Presentation Material for Business Plan and Growth Potential

StemRIM Inc. (Stock code: TSE4599)

October 31,2025



Overcoming Refractory Diseases by "Regeneration-Inducing Medicine™"



<u>Stem</u> cell <u>Regeneration-Inducing</u> <u>Medicine</u>

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

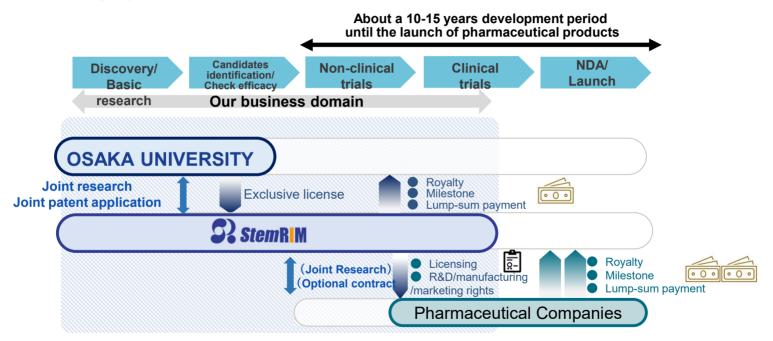
"Regeneration-Inducing MedicineTM" is new class of medicine that induces functional regeneration of damaged tissues or organs by maximizing the patient's innate ability of tissue repairing.

We aim for a future in which "Regeneration-Inducing Medicine $^{\text{\tiny TM}}$ " helps patients all over the world suffering from refractory diseases.

1. Business Model and R&D Structure

Business Model

A business model that generates income by licensing out product development, manufacturing, and marketing rights to pharmaceutical companies in Japan and overseas.



Main Contracts with Pharmaceutical Companies

Contract Name (Date of Agreement)	Company	Contract Details (Excerpt)	Total Contract Amount	Received Contract Amount
Implementation License Agreement(November 2014)	Shionogi & Co. Ltd.	A license is granted for the exclusive development, manufacturing, use, or sale of prior compounds and products for pharmaceutical applications worldwide, based on patents related to the pharmaceutical use of Redasemtide (HMGB1 peptide) or compounds containing it, as well as their methods of manufacture or formulation. As compensation for the license, Stemrim will receive upfront payments, milestone revenues, and royalty income.	Not disclosed*	4,046 million yen
Contract for the accelerated clinical development of the "Regeneration-Inducing Medicine TM "candidate Redasemtide for multiple diseases(June 2020)	Shionogi & Co. Ltd.	Utilizing non-clinical research evidence related to the Redasemtide (HMGB1 peptide), physician-led clinical trials will be conducted targeting cardiomyopathy, osteoarthritis of the knee, and chronic liver disease. As compensation for the license, Stemrim will receive a one-time payment based on the achievement of specified conditions.	3,100 million yen	3,100 million yen

^{*}The total contract amount related to this agreement is not disclosed due to confidentiality obligations.

Summary of Financial Results

- •For FY 2025, 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 bioventure, we have an unstable revenue structure considering our business model.
- As of the end of FY 2025, we hold **6,994 million yen** in cash and deposits. The estimated annual expenditure for the FY 2025 is between 1.5 billion yen and 2 billion yen (cash outflows related to R&D: 1.3 billion yen to 1.7 billion 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)

	FY 2021.7	FY 2022.7	FY 2023.7	FY 2024.7	FY 2025.7	Function (FY on FY)
Operating revenue	1,400	22	2,350	_	_	_
R&D expenses	1,523	1,421	1,567	1,453	1,394	-57
Total operating expenses	1,993	2,003	2,207	2,076	1,971	-104
Operating Income (loss)	(593)	(1,980)	142	(2,076)	(1,971)	+104
Ordinary Income (loss)	(583)	(1,972)	145	(2,077)	(1,970)	+107
Net Income (loss)	(582)	(1,948)	168	(2,022)	(1,929)	+92
Cash and deposit	10,172	8,880	10,217	8,410	6,994	

Scientific founder: Prof. Katsuto Tamai

Katsuto Tamai, our current Director and Chief Scientific Officer (CSO), was inspired to explore the potential of skin regeneration using bone marrow-derived stem cells after encountering a patient with the rare and debilitating disease. Dystrophic Epidermolysis Bullosa, He elucidated the Regeneration-Inducing Mechanism of the HMGB1 protein and subsequently developed "Redasemtide." a peptide that excludes the inflammatory domain of HMGB1. Through clinical trials. Redasemtide demonstrated both efficacy and safety, leading to the establishment of a new therapeutic concept known as "Regeneration-Inducing Medicine™."

Academic Society

The Japanese Dermatological Association

The Japanese Society for Matrix Biology and Medicine

The Japanese Cancer Association

The Japanese Society for Regenerative Medicine

Japan Society of Gene and Cell Therapy

The Japanese Society of Inflammation and Regeneration

Japan Organization of Clinical Dermatologists

Society for Skin Structure Research

Society for Investigative Dermatology

American Society of Gene & Cell Therapy

Career

April 1990

Assistant, Department of Dermatology, Hirosaki University Hospital, Faculty of Medicine October 1990

Postdoctoral Fellow, Jefferson Medical College, United States

December 1992

Assistant, Department of Dermatology, Hirosaki University, Faculty of Medicine February 1995

Lecturer, Department of Dermatology, Hirosaki University Hospital, Faculty of Medicine August 1998

Associate Professor, Department of Dermatology, Hirosaki University, Faculty of Medicine April 2002

Associate Professor, Department of Gene Therapy, Graduate School of Medicine, Osaka

University May 2003

Associate Professor (tenure-track), Department of Gene Therapy, Graduate School of

Medicine. Osaka University

February 2007

Director, Genomix Co., Ltd. (now StemRIM Inc.)

October 2009

Professor, Endowed Chair of Regenerative Medicine, Graduate School of Medicine,

Osaka University

October 2022

Director and Chief Scientific Officer (CSO), StemRIM Inc.

October 2023

Visiting Professor, Graduate School of Medicine, Osaka University



Research and Development system

At Stemrim, in collaboration with Osaka University and the Institute for Advanced Co-Creation Studies in "Regeneration-Inducing Medicine™", we are comprehensively promoting the entire research and development process toward the practical application of "Regeneration-Inducing Medicine™". This process spans from the molecular biological elucidation of stem cell mobilization mechanisms, through the discovery of next-generation regenerative induction drugs, to the verification of efficacy and safety in non-clinical studies.

