use of all management resources. Additionally, by thoroughly implementing waste separation and reducing electricity consumption, we aim to lower CO2 emissions and contribute to creating a better society.Regarding the efficient use of valuable resources such as paper used within the company, we are promoting company-wide efforts toward sustainable use and resource recycling. Going forward, we will continue to review the consumption of unnecessary items and work towards maximizing the use of precious resources in order to contribute to both societal and business sustainability.

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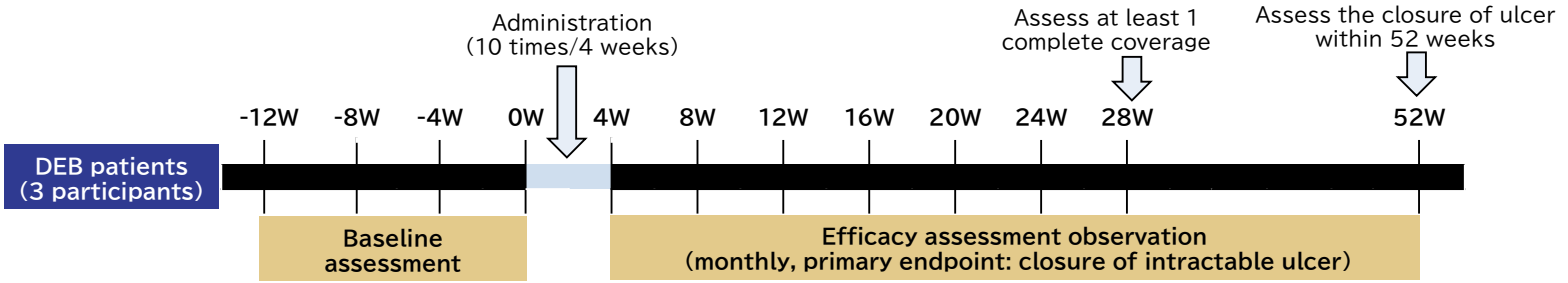
Appendix

PJ1-01:Redasemtide(Dystrophic Epidermolysis Bullosa)

Additional Phase 2 Protocol	
Study objectives	Evaluation of efficacy and safety of Redasemtide in patients with dystrophic epidermolysis bullosa having intractable ulcers
Study design	Single arm, multicenter, open label, uncontrolled
Intervention	Redasemtide (1.0 mg/kg) group: 3 participants
Regimen	30-minute intravenous infusion once a day, total 10 times/4 weeks [1st week of administration: 4 times/week, 2nd-4th weeks of administration: twice/week (once every 3-4 days)]
Primary endpoint	Closure of intractable ulcer



Status

February 2023: Initiated the administration to the first patient

* Shionogi & Co. Ltd., *Shionogi R&D Day 2022*, Oct. 12, 2022, pp.65
** jRCT2031220378

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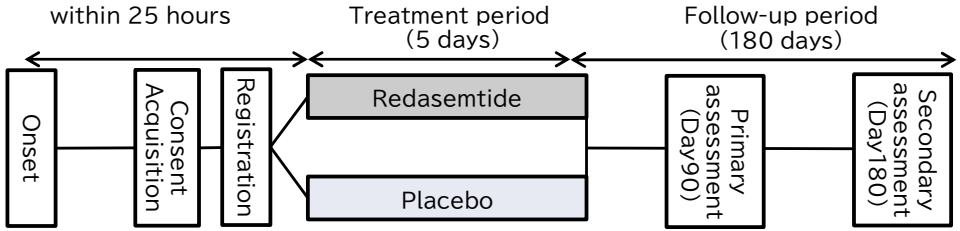
PJ1-02:Redasemtide(Acute Ischemic Stroke)

Global Phase 2b Protocol	
Study objectives	Verification of efficacy of Redasemtide in patients with acute ischemic stroke
Subject population	・Can be administered within 25 hours from the onset of symptoms to the patients at age 18 or older ・Baseline NIHSS score* between 8 and 22 ・Intravascular recanalization therapy (t-PA treatment, endovascular treatment) is not applicable
Study design	Multicenter, randomized, placebo-controlled, double-blind
Intervention	・**Redasemtide (1.5 mg/kg) group** ・**Redasemtide (0.75 mg/kg) group** ・**Placebo group** **total 627 participants**
Regimen	90-minute intravenous infusion once a day for 5 days
Primary endpoint	Modified Rankin Scale (mRS) 90 days after administration
Country	**Japan, Europe, North America, China, etc.**



Status

Global Phase 2b study started in March 2023 in Japan and US, and in July 2023 in EU and China; the first patient was dosed in July (Japan).

* modified Rankin Scale(mRS):General prognostic rating scale (degree of social reintegration) "Score 0 (no symptoms) to score 6 (death)" in 7 grades
** National Institutes of Health Stroke Scale (NIHSS): Stroke Neurological Severity Rating Scale (42 points in total, the higher the score, the more severe)
*** Barthel Index (BI) : Evaluation scale for activities of daily living such as eating, bathing, and toileting (total 100 points, the higher the score, the more independent the person is, and the guideline for complete independence is 95 points)
**** Shionogi & Co. Ltd., *Shionogi R&D Day 2022*, Oct. 12, 2022, pp.64

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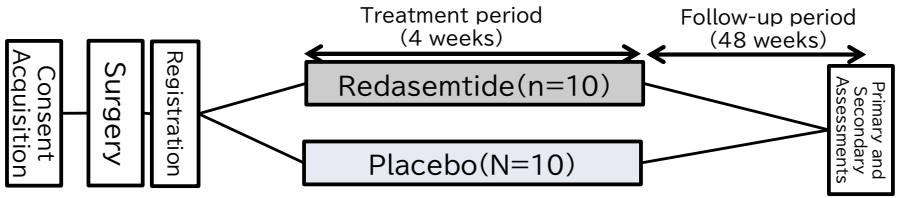
PJ1-04:Redasemtide(Knee Osteoarthritis)

Phase 2 Protocol	
Study objectives	Evaluation of efficacy and safety of Redasemtide in patients with Osteoarthritis (OA) of the knee
Subject population	Patients with knee OA who have undergone high tibial osteotomy (HTO) and arthroscopic microfracture
Study design	Multiple arms, Single center, randomized, placebo-controlled, double blinded
Intervention	Redasemtide (1.5 mg/kg) : 10 participants Placebo : 10 participants total 20 participants
Regimen	90-minute intravenous infusion, total 8 times / 4 weeks [once every 3-4 days]
Primary endpoint	Presence/absence and percentage of adverse events
Secondary endpoint	Morphological assessment (based on MRI images) and functional assessment (KOOS)
Location	Department of Orthopaedic Surgery, Hirosaki University



Status

Confirmation of the result that there are no safety issues in March 2023.

* High tibial osteotomy(HTO): Surgery to reduce knee pain by making an incision on tibia to correct the surface angle of the tibial joint of the O-leg so that the weight is applied to the lateral side of the joint where intact cartilage and meniscus are left.
** Arthroscopic microfracture: A treatment procedure that promotes the recruitment of bone marrow stem cells for tissue repair by making small holes in the subchondral bone at the mother bed of the damaged cartilage to flow out the blood and bone marrow fluid.
*** Knee Injury and Osteoarthritis Outcome Score (KOOS):One of the scores to measure the outcome of knee injury and osteoarthritis
**** jRCT2021200034

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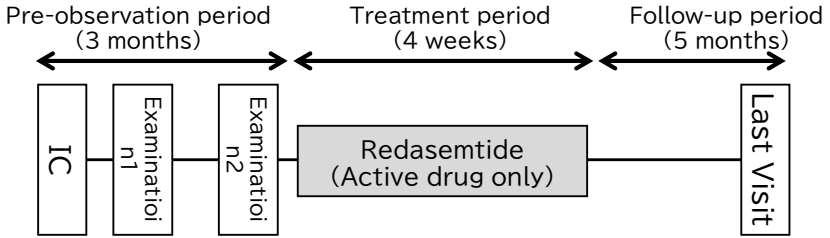
PJ1-05:Redasemtide(Chronic Liver Disease)

Phase 2 Protocol	
Main purpose	Evaluate the safety and exploratory efficacy in patients with chronic liver disease
Clinical trial design	Single arm study, Open label, Uncontrolled
Target patient	Patients with chronic liver disease with liver hardness test results of 4 kPa or greater by MR elastography.
Administration group/number of cases	1.5 mg/kg (free form), 90minutesintravenous infusion •Cohort A: 4 times / 4 weeks [once a week] •Cohort B: 7 times / 4 weeks [Week 1: 4 days, Week 2-4: once a week (1 dosage/3-4 days)]
Endpoint	**Rate of change in liver stiffness, rate of change in liver stiffness using ultrasound elastography, and rate of change in Child-Pugh score, etc.**
Site	Division of Gastroenterology and Hepatology, Niigata University Medical and Dental Hospital



Status

Confirmation of the result that there are no safety issues in April 2023.

* MR elastography: Magnetic Resonance Elastography (MRE) is one test that can quantitatively evaluate liver fibrosis.
** Child-Pugh score: Child-Pugh score is an assessment method mainly used to evaluate liver reserve function in patients with chronic liver diseases such as liver cirrhosis. It scores the severity of liver dysfunction using hepatic encephalopathy, ascites, serum bilirubin level, serum albumin level, and prothrombin activity, and classifies it into three stages, A to C.
*** jRCT2031200232

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Discovery of in-vivo mechanism inducing tissue regeneration

・Differences between normal skin and epidermolysis bullosa skin

In normal skin (Figure A), type 7 collagen functions like an adhesive, bonding the epidermis and dermis, the superficial layers of skin. In epidermolysis bullosa congenita (Figure B), the epidermis and dermis are easily detached with the slightest irritation due to abnormal type 7 collagen.
Since epidermal stem cells, which are responsible for supplying epidermal cells, reside in the epidermis, the epidermal stem cells are lost from the skin of patients with epidermolysis bullosa, and the epidermis loses its regenerative capacity.

Fig. A

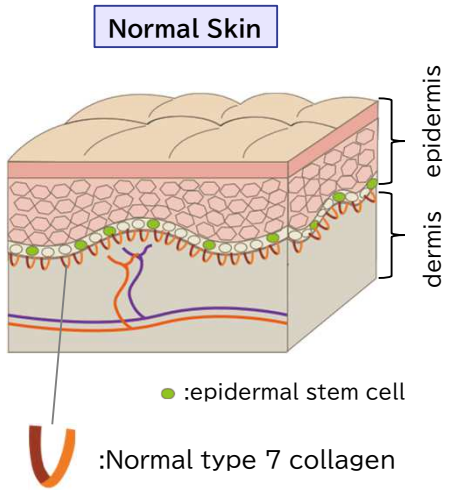
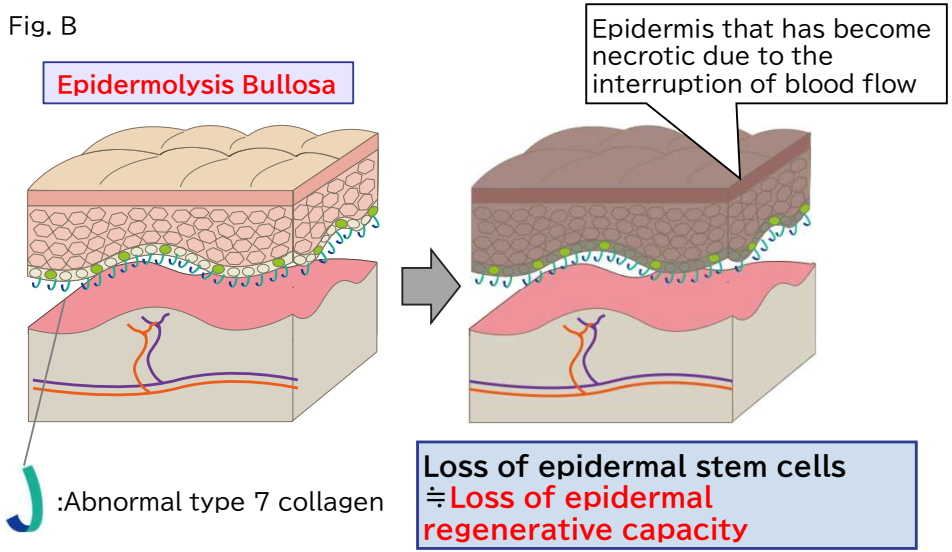