OSAKA UNIVERSITY

- ·Basic Research in
- "Regeneration-Inducing Medicine™".
- •Elucidation of the mechanism of action



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



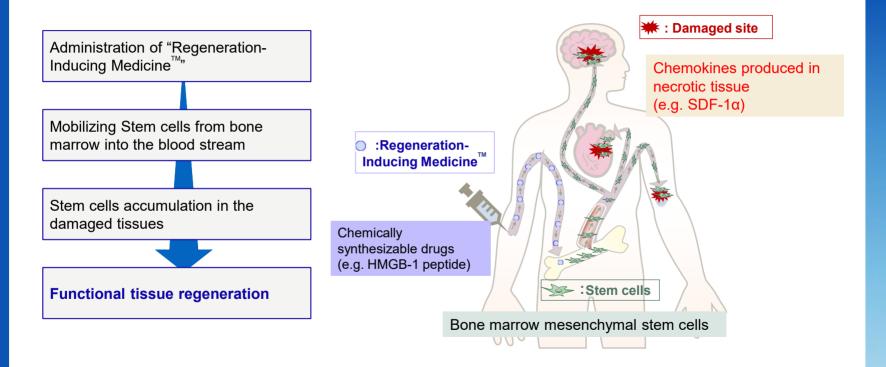
- •Consistent promotion from basic research to clinical research
- Collaboration with other domestic and international universities and research institutions

*POC: Proof of Concept

2. Mechanism of Action of "Regeneration-Inducing Medicine™"

Mechanism of Action of "Regeneration-Inducing Medicine™"

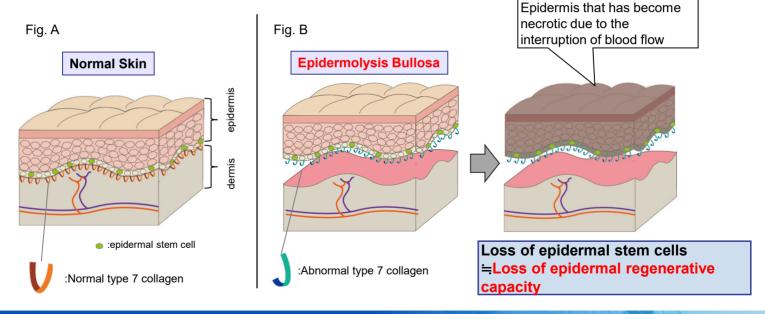
Bone marrow mesenchymal stem cells mobilized into the peripheral blood stream induce the tissue regeneration.



Discovery of in-vivo mechanism inducing tissue regeneration

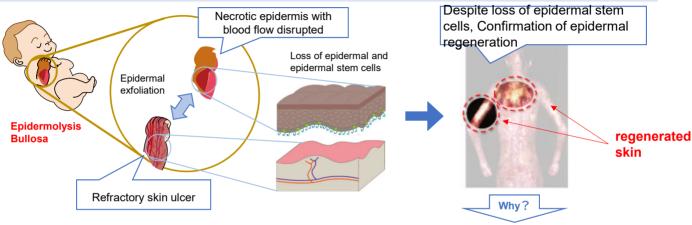
•Differences between normal skin and epidermolysis bullosa skin

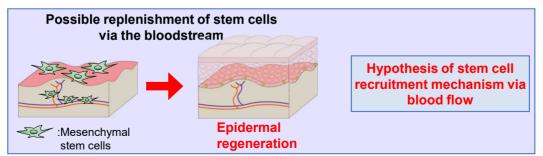
In normal skin (Figure A), type 7 collagen functions like an adhesive, bonding the epidermis and dermis, the superficial layers of skin. In epidermolysis bullosa congenita (Figure B), the epidermis and dermis are easily detached with the slightest irritation due to abnormal type 7 collagen. Since epidermal 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.



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.

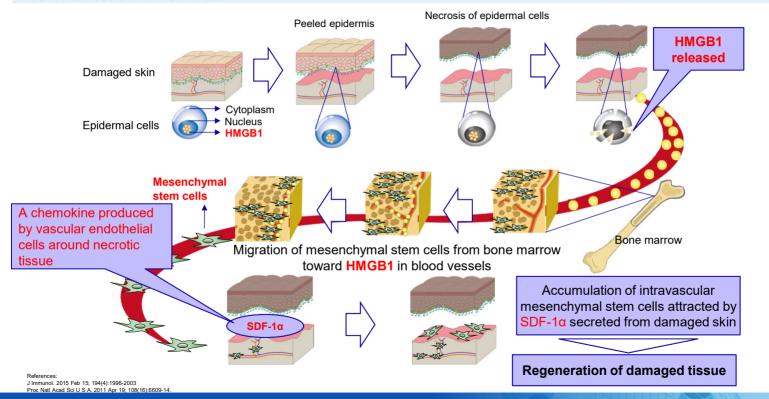




References: "gaku-no-ayumi" Vol.265 No.5 463-468; 2018 Skin Diseases :41(1); 7-12,2019 Photo courtesy of Osaka University

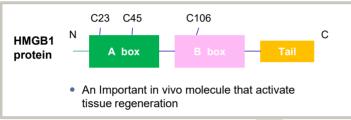
Discovery of in-vivo mechanism inducing tissue regeneration

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



HMGB1 peptide drugs with improved safety

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

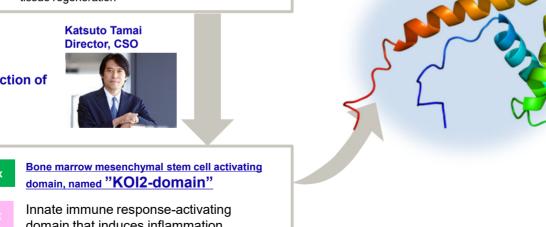


Identifying the function of protein domains

References:

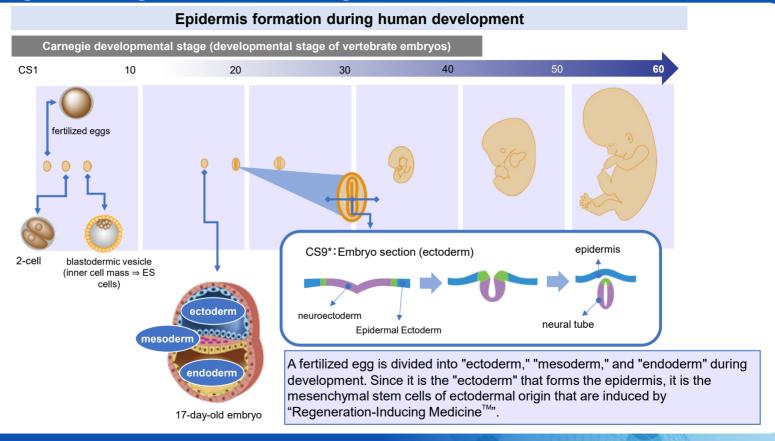
J Intern Med. 2004 Mar: 255(3):351-66.

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



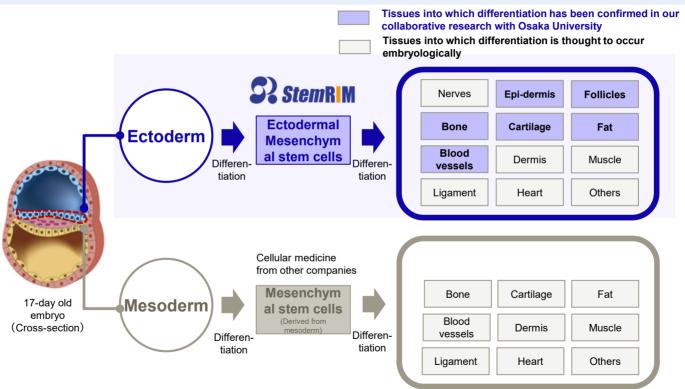
3. Advantages of "Regeneration-Inducing Medicine™"

Advantages of "Regeneration-Inducing Medicine™"

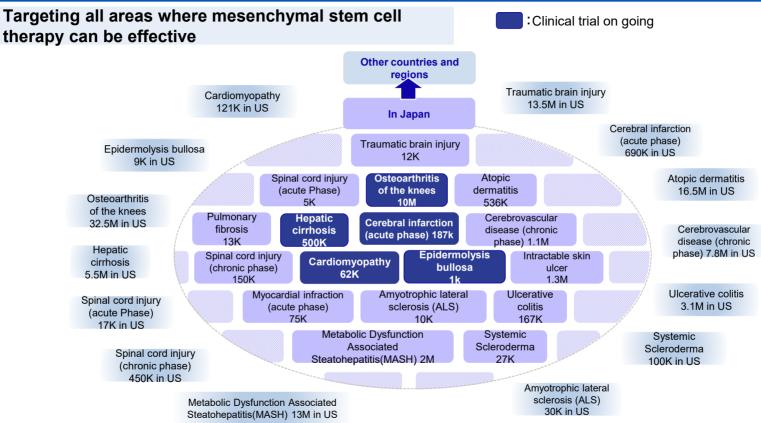


Advantages of "Regeneration-Inducing Medicine™"

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



Expanding Indications and Markets (Number of patients)

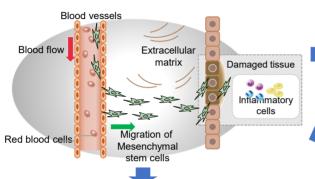


Functions of mesenchymal stem cells

In-vivo mesenchymal stem cells have 5 distinctive capabilities

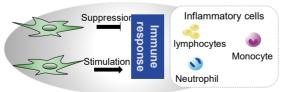
1. Cell migration ability

Mesenchymal stem cells migrate to damaged tissue via the bloodstream



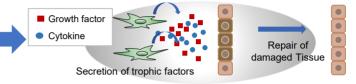
2. Immunomodulatory ability

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



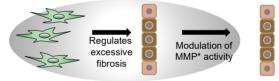
3. Trophic factor secretion ability

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

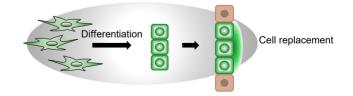


4. Fibrosis regulation ability

Regulates and inhibits excessive fibrosis of damaged tissue



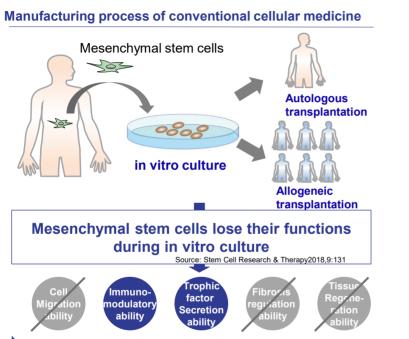
5. Tissue regeneration ability

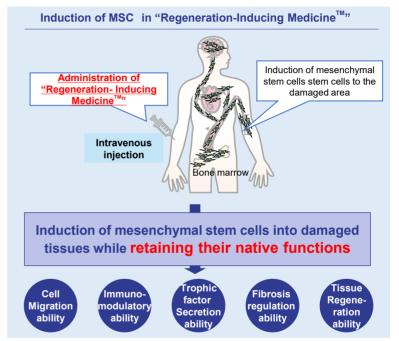


* MMP: Matrix metalloproteases

In vitro culture reduces the functions of MSCs

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





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

「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.

Advantages of "Regeneration-Inducing Medicine™"

"Regeneration-Inducing Medicine[™]" products have an advantage over conventional regenerative medicine products in terms of global expansion

Issues in the Global Development of Regenerative Medicine Products Using Living Cells

Transportation Need to be frozen from CPC and other manufacturing facilities and transported with thorough quality control These problems do not occur in "Regeneration-Inducing Medicine™" Product Transportation Advantages Manufacturing Need for mass culture with uniformity in cell properties In the case of Allogeneic transplantation, the need for mass production while keeping costs down Manufacturing Manufacturing Manufacturing Advantages

Potential for global development "Regeneration-Inducing Medicine™"

Summary of advantages of "Regeneration-Inducing Medicine™"

"Regeneration-Inducing

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

		Medicine™"	Cell therapy	Chemicals
	<u>Tissue</u> regeneration	Applicable for large-scale tissue damage	Applicable for large tissue damage with large number of cells	No regeneration
Efficacy	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	<u>Noninvasive</u>	Compound mobilizes the patient's cells in vivo and no rejection	Invasive in cell collection Immune- rejection in allogenic case	C 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	Cost	Normal industrial drug production	CPC and cell collection and transplantation facility is required	Affordable and large-scale production
benefit	Regulatory affairs	Same as general compound drugs	No standard, and case-by-case regulation is required	Standardized regulation

Summary of advantages of "Regeneration-Inducing Medicine™"

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

Cancerization risk

Risk of cancer depending on the site of gene insertion

iPS cell



"Regeneration-Inducing Medicine™"



Immunogenicity issues

Risk of immune rejection due to use of someone else's cells



Somatic stem cells

Limit of differentiation ability

Limited ability to proliferate and differentiate limited to specific embryonic tissues

Ethical issues

Ethical issues in the creation of human embryos by breaking and extracting them

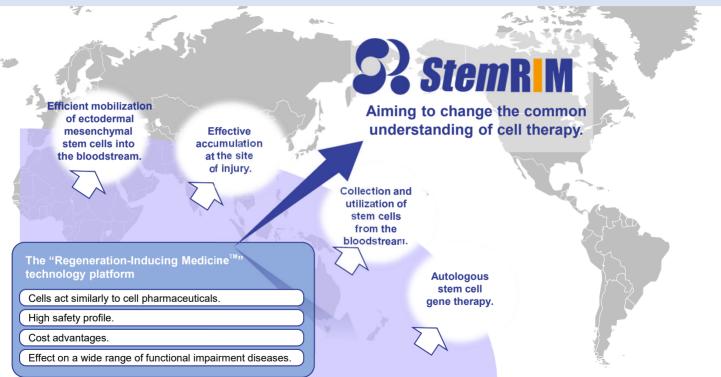
ES cell

Allogeneic cell

23

Summary of advantages of "Regeneration-Inducing Medicine™"

The "Regeneration-Inducing Medicine™" technology platform aims to be a game-changer in the field of cell therapy.



4. Business Areas and Pipeline Progress Status

Reconstruction of the Research Projects

Development Code Categorization of the Pipeline for the Optimal Allocation of R&D Resources

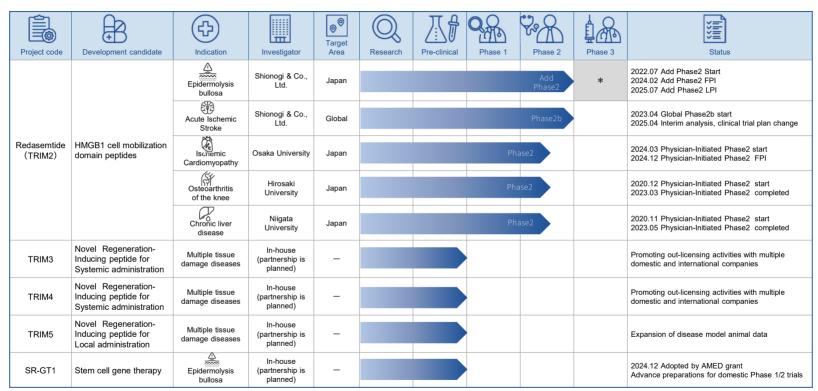
We have reevaluated the priorities of our pipeline by selecting and focusing our research resources, with the aim of maximizing business value and improving development efficiency. As a result, we have removed the lower-priority "therapeutic autologous cell collection device" from our pipeline. Going forward, we will concentrate our research and development efforts on five themes: Redasemtide (TRIM2), TRIM3, TRIM4, TRIM5, and SR-GT1. This approach will allow us to allocate our limited resources to areas with greater market potential and technological maturity, and is expected to further accelerate our development speed.