Fig. B



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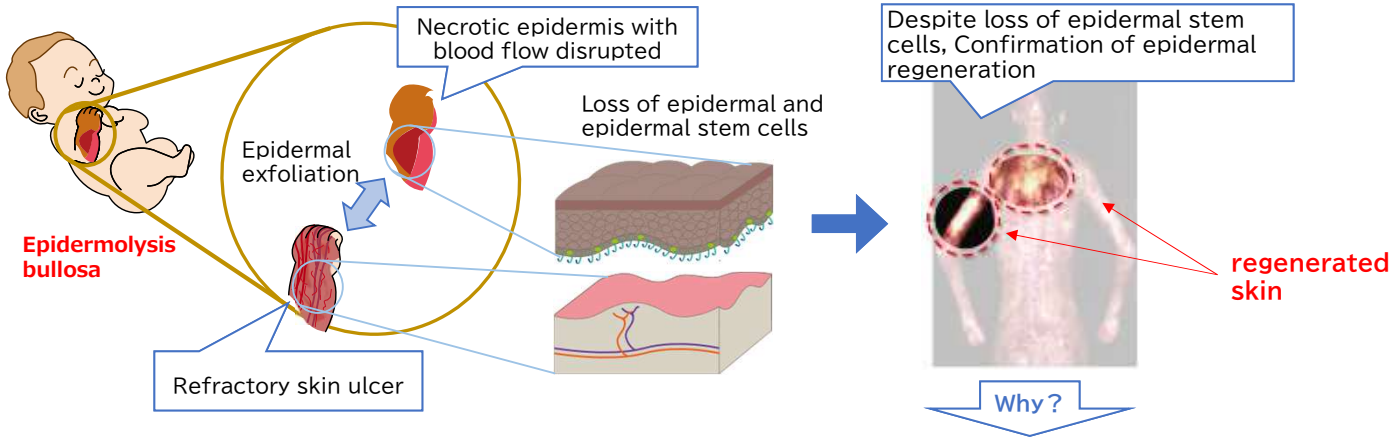
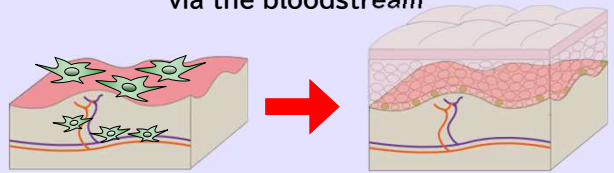
Discovery of in-vivo mechanism inducing tissue regeneration

The beginning of the research and development on “Regeneration-Inducing Medicine™” : Hypothesis of stem cell recruitment mechanism from bone marrow to damaged skin.



Possible replenishment of stem cells via the bloodstream



Hypothesis of stem cell recruitment mechanism via blood flow

References:
“Igaku-no-ayumi” Vol.265 No.5 463-468;2018
Skin Diseases :41(1);7-12,2019
Photo courtesy of Osaka University

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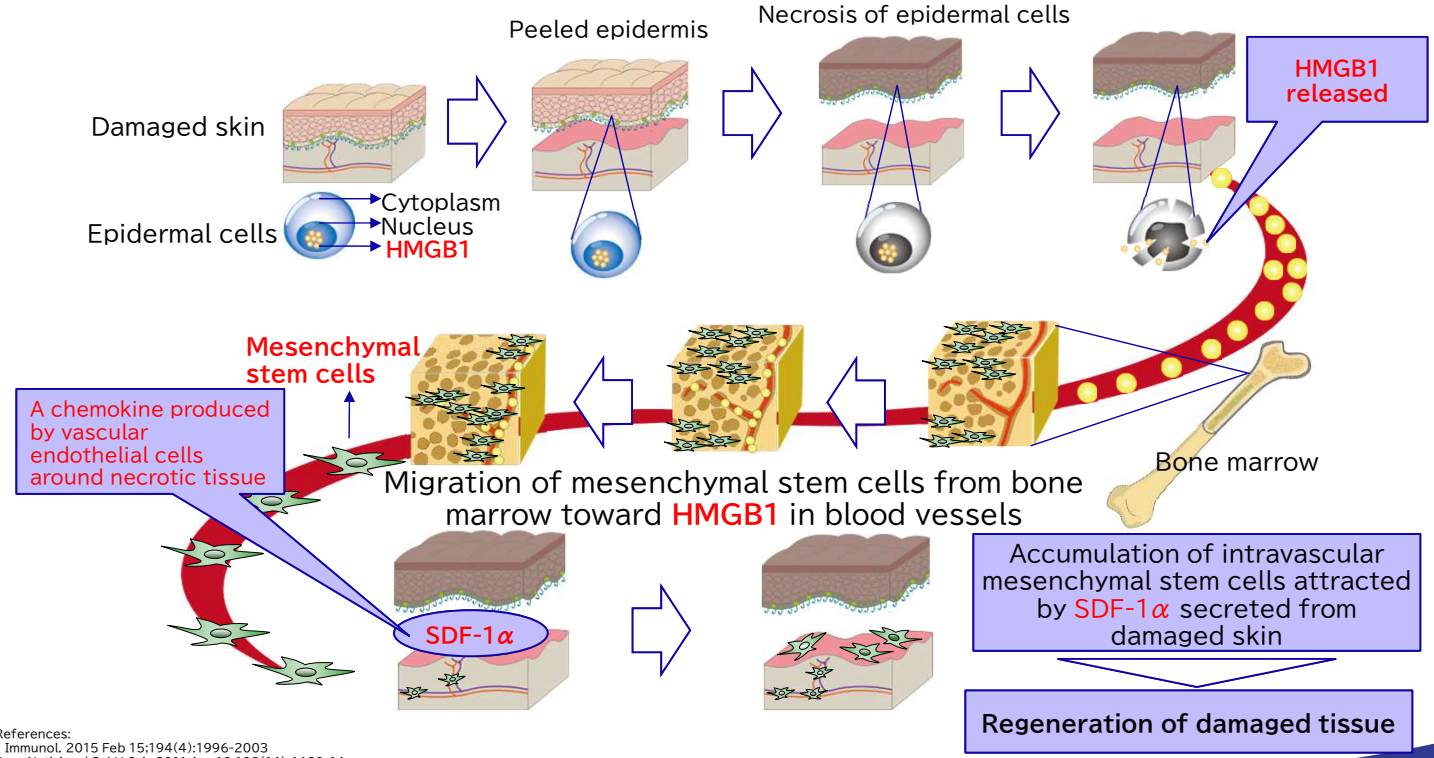
Discovery of in-vivo mechanism inducing tissue regeneration