Development Pipeline (New)

	,			
Project code	Development candidate	Indication	Investi-gator	Target Area
		Epidermolysis Bullosa	Shionogi & Co., Ltd.	Japan
		Acute Ischemic Stroke	Shionogi & Co., Ltd.	Global
Redasemtide (TRIM2)	HMGB1 cell mobilization domain peptides	Ischemic Cardiomyopathy	Osaka University	Japan
		Osteoarthritis of the Knee	Hirosaki University	Japan
		Chronic Liver Disease	Niigata University	Japan
TRIM3	Novel Regeneration- Inducing peptide for Systemic administration	Multiple tissue damage diseases	In-house (partnership is planned)	_
TRIM4	Novel Regeneration- Inducing peptide for Systemic administration	Multiple tissue damage diseases	In-house (partnership is planned)	_
TRIM5	Novel Regeneration- Inducing peptide for Local administration	Multiple tissue damage diseases	In-house (partnership is planned)	_
SR-GT1	Stem cell gene therapy	Epidermolysis Bullosa	In-house (partnership is planned)	_

	Development Pipeline (Old)						
	Project code		Development candidate	Indication			
		01		Epidermolysis Bullosa			
		02	Redasemtide	Acute Ischemic Stroke			
	PJ1	03	(HMGB1 cell mobilization domain	Ischemic Cardiomyopathy			
		04	peptides)	Osteoarthritis of the Knee			
		05		Chronic Liver Disease			
1	D 10	01	TRIM3 (Novel Regeneration-Inducing peptide for Systemic administration)	Multiple tissue damage diseases			
	PJ2 02		TRIM4 (Novel Regeneration-Inducing peptide for Systemic administration)	Multiple tissue damage diseases			
	PJ3		TRIM5 (Novel Regeneration-Inducing peptide for Local administration)	Multiple tissue damage diseases			
	PJ4		Autologous cell collection device for treatment	Refractory Ulcerative Bone Disease			
	PJ5		SR-GT1 (Stem cell gene therapy)	Epidermolysis Bullosa			

Overview of Development Pipeline



^{*}The number of patients with dystrophic epidermolysis bullosa (DEB) targeted for this study is estimated to be around 400 nationwide, making it difficult to plan a large-scale Phase III clinical trial. Furthermore, since DEB is a rare and intractable disease with no effective treatment currently available, we expect to file a new drug application (NDA) based on the results of the additional Phase 2 trial.

One-year progress in the development pipeline

Project code	Development candidate	Indication	Investigator	Target Area	Progress (as of October 2025)	(Reference) From "Presentation Material for Business Plan and Growth Potential " disclosed on October 31, 2024
		Epidermolysis bullosa	Shionogi & Co., Ltd.	Japan	Additional Phase 2 trial currently underway	Additional Phase 2 trial currently underway
		Acute Ischemic Stroke	Shionogi & Co., Ltd.	Global	Global Phase 2b clinical trial currently underway	Global Phase 2b clinical trial currently underway
Redasemtide (TRIM2)	HMGB1 cell mobilization domain peptides	Ischemic Cardiomyopathy	Osaka University	Japan	Physician-Initiated Phase2 trial currently underway	Physician-Initiated Phase2 trial begins (March 2024)
		Osteoarthritis of the knee	Hirosaki University	Japan	Physician-Initiated Phase2 trial completed	Physician-Initiated Phase2 trial completed
	Chronic liver disease	Niigata University	Japan	Physician-Initiated Phase2 trial completed	Physician-Initiated Phase2 trial completed	
TRIM3	Novel Regeneration- Inducing peptide for Systemic administration	Multiple tissue damage diseases	In-house (partnership is planned)	_	Non-clinical	Non-clinical
TRIM4	Novel Regeneration- Inducing peptide for Systemic administration	Multiple tissue damage diseases	In-house (partnership is planned)	-	Non-clinical	Non-clinical
TRIM5	(Novel Regeneration- Inducing peptide for Local administration)	Multiple tissue damage diseases	In-house (partnership is planned)	_	Non-clinical	Non-clinical
SR-GT1	SR-GT1 (Stem cell gene therapy)	Epidermolysis Bullosa	In-house (partnership is planned)	-	Preparing for clinical trials	Preparing for clinical trials

Redasemtide: Additional Phase 2 Trial for DEB

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: More than 3 participants		
Dogimon	30-minute intravenous infusion once a day, total 10 times/4 weeks		
Regimen	[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		

Clinical Trial Timeline to Date

December 2017: Initiation of Phase 2 investigator-initiated clinical trial September 2019: Completion of Phase 2 investigator-initiated clinical trial

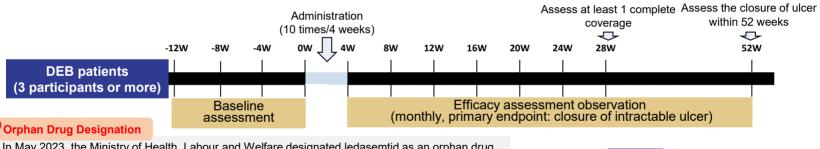
March 2020: Completion of follow-up study for Phase 2 investigatorinitiated clinical trial

July 2022: Initiation of additional Phase 2 clinical trial

March 2023: First patient enrolled in the additional Phase 2 clinical trial

May 2023: Orphan Drug Designation

July 2025: Final patient enrolled in the additional Phase 2 clinical trial



Orphan Drug Designation

In May 2023, the Ministry of Health, Labour and Welfare designated ledasemtid as an orphan drug for hypoparathyroidism-related epidermolysis bullosa. This designation reflects the Ministry's recognition of the development plan's validity for treating hypoparathyroidism-related epidermolysis bullosa. Eligibility for the priority review system is expected to shorten the review period, facilitating earlier approval.

Status

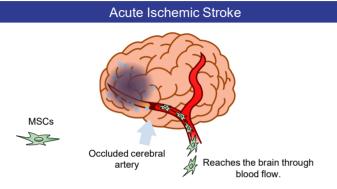
Planned Market Launch by March 2028

** iRCT2031220378

^{*} Shionogi & Co. Ltd., 1st Quarter of Fiscal 2025 Financial Results, July 28, 2025, pp.31

Redasemtide: Global Phase 2b Trial for Acute Ischemic Stroke

Developing a stroke treatment that alleviates time constraints compared to conventional therapies.



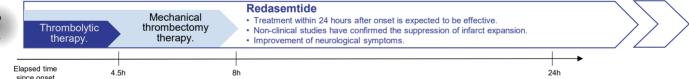
Market Size in Japan

187 thousand people



Mechanism of action

- Suppression of inflammation
- Promotion of angiogenesis and secretion of trophic factors to remaining nerve cells
- / Inhibition of fibrosis to suppress the expansion of the infarct area in stroke.



Onset to 4.5 hours

Thrombolytic therapy (t-PA intravenous therapy): A treatment method that dissolves clots and restores blood flow by administering a thrombolytic agent (t-PA).

Onset to 8 hours

Mechanical thrombectomy therapy: A treatment method that retrieves clots using a catheter and thrombectomy device.

Compared to conventional therapies, Redasemtide offers more relaxed time constraints and is expected to be used in combination with t-PA during the acute phase, as a first-line treatment for t-PA contraindications, and as a standalone treatment in the subacute phase.