Discovery of crosstalk mechanism between damaged skin and bone marrow mesenchymal stem cells via necrotic tissue-derived factor



References:
J Immunol. 2015 Feb 15;194(4):1996-2003
Proc Natl Acad Sci U S A. 2011 Apr 19;108(16):6609-14.

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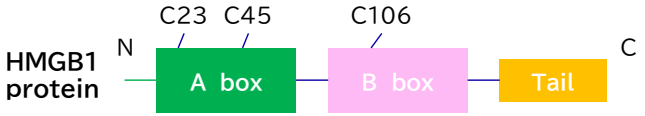
HMGB1 peptide drugs with improved safety

Designing highly safe, chemically synthesized peptide drug from A-Box domain of HMGB1 protein

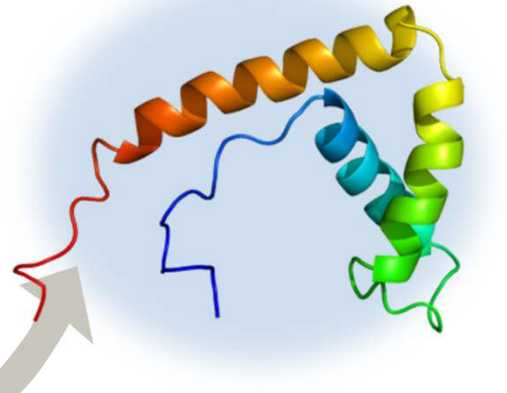


- An Important in vivo molecule that activate tissue regeneration

Identifying the function of protein domains

Prof. Katsuto Tamai
Osaka University

A box	Bone marrow mesenchymal stem cell activating domain, named "KOI2-domain"
B box	Innate immune response-activating domain that induces inflammation



HMGB1 peptide drug excluding the domains causing side effects in HMGB1 protein

References:
J Intern Med. 2004 Mar ;255(3):351-66.

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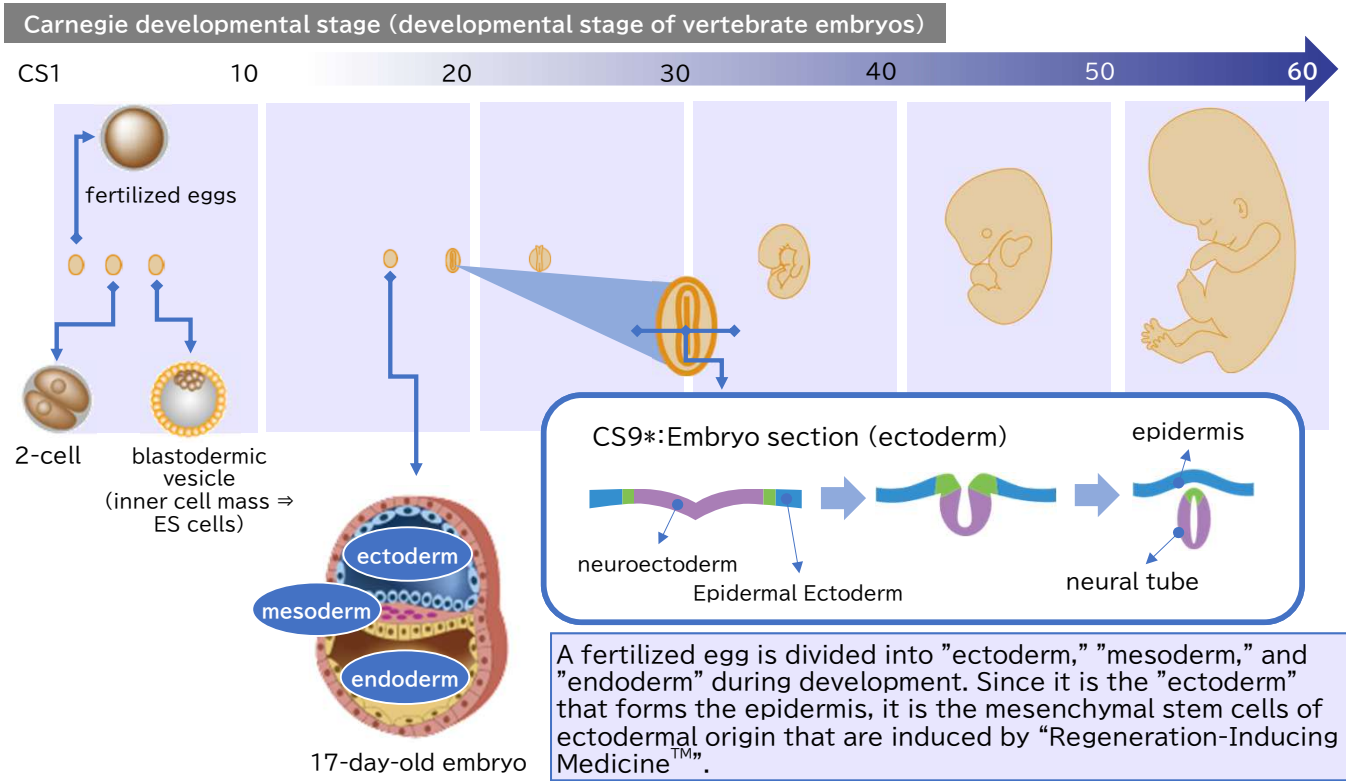
Advantages of “Regeneration-Inducing Medicine™”

Epidermis formation during human development



A fertilized egg is divided into ”ectoderm,” ”mesoderm,” and ”endoderm” during development. Since it is the ”ectoderm” that forms the epidermis, it is the mesenchymal stem cells of ectodermal origin that are induced by “Regeneration-Inducing Medicine™”.

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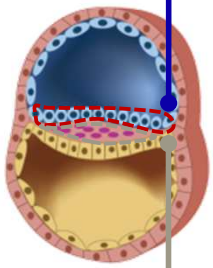
Advantages of “Regeneration-Inducing Medicine™”

Ectodermal mesenchymal stem cells have high pluripotency and differentiation ability to various tissues.

Tissues into which differentiation has been confirmed in our collaborative research with Osaka University

Tissues into which differentiation is thought to occur embryologically



17-day old embryo (Cross-section)

Ectoderm

Differen-tiation

Ectodermal Mesenchymal stem cells

Differen-tiation

Nerves	Epi-dermis	Follicles
Bone	Cartilage	Fat
Blood vessels	Dermis	Muscle
Ligament	Heart	Others

Mesoderm

Differen-tiation

Cellular medicine from other companies

Mesenchymal stem cells (Derived from mesoderm)

Differen-tiation

Bone	Cartilage	Fat
Blood vessels	Dermis	Muscle
Ligament	Heart	Others

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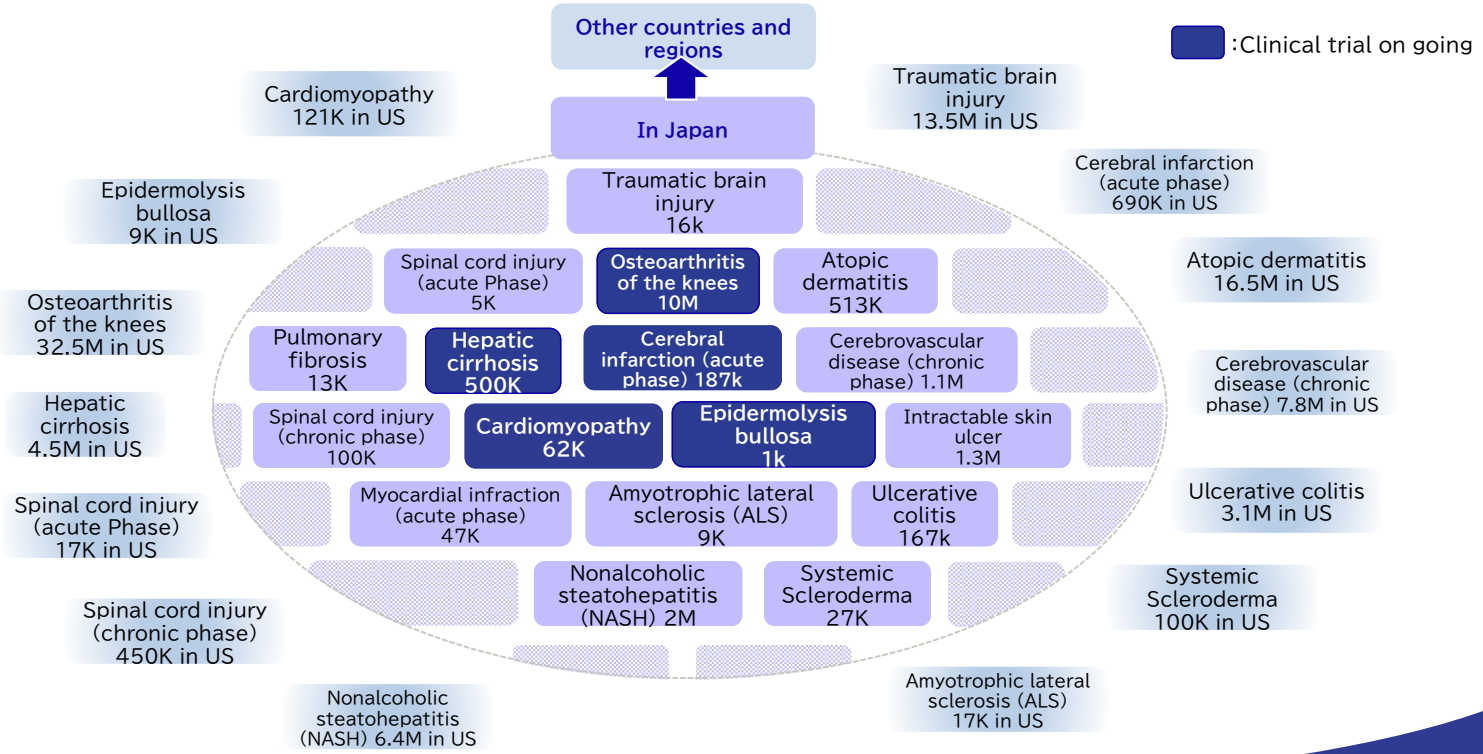
Expanding Indications and Markets(Number of patients)