Redasemtide: Global Phase 2b Trial for AIS

April 2019:

Initiation of Phase 2 corporate-sponsored clinical trial (In Japan)

October 2021:

Completion of Phase 2 corporate-sponsored clinical trial (In Japan)

April 2023:

Initiation of global Phase 2b clinical trial

February 2025:

Amendment to the global Phase 2b clinical trial protocol

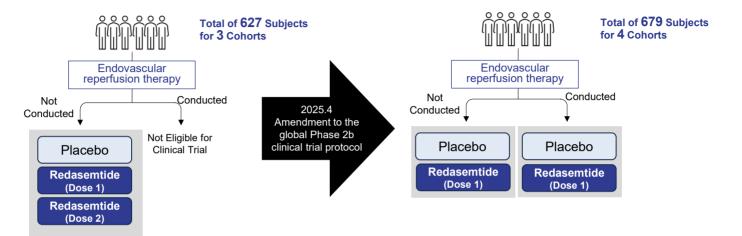
April 2025:

Interim analysis of the global Phase 2b clinical trial

Background to the Clinical Trial Plan Change

- Advances in endovascular recanalization therapy have changed the treatment system
- Considering adding a cohort of patients who underwent endovascular recanalization therapy to respond to a wide range of patient groups
- Conduct an interim analysis and perform a "Futility Analysis" of the existing cohort.

Redasemtide: Global Phase 2b Trial for AIS



1. Addition of Clinical Trial Subjects and Case Numbers

Due to Changes in the Stroke Treatment Paradigm, a new patient group that underwent thrombolytic therapy and mechanical thrombectomy has been added. As a result, the number of enrolled cases in the clinical trial has increased.

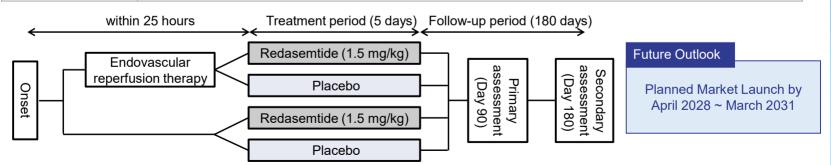
2. Reduction in the Number of Cases Due to Discontinuation of Dose 2

For acute ischemic stroke patients ineligible for endovascular recanalization therapy, futility analysis was conducted, and based on the results, dose 2 was discontinued. Relaxation of patient inclusion criteria, increased trial patient population, and efficient patient enrollment following discontinuation of Dose 2 are expected to prevent a significant extension of the trial period.

*jCRT:2031230083

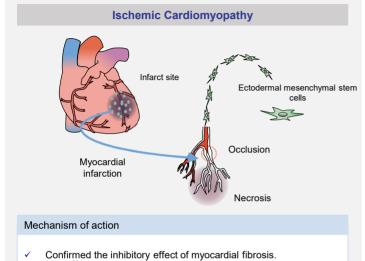
Redasemtide: Global Phase 2b Trial for AIS

Phase 2b Trial Proto	col (After interim analysis)	
Study objectives	Evaluation of the Efficacy, Safety, and Tolerability of Redasemtide in Patients with Acute Ischemic Stroke	
Subject population	Patients aged 18 years or older who can receive treatment within 25 hours of stroke onset, with a baseline NIHSS* score between 8 and 22.	
Study design	Multicenter, Randomized, Placebo-Controlled, Double-Blind	
Intervention	Cohort A: Patients Who Did Not Received Thrombolytic Therapy and/or Mechanical Thrombectomy	
Dose	Intravenous Administration Once Daily for 90 Minutes Over 5 Days	
Primary End Point	Modified Rankin Scale (mRS) at 90 Days After Initial Dosing	
Region	Japan, Europe, North America, China, etc.	

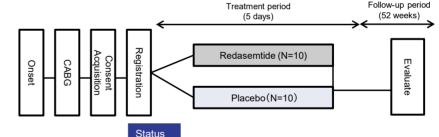


*NIHSS(National Institutes of Health Stroke Scale): Stroke Neurological Severity Rating Scale (42 points in total, the higher the score, the more severe)

Redasemtide: Phase 2 Clinical Trial in Ischemic Cardiomyopathy



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		



- √ 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.

*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.

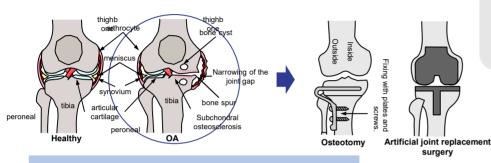
*2 CABG(coronary artery bypass grafting); Surgery to bypass a blockage in a coronary artery and install a new blood vessel (bypass).

March 2024:
Phase 2 Clinical Trial started in Japan

Redasemtide: Osteoarthritis of the Knee

Developing a treatment for osteoarthritis of the knee that does not rely on surgical interventions.

Osteoarthritis of the Knee(OA)



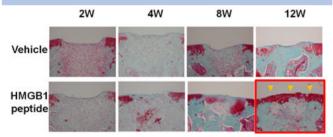
Market size in Japan

- Number of patients with symptoms: approximately 8 million
- •Estimated number of potential patients: approximately 25 million

Mechanism of action

Regeneration of articular cartilage tissue.

Cartilage regeneration with Redasemtide in a mouse model



(Note) Joint research between our company and Osaka University

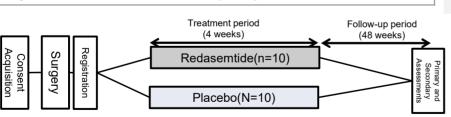
Cartilage regeneration by blood-induced bone marrow-derived mesenchymal stem cells following Redasemtide administration (the red-stained area indicated by \checkmark)

Conventional treatment methods.

- •For mild cases, analgesics (oral or topical) and hyaluronic acid injections into the knee joint are prescribed.
- •There is no radical treatment available, and in severe cases, the decline in quality of life (QOL) is significant, necessitating surgical interventions (such as total knee arthroplasty and high tibial osteotomy).
- A radical treatment for osteoarthritis of the knee through the administration of pharmaceuticals, without the need for surgical intervention, is anticipated

Redasemtide: Osteoarthritis of the Knee

Phase 2 Protoc	ol
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)



Phase 2 Clinical Trial Results

Safety Evaluation

No severe adverse events or side effects related to Redasemtide were identified. The safety of Redasemtide administration for osteoarthritis of the knee was confirmed.

Morphological and Functional Evaluation

As a morphological assessment of cartilage damage, a primary cause of osteoarthritis of the knee, MRI imaging was conducted. At 52 weeks after the start of administration, the median change in the defect area of the medial femoral condyle cartilage was -3.5% in the placebo group, compared to -7.5% in the Redasemtide group, showing a tendency toward greater reduction in defect area with Redasemtide. Additionally, endoscopic observation by specialists revealed favorable cartilage regeneration in 5 cases in the Redasemtide group (compared to 2 cases in the placebo group).

Status

We are currently reviewing our future development strategy following favorable results from a physician-initiated Phase 2 clinical trial.

^{*} 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.

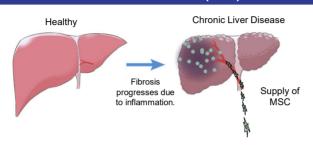
^{***} Knee Injury and Osteoarthritis Outcome Score (KOOS): One of the scores to measure the outcome of knee injury and osteoarthritis

^{****} iRCT2021200034

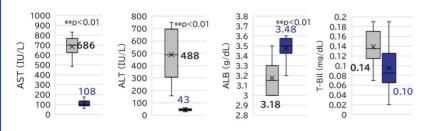
Redasemtide: Chronic Liver Disease

Developing a treatment for chronic liver disease that works by inhibiting fibrosis.