Targeting all areas where mesenchymal stem cell therapy can be effective



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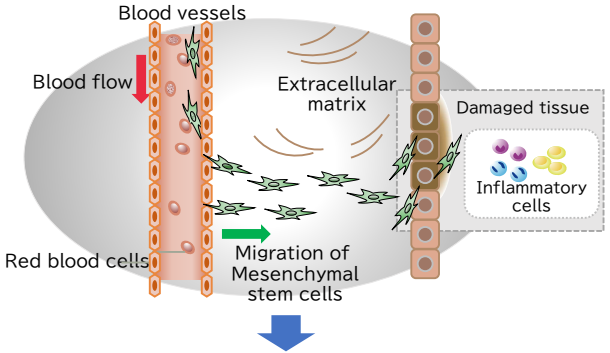
Functions of mesenchymal stem cells

In-vivo mesenchymal stem cells have 5 distinctive capabilities

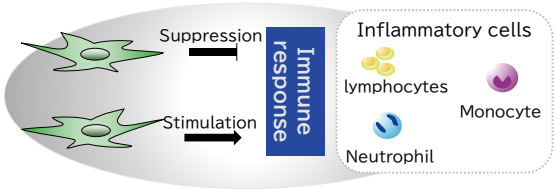
1. Cell migration ability

Mesenchymal stem cells migrate to damaged tissue via the bloodstream



2. Immunomodulatory ability

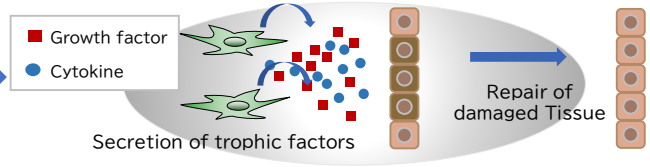
Modulates immune response and inhibits the spread of tissue damage caused by excessive inflammation



* MMP:Matrix metalloproteases

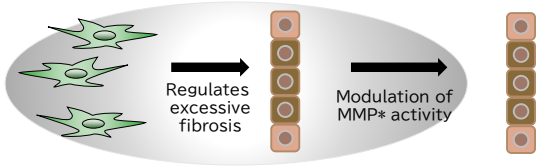
3. Trophic factor secretion ability

Promotes cell proliferation and tissue repair by secreting growth factors and cytokines to cells in damaged tissue



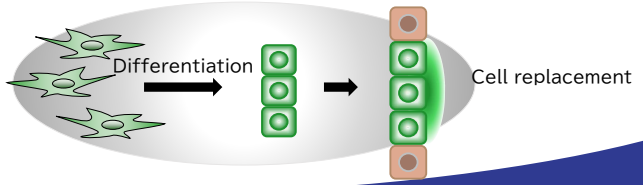
4. Fibrosis regulation ability

Regulates and inhibits excessive fibrosis of damaged tissue



5. Tissue regeneration ability

Mesenchymal stem cells themselves differentiate into various cell types to Replacing cells in damaged tissues and regenerating tissues



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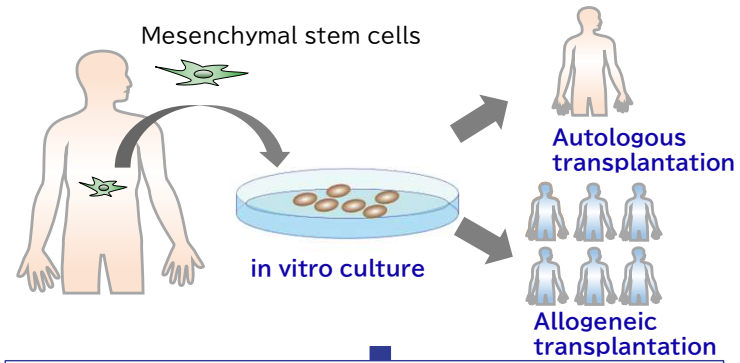
In vitro culture reduces the functions of MSCs

"Regeneration-Inducing Medicine™" can avoid functional degradation of mesenchymal stem cells due to in vitro culture

Manufacturing process of conventional cellular medicine

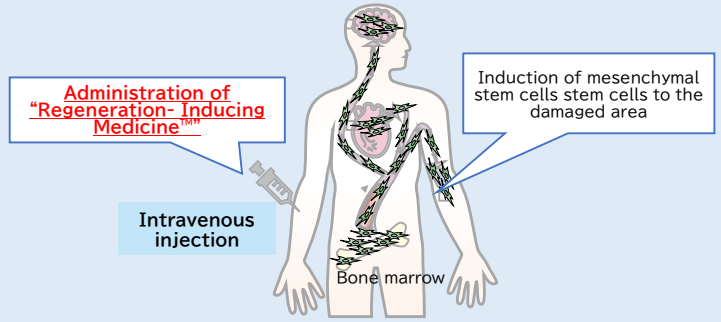


Mesenchymal stem cells lose their functions during in vitro culture

Source: Stem Cell Research & Therapy2018,9:131

~~Cell Migration ability~~ | Immuno-modulatory ability | Trophic factor Secretion ability | ~~Fibrosis regulation ability~~ | ~~Tissue Regene-ration ability~~

Induction of MSC in "Regeneration-Inducing Medicine™"



Induction of mesenchymal stem cells into damaged tissues while retaining their native functions

Cell Migration ability | Immuno-modulatory ability | Trophic factor Secretion ability | Fibrosis regulation ability | Tissue Regene-ration ability

"The effects of MSC cell therapy are limited to inflammation suppression and supply of growth factors to the remaining cells", reported by Caplan AI

「Mesenchymal Stem Cells: Time to Change the Name!」 Arnold Caplan June 2017

Source: Stem Cells Transl Med. 2017 Jun;6(6):1445-1451. doi: 10.1002/sctm.17-0051. Epub 2017 Apr 28.

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Summary of advantages of “Regeneration-Inducing Medicine™”

“Regeneration-Inducing Medicine™” includes advantages in both cell therapy and chemicals

		“Regeneration-Inducing Medicine™”	Cell therapy	Chemicals
Efficacy	Tissue regeneration	○ Applicable for large-scale tissue damage	▲ Applicable for large tissue damage with large number of cells	↓ No regeneration
	Mechanism of action	○ Use in vivo native regeneration mechanism	○ Cellular physiological activity	↓ Targeting molecules often including side-effect and off-target
	Indications	○ Same compound can cover a wide range of indications	○ Same platform can cover a wide range of indications	↓ In general, targeting limited indications caused by same mechanism
Safety	Noninvasive	○ Compound mobilizes the patient’s cells in vivo and no rejection	↓ Invasive in cell collection Immune-rejection in allogenic case	○ Low noninvasive
Quality	Quality control	○ Easy quality control and stable production	↓ Cell culture includes risk of cellular change	○ Easy quality control and stable production
Other benefit	Cost	○ Normal industrial drug production	↓ CPC and cell collection and transplantation facility is required	○ Affordable and large-scale production
	Regulatory affairs	○ Same as general compound drugs	↓ No standard, and case-by-case regulation is required	○ Standardized regulation

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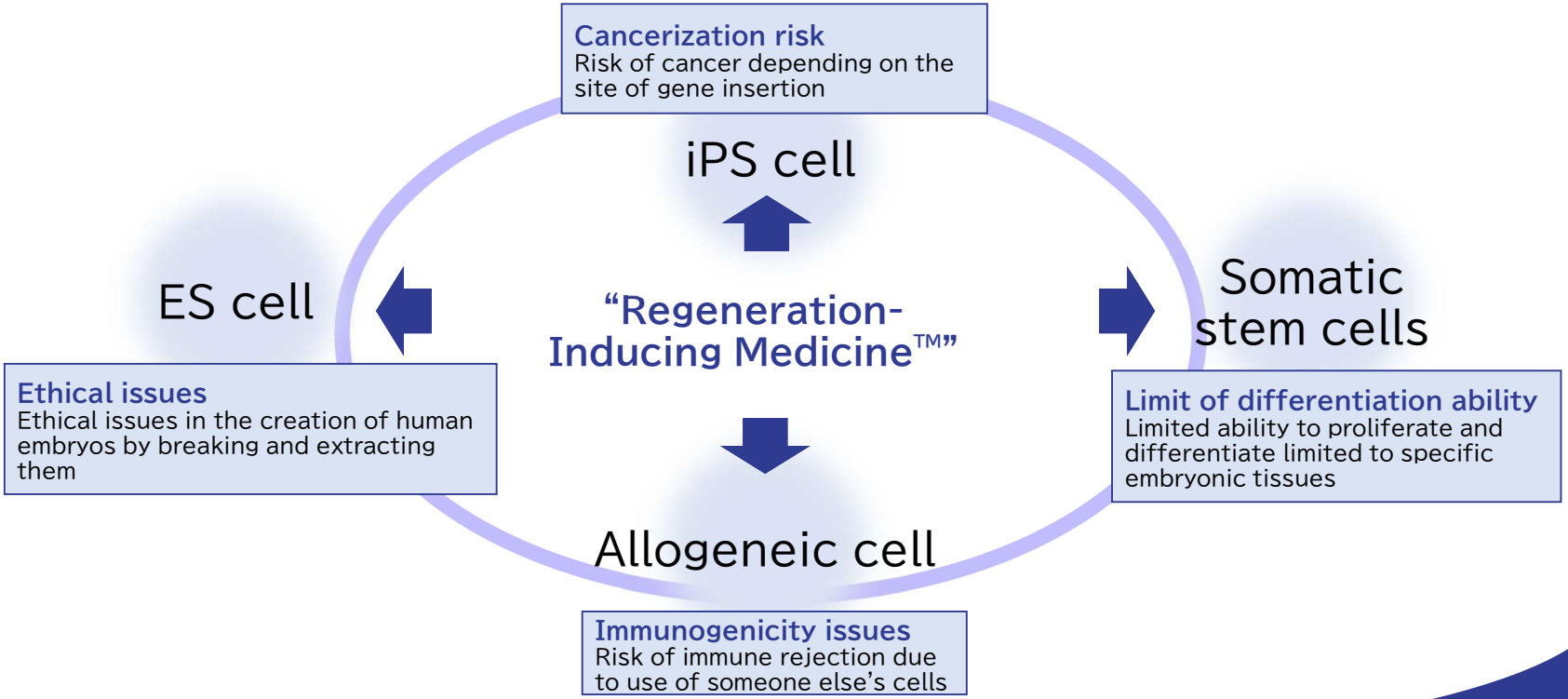
Summary of advantages of “Regeneration-Inducing Medicine™”

“Regeneration-Inducing Medicine™” can solve the four major problems of conventional cell therapy



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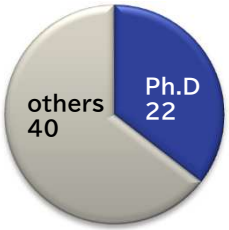
Corporate information

Company name	StemRIM Inc.
Chief Executives	Masatsune Okajima（Representative Director）
Address	Saito Bio-Incubator 3F, 7-7-15 Saito-Asagi, Ibaraki City, Osaka, 567-0085 Japan
Established	October 30, 2006
Shareholders' equity	7,579 million yen(as of July 2024)
Number of Employees	71 (as of July 2024)
Number of R & D staff	62 research staff  *22 staff with Ph.D, including MD and Veterinarian *In-house patent attorney and pharmacist *Numbers as of July 2024