Chronic Liver Disease (CLD)



In a cirrhotic mouse model, improvements in serum liver damage markers (AST, ALT) and liver function indicators (ALB, T-Bil) were confirmed with Redasemtide treatment.



Redasemtide: n=8

The numbers in the figure represent average values.

*Nojiri S, Tsuchiya A, Tamai K, Terai S et al. Inflamm Regen. 2021

Market size in Japan

Approximately 400,000 to 500,000 people



Mechanism of action

- Exhibits strong anti-inflammatory effects
- ✓ Improves liver tissue fibrosis
- Regenerates liver function through stem cell activation

Conventional treatment methods

No established treatment can be expected to completely cure the condition. Liver transplantation is effective for advanced cirrhosis with fibrosis, but there is a concern about the shortage of organ donors.



Industrially producible Redasemtide is expected to provide a fundamental treatment for chronic liver disease through drug administration.

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 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 1: 4 days, Week 2: 4 days)]						
Rate of change in liver stiffness, rate of change in liver stiffness using ultrasound elastography, and rate of change in Change in Change in liver stiffness using ultrasound elastography, and rate of change in Change in Change in Change in liver stiffness using ultrasound elastography, and rate of change in C						
Site Division of Gastroenterology and Hepatology, Niigata University Medical and Dental Hospital						
Pre-observation period (3 months)	Treatment period (4 weeks)	Follow-up period (6 months)				
Examination 1	Redasemtide (Active drug only)	Last Visit				

^{*} 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

Phace 2 Clini

Phase 2 Clinical Trial Results

- Safety Evaluation: Presence and Incidence of Adverse Events
 2 mild adverse events (voice disorder and fever) with a possible relationship to the investigational drug were observed, both of which resolved. 1 severe adverse event (bleeding during liver biopsy) occurred, but it resolved without treatment and was deemed unrelated to the investigational drug. These findings confirm the tolerability of Redasemtide administration for chronic liver disease.
- Efficacy Evaluation: Rate of Change in Liver Stiffness, Change in Liver Stiffness by Ultrasound Elastography, and Change in Child-Pugh Score
 In Cohort A (5 cases), an improvement in liver stiffness based on MR elastography was observed at 78 days and 162 days after the start of treatment, showing an average reduction of 12% and 8%, respectively, compared to baseline. In addition to improvements in liver stiffness by MR elastography, several cases showed an accompanying improvement trend in other fibrosis indicators (Fibrosis Index, Fibrosis Markers, and modified HAI Fibrosis Stage values). Based on these various efficacy evaluation indicators, the principal investigator's overall assessment suggested an improvement trend in liver fibrosis in 3 of 5 cases (60%) in Cohort A and 2 of 5 cases (40%) in Cohort B.

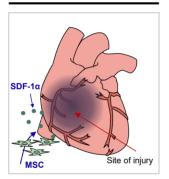
Status

We are currently reviewing our future development strategy following favorable results from a physician-initiated Phase 2 clinical trial.

TRIM5: Novel Regeneration-Inducing Peptide for Local Administration

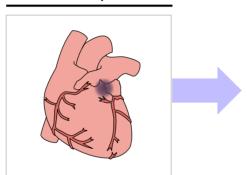
Developing protein drugs that accumulate mesenchymal stem cells at the site of injury

Large injury



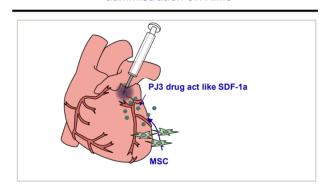
- SDF1-a is released, and mesenchymal stem cells mobilized in the blood accumulates at the injury
- = Mechanism of action in Redasemtide, TRIM3, or TRIM4 is effective

Small injury or chronic phase



- SDF1-a is not released, and mesenchymal stem cells cannot accumulate efficiently
 - = Combination therapy that maximizes the effects of "Regeneration-Inducing Medicine" is effective

Efficient accumulation of mesenchymal stem cells by topical administration ofTRIM5



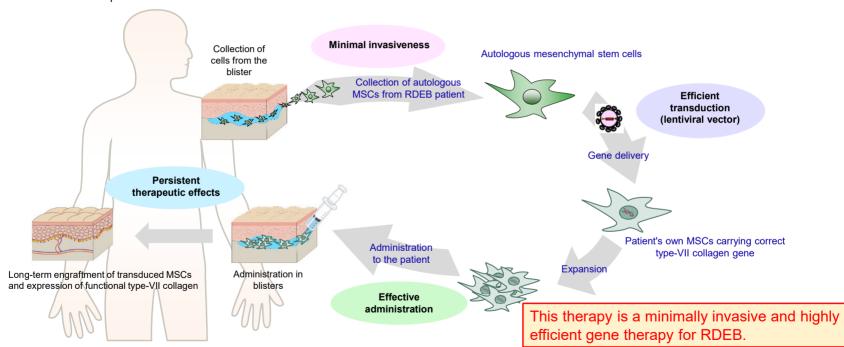
- Effective accumulation of mesenchymal stem cells at the site of injury by topical administration or intravenous injection
 - = Maximize damage repair effect of mesenchymal stem cells

- Multiple candidate proteins have been identified so far
- ✓ Confirmed good results in animal experiments
- Currently, the most suitable indication is being selected through multiple animal model experiments

Aim to cure intractable genetic disease by stem cell gene therapy

Concept

Ex vivo gene therapy involving the introduction of correct type VII collagen gene into autologous mesenchymal stem cells (MSCs) and administration of the cells in the blisters of the patient.

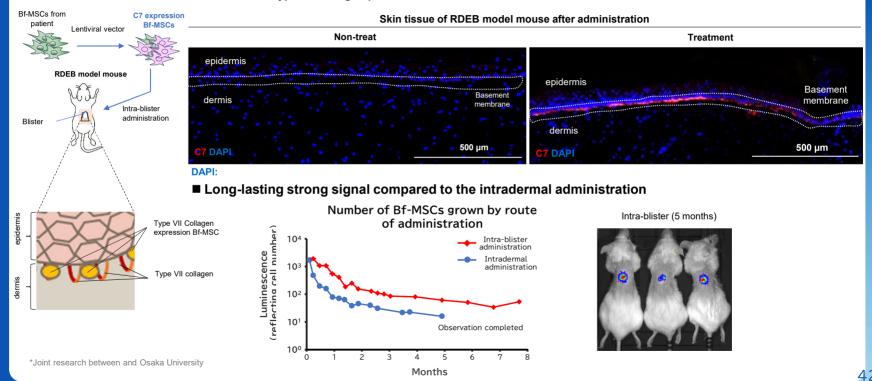


Ex vivo gene therapy with minimal invasiveness, high efficacy, and persistent effect
This therapy employs a novel method of isolating Bf-MSCs from a patient, efficient delivery of functional type VII collagen gene to the cells, and novel administration method to the patient with minimal invasiveness.