Month/ Year	History
Oct. 2006	Established a company aiming to develop new drugs based on the discovery of bone marrow multi-potent stem cell mobilization factors identified by Professor Katsuto Tamai of the Graduate School of Medicine, Osaka University.
Apr. 2010	Transferred our head office to Saito Bio Incubator (Ibaraki City, Osaka Prefecture) and set up a laboratory there. Signed joint research agreement with Shionogi & Co., Ltd. on bone marrow-derived stem cell mobilization factors
Nov. 2014	Signed a license agreement with Shionogi & Co., Ltd. regarding Redasemtide (HMGB1 peptides)
Jan. 2018	An investigator-initiated phase 2 clinical trial of Redasemtide for dystrophic epidermolysis bullosa patients started at Osaka University. (to be completed in March 2020)
Apr. 2019	A company-initiated phase 2 clinical trial of Redasemtide for cerebral infarction patients started at Shionogi & Co., Ltd. (to be completed in December 2021)
Aug. 2019	Listed on the Tokyo Stock Exchange Mothers
June 2020	Established a new R&D base, "StemRIM Institute of Regeneration-Inducing Medicine, Osaka University".
Nov. 2020	An investigator-initiated phase 2 clinical trial of Redasemtide for Osteoarthritis of the knee patients started at Hirosaki University.
Nov. 2020	An investigator-initiated phase 2 clinical trial of Redasemtide for Chronic liver disease patients started at Niigata University.
Feb. 2021	Signed joint research agreement with Shiseido Co., Ltd. and Osaka University on anti-aging skin.
July 2022	An investigator-initiated additional phase 2 clinical trial of Redasemtide for DEB* patients started.
Mar. 2023	Notification of Preliminary Results of Data Analysis of Physician-Initiated Clinical Trial (Phase 2) on Redasemtide in Patients with Knee Osteoarthritis
April 2023	A global Phase 2b clinical trial of Redasemtide for Acute Ischemic Stroke started in Japan and US.
April 2023	Notification of Preliminary Results of Data Analysis of Physician-Initiated Clinical Trial (Phase 2) on Redasemtide in Patients with Chronic Leaver Disease.
July 2023	A global Phase 2b clinical trial of Redasemtide for Acute Ischemic Stroke started in EU and China.
Mar. 2024	A Phase 2 investigator-initiated trial of Redasemtide in ischemic cardiomyopathy has been initiated.

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StemRIM Management

Director

Masatsune Okajima, President and CEO

President and CEO, StemRIM Inc. (Oct. 2023 – Present)
President, StemRIM Inc. (March 2019 – Oct. 2023)
Vice president, Medicinova Inc. (Sep. 2006 – March 2019)
Deputy General Manager, Daiwa Securities SMBC Co., Ltd.(April 2002 – Aug. 2006)
Manager, Daiwa Securities SB Capital Markets Co., Ltd. (currently Daiwa Securities SMBC Co., Ltd.) (April 1999 – March 2002)
Sumitomo Capital Securities Co., Ltd. (Oct. 1996 – April 1999)
Sumitomo Bank, Ltd. (currently Mitsui Sumitomo Bank) (April 1991 – Oct. 1996)

Kensuke Tomita, Chairman

Chairman, StemRIM Inc. (Oct. 2023 – Present)
Chairman and CEO, StemRIM Inc. (March 2019 – Oct. 2023)
President, StemRIM Inc. (April 2018 - March 2019)
Director, StemRIM Inc. (July 2013 - April 2018)
External director, MEDINET Co., Ltd. (Oct. 2014 – Jan. 2016)
Advisor, StemRIM Inc. (April 2012 – June 2013)
President and CEO, OncoTherapy Science, Inc. (April 2003 – June 2012)
President and CEO, Anges MG (currently Anges Inc.) (June 2000 – March 2003)
Vice president, Rhône Poulenc Roller Inc.(currently Sanofi S.A.) (Aug. 1994 – March 2000)
Sandoz KK (currently Novartis Pharma KK) (Nov. 1991 – July 1992)
Roller Japan Inc.(currently Sanofi S.A.) (July 1989 – Sep. 1991)
Eli Lilly Japan KK (July 1987 – April 1989)
Sankyo Co., Ltd.(currently Daiichi Sankyo Co., Ltd.) (April 1974 – July 1987)

Katsuto Tamai, Founder, Director

Director, StemRIM Inc. (Oct. 2022 – Present)
Professor, Endowed course of Regeneration-Inducing Medicine Graduate School of Medicine/ Faculty of Medicine, Osaka University (Oct. 2010 – Present)
Director, StemRIM Inc. (Feb. 2007 – Aug. 2010)
Associate professor, Department of Gene Therapy, Graduate School of Medicine/ Faculty of Medicine, Osaka University (May 2003 – Sep. 2009)

Noriko Sawai, External director

Head of healthcare team, Social Innovation and Investment Foundation (Aug. 2022 – present)
Impact Officer, Social Innovation and Investment Foundation (Feb. 2020 – July 2022)
External director, StemRIM Inc. (Oct. 2019 – Present)
DeNA Co. (June 2014 – Jan. 2020)
CSK Venture Capital Co. (April 1995 – May 2014)

Hirotada Nagai, External director

President, HyakusanSoken KK (July 2022 - Present)
External directors, StemRIM Inc. (Oct. 2020 - Present)
Auditor, Regional Fish Institute, Ltd. (May 2020 – Present)
Director, PRDM Co., Ltd. (March 2018 – Present)
Director, PorMedTec Co., Ltd. (Dec. 2017 – Present)
Director, Kyoya KK (Dec. 2017 - Present)
Pharmaceuticals and Medical Devices Agency (PMDA) (Sep. 2012 – July 2014)
Pharmaceutical and Food Safety Bureau of Ministry of Health, Labour and Welfare (April 2001 – Sep. 2017)

External Audit & Supervisory Board Member

Yoji Kudo, External audit

Akihiro Mizukami, External audit

Yoichiro Shimada, External audit

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