Carrinanii	Brand, Generic or	in/ex	Township and	Familiation	ation Administration route	Comparison with StemRIM				
Company	Code name	vivo	Target cell	Formulation		Area	Patient's burden	Effective length	Efficacy	
StemRIM	SR-GT1	ex vivo	Mesenchymal stem cells	Cell suspension	Intra-blister administration	Non-ulcer surface	Low	Long-term (sustained)	High	
Krystal Biotech	Vyjuvek	in vivo	-	Virus containing gel	Local application	Ulcer surface	Low	Long-term (limited)	High	
Abeona Therapeutics	prademagene zamikeracel	ex vivo	Skin keratinocytes	Epidermal Sheet	Epidermal sheet transplantation	Ulcer surface	High	Long-term (limited)	High	
Castle Creek Biosciences	dabocemagene autoficel	ex vivo	Dermal fibroblasts	Cell suspension	Intradermal administration	Ulcer surface	High	Long-term (limited)	Low	
Amryt Pharma	AP-103	in vivo	-	Protein solution	Intravenous administration	Whole body	Low	Short-term	High	

Verification of therapeutic efficacy and duration of drug effect of this treatment using RDEB model mice

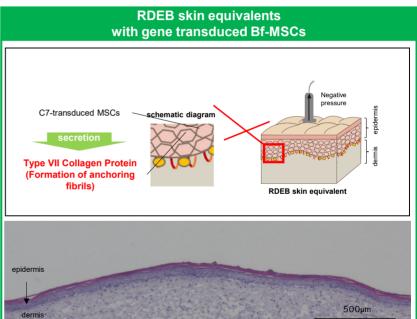
■ Restoration of the type-VII collagen protein (C7) at the basement membrane on RDEB model mouse



Therapeutic effects on RDEB skin model

 We confirmed the effect of gene therapy using patient-derived Bf-MSCs by RDEB skin model and artificially forming blisters by suction method.

RDEB skin equivalents schematic diagram Lack of Type VII collagen protein (anchoring fibrils) RDEB skin equivalent * : Blister epidermis



Joint research between and Osaka University

5. Future Growth Strategy

Future Growth Strategy

Growth Strategy to Maximize the Potential Value of "Regeneration-Inducing Medicine™"

Out-Licensing of Next-Generation Regeneration-Inducing Medicine[™]

TRIM3, TRIM4, and TRIM5 are next-generation "Regeneration-Inducing MedicineTM" candidates discovered through joint research with Osaka University and proprietary screening efforts. TRIM3 and TRIM4 have demonstrated efficacy in non-clinical studies, and we plan to continue early-stage development in-house, followed by out-licensing to pharmaceutical companies. Similarly, for TRIM5, we intend to pursue out-licensing after selecting appropriate target indications. Through these out-licensing activities, we aim to establish diverse revenue streams including upfront payments, milestone payments, and royalties.

Support for the development of Redasemtide.

To support the smooth progress of clinical development by Shionogi & Co., Ltd., we will continue to provide assistance for investigator-initiated clinical trials at universities and other institutions (for ischemic cardiomyopathy, chronic liver diseases, and osteoarthritis). In the case of epidermolysis bullosa, we aim for early approval and commercialization by utilizing the designation as an orphan drug. As these programs advance, we aim to maximize milestone and royalty revenues.

The clinical development of stem cell gene therapy (SR-GT1)

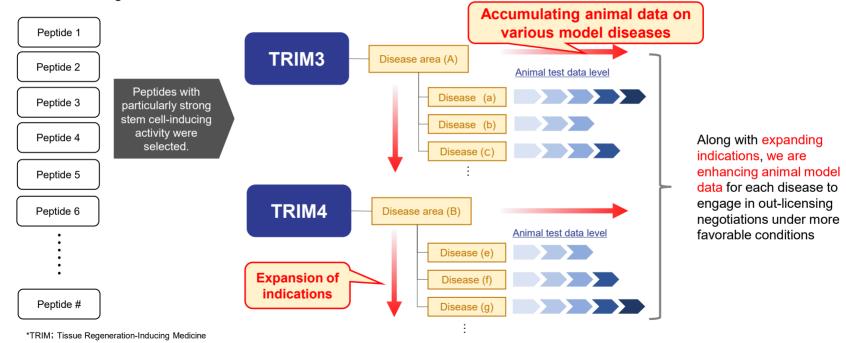
SR-GT1 is a therapeutic product designed for the treatment of severe genetic disorders, utilizing a process in which the patient's own stem cells are genetically edited ex vivo and then reintroduced into the body. Development is currently focused on severe epidermolysis bullosa as the initial indication, with efficacy and safety confirmed in animal studies. Non-clinical studies are ongoing in preparation for the start of clinical trials. Following initial in-house development, we aim to out-license the program and are also considering applications to other genetic disorders.

Expansion of the development pipeline.

To complement the existing pipeline, enhance corporate value, and diversify risk, we are actively pursuing the discovery of new "Regeneration-Inducing Medicine medical compounds, filing patent applications, and advancing non-clinical studies. Utilizing single-cell functional evaluation technologies, we are developing high-performance stem cell-based pharmaceuticals. By sharing these technologies with both domestic and international academic institutions and pharmaceutical companies, we aim to establish business partnerships and license-out opportunities, thereby diversifying revenue sources and achieving sustainable growth.

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.



Business Development

Continuing from last year, out-licensing negotiations were conducted with multiple pharmaceutical companies both domestically and internationally.

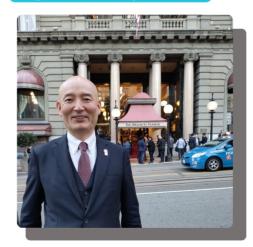


2024.10.9~11 @ Yokohama, JPN



J.P.Morgan
Healthcare Conference

2025.1.13~16 @ San Francisco, CA





2025.6.15~21 @ Boston, MA



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.



* As of July 2025

Activities of "StemRIM Institute of Regeneration-Inducing Medicine, Osaka University"



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 multifaceted development of "Regeneration-Inducing Medicine TMn. To date, several collaborative research projects have made significant progress.

Joint Research Projects

,		_	,
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							(Hullibel of events
	FY 2021	FY 2022	FY 2023	FY 2024	FY 2025	FY on FY	Notes
Division of Health Sciences	1	2	3	2	2	±0	Neonatal-Associated Diseases
Division of Biofunctional Research	_	_	_	_	_	±0	
Division of Medical Research	_	1	2	2	3	+1	Nervous System Diseases, Orthopedic-Related Diseases
Division of Dentistry	3	5	5	5	6	+!	Periodontitis-Related Diseases
Total	4	8	10	9	11	+2	



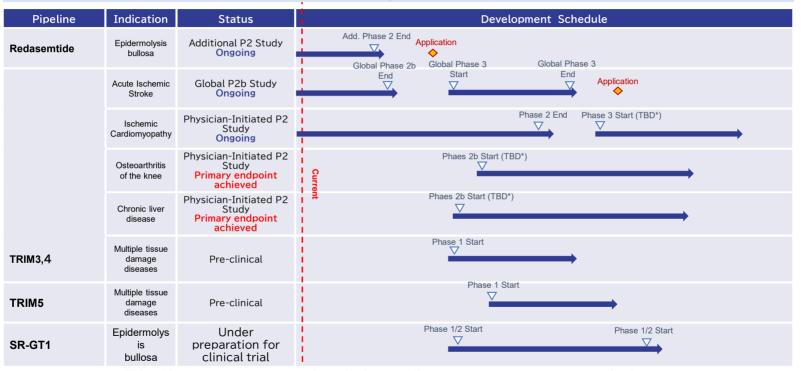
Website (Japanese):

https://stemrim -osaka-u.jp/



Pipeline Development Plan

医Given the long development timeline for pharmaceuticals, a pipeline development plan is formulated based on a longterm management vision.



*TBD: to be determined This table represents our company's projections and does not guarantee progress as outlined.

Forecast for the fiscal year ending July 2026

Research and Development Progress for the Fiscal Year Ended July 2025

Previous Disclosure (October 31, 2024)

Research Progress Outlook for the Fiscal Year Ending July 2025

Research and development for Redasemtide is progressing in clinical trials and toward expanded indications. Additionally, negotiations for clinical trials and licensing for candidate "Regeneration-Inducing MedicineTM" following Redasemtide continue to advance.

Cash Outflow Forecast for the Fiscal Year Ending July 2025

Cash Outflow for R&D	1,200 million to 1,600 million yen
Cash Outflow for General and Administrative Expenses	230 million to 310 million yen

Actual Results

Research Progress Results for the Fiscal Year Ended July 2025

A physician-led Phase 2 clinical trial targeting ischemic cardiomyopathy with Redasemtide has started. Additionally, negotiations for licensing next-generation regenerative induction pharmaceutical candidates were conducted at multiple conferences with domestic and international pharmaceutical companies.

Cash Outflow for the Fiscal Year Ended July 2025

Cash Outflow for R&D	1,362 million yen
Cash Outflow for General and Administrative Expenses	256 million yen

Research and Development Progress Forecast for the Fiscal Year Ending July 2026

Most business revenue relies on development milestones, which are highly dependent on the development strategy and schedule of partners, making it difficult to predict the timing of receipts. Additionally, there is a possibility of receiving upfront payments from new partnerships, but the timing of contract finalization is uncertain. For these reasons, it is challenging to reasonably forecast earnings for the fiscal year ending July 2026, so earnings projections are not disclosed.

Research Progress Outlook for the Fiscal Year Ending July 2026

Research and development for Redasemtide is progressing in clinical trials and toward expanded indications. Additionally, negotiations for clinical trials and licensing for candidate "Regeneration-Inducing MedicineTM" following Redasemtide continue to advance.

Cash Outflow Forecast for the Fiscal Year Ending July 2026

Cash Outflow for R&D	1,200 million to 1,600 million yen
Cash Outflow for General and Administrative Expenses	230 million to 310 million yen

Allocation Status of Raised Funds

(Amount: million yen)

Funding Method	Amount Raised	Use of Funds	Planned Disbursement Amount(Timing)	Actual Disbursement Amount(Timing)	Undisbursed Amount(Timing)
		Funds for establishing the "Regeneration-Inducing Medicine™" research institute and an animal	7,195	_	_
Stock issuance associated with new listing (August 2019) 8,625	0.605	testing facility	(FY 2020)	-	_
	0,025	Costs for promoting R&D for the existing pipeline	1,430	-	_
, , ,		and R&D for new pipeline development.	(FY 2020)		_



Change in Use of Funds Raised through Listing on November 11, 2021., and October 31, 2025

(Amount: million yen)

					(· j j
		Funds for the establishment and maintenance of the "Regeneration-Inducing Medicine™" research institute and an animal	3,050	2,149 [Breakdown] Establishment Costs 940 Maintenance Costs 1,209	901
Stock issuance associated with new listing (August 2019)	testing facility.	(FY 2020 to FY 2030)	(FY 2020 to FY 2025)	(FY 2025 to FY 2030)	
	8,625	Costs for promoting R&D for the existing pipeline and R&D for new pipeline	5,471	3,409 [Breakdown] Outsourcing Costs 603 Research Material Costs 1,122 Collaborative Research Costs 1,683	2,320
		development.	(FY 2020 to FY 2026)	(FY 2020 to FY 2025)	(FY 2026 to FY 2029)

The plan for establishing the "Regeneration-Inducing Medicine™" research institute was changed from in-house purchase to leasing (collaborative research institute), resulting in an earlier opening and reduced establishment costs. Sufficient funds have been secured for pipeline development.

6. Risk Information

Risk Information

	Risk	Possibility and Timing of Materialization	Countermeasures
A) Uncertainty in the development of the pharmaceutical pipeline and associated revenue generation	 Risk of development delays or discontinuation due to the inability to discover beneficial effects in clinical trials. If the commercialization of our developed pharmaceutical candidates or those licensed out to other companies is delayed or canceled, there is a significant risk of adversely impacting our performance and financial condition. 	Medium / As needed	 We aim to maintain multiple pipelines in clinical development stages. We will advance non-clinical pipeline projects swiftly to the clinical development stage.
B) Business plan reliant on specific partnership agreements	 Risk of dependence on limited joint research and licensing agreements with specific pharmaceutical companies. Risk of early termination of contracts before the expiration date due to factors beyond our control, such as significant deterioration in the business environment or changes in the management policies of the licensing partner company. 	Medium / As needed	We aim to generate revenue from subsequent pipelines to reduce dependence on income from current partnership agreements. We will minimize the impact on our business plan by establishing new partnerships with other pharmaceutical companies.
C) Cash Flow Management	Research and development-oriented companies like ours require significant R&D funding, and due to the burden of R&D costs, there is a prolonged period of upfront investment. During this period, there is a risk of incurring continuous operating losses and negative cash flow from operations. Currently, our company lacks stable revenue sources, such as ongoing royalty income, and future revenue generation heavily depends on the progress of Redasemtide development and the outcomes of licensing negotiations for other pipeline projects. Therefore, we are not yet in a position to consistently generate funds from operating activities.	Low / As needed	•We aim to secure necessary funds by obtaining upfront payments and milestone revenue from existing pipelines, along with planned fundraising activities.

Appendix

StemRIM Management



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)



Katsuto Tamai, Founder, Director and CSO

(May 2003 - Sep. 2009)

Director, StemRIM Inc. (Oct. 2022 – Present)
Guest Professor, Endowed course of Regeneration-Inducing
Medicine Graduate School of Medicine/ Faculty of Medicine,
Osaka University (Oct. 2023 – Present)
Professor, Endowed course of Regeneration-Inducing
Medicine Graduate School of Medicine/ Faculty of Medicine,
Osaka University (Oct. 2010 – Sep. 2023)
Director, StemRIM Inc. (Feb. 2007 – Aug. 2010)
Associate professor, Department of Gene Therapy, Graduate
School of Medicine/ Faculty of Medicine, Osaka University



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)

Yoji Kudo, External audit Akihiro Mizukami, External audit Yoichiro Shimada, External audit

Corporate Information

Corporate Name	StemRIM Inc.
■ Chief Executives	Masatsune Okajima (Representative Director)
■ Established	October 30, 2006
■ Business Description	Research and Development of "Regeneration Inducing-Medicine™"
■ Shareholders' Equity	5,861 million yen
Equity Ratio	77.9 %
Number of Employees	69

Head Office

7-7-15, Saito-Asagi, Ibaraki-City, Osaka, Japan



StemRIM Institute of Regeneration-Inducing Medicine,

Osaka University

Techno-Alliance Building, 2-8, Yamadaoka, Suita-City, Osaka, Japa



■ Endowed Chair for Regeneration-Inducing Medicine / Joint Research Course in Stem Cell and Gene Therapy

The Center of Medical Innovation and Translational Research, 2-2, Yamadaoka, Suita-City, Osaka, Japan



As of the End of July 2025

Disclaimer

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