StemRIM

(TSE Growth : 4599)

# Presentation Material for Business Plan and Growth Potential

*StemRIM aims to bring a brighter future to patients suffering from intractable diseases.*

October 31, 2024

# StemRIM

Stem cell Regeneration-Inducing Medicine

## Overcoming Refractory Diseases by “Regeneration-Inducing Medicine™”

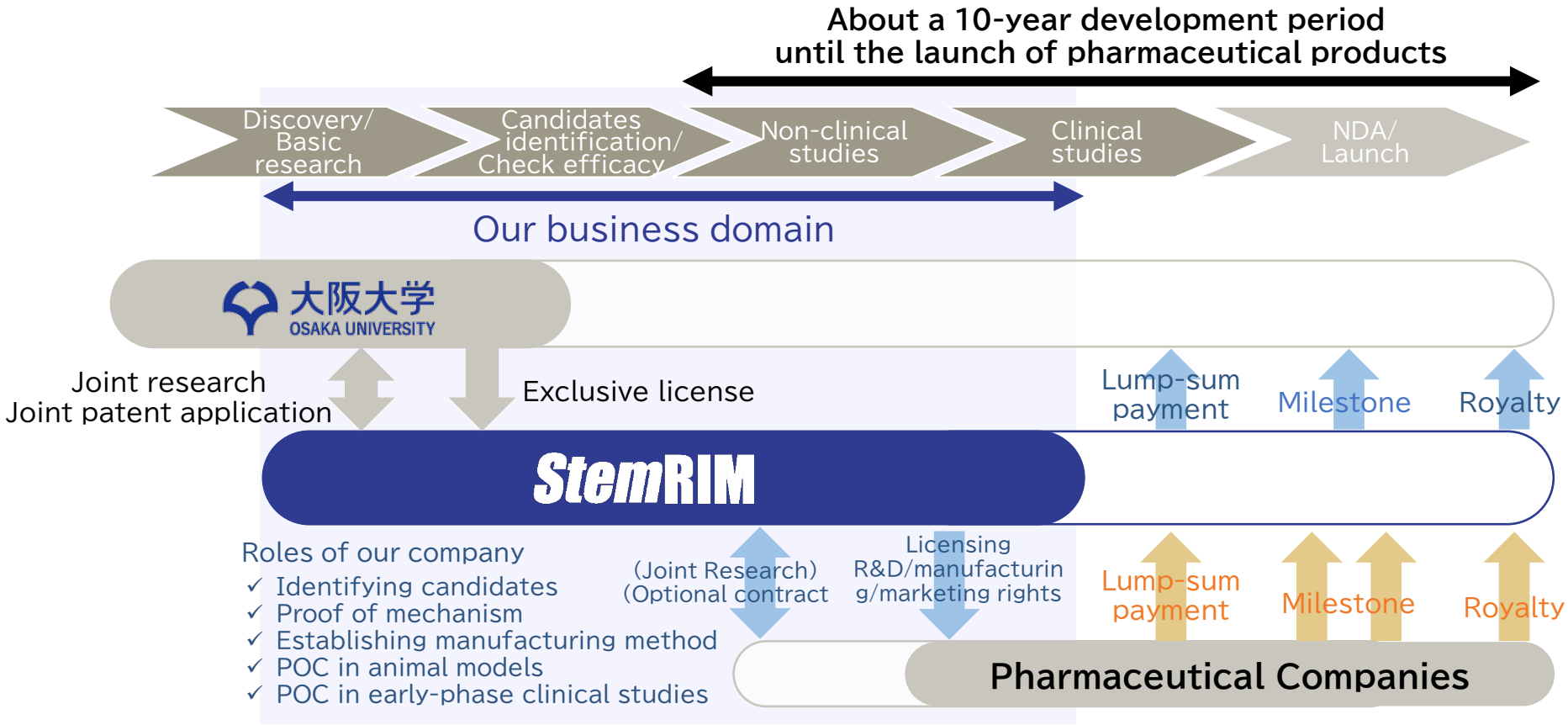
StemRIM is a biotech company aiming to develop
“Regeneration-Inducing Medicine™ ”
a next generation of regenerative medicine.

“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.

# 1 Business Model and R&D Structure

# Our Business Model




A business model that generates income by licensing out product development, manufacturing, and marketing rights to pharmaceutical companies in Japan and overseas. The main revenues are as follows;

- ✓ Lump-sum payment: Income earned as a lump-sum payment upon signing a joint research or licensing agreement.
- ✓ Milestone: Income earned when drug development stage/sales goals are achieved
- ✓ Royalty: Income earned on sales after the product is launched on the market.
- ✓ Joint research income: Conducting joint research utilizing our intellectual property and income earned as compensation

# 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.<br>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™”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.<br>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 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 |

# Scientific founder： Prof. Katsuto Tamai

大阪大学 OSAKA UNIVERSITY

**StemRIM scientific founder**
**Professor Katsuto Tamai**
Graduate School of Medicine
Faculty of Medicine, Osaka Univ.

## <Academic Society>

The Japanese Dermatological Association
The Japanese Society of Investigative Dermatology
The Japanese Society for Matrix Biology and Medicine
The Japanese Cancer Association
The Japanese Society for Regenerative Medicine
The Japanese Society of Inflammation and Regeneration
Japan Organization of Clinical Dermatologists
The Society for Skin Structure Research
The Society for Investigative Dermatology
The American Society of Gene & Cell Therapy

## <List of main papers>


Stem Cells 26:223-234, 2008.
Circulating bone marrow-derived osteoblast progenitor cells are recruited to the bone-forming site by the CXCR4/stromal cell-derived factor-1 pathway.

Biochem Biophys Res Commun 354:453-458, 2007.
Bone marrow-derived osteoblast progenitor cells in circulating blood contribute to ectopic bone formation in mice.

Am J Pathol 173:803-814,2008. Epub 2008 Aug 7.
Bone marrow cell transfer into fetal circulation can ameliorate genetic skin diseases by providing fibroblasts to the skin and inducing immune tolerance.

# R&D Structure and Facilities

Osaka University and StemRIM Institute of Regeneration-Inducing Medicine promote joint research and development in “Regeneration-Inducing Medicine™”.

大阪大学 OSAKA UNIVERSITY


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

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

Other domestic and international university research institutions

Collaboration

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

# 2 Mode of Action of “Regeneration-Inducing Medicine™”

# Mode of Action of “Regeneration-Inducing Medicine™”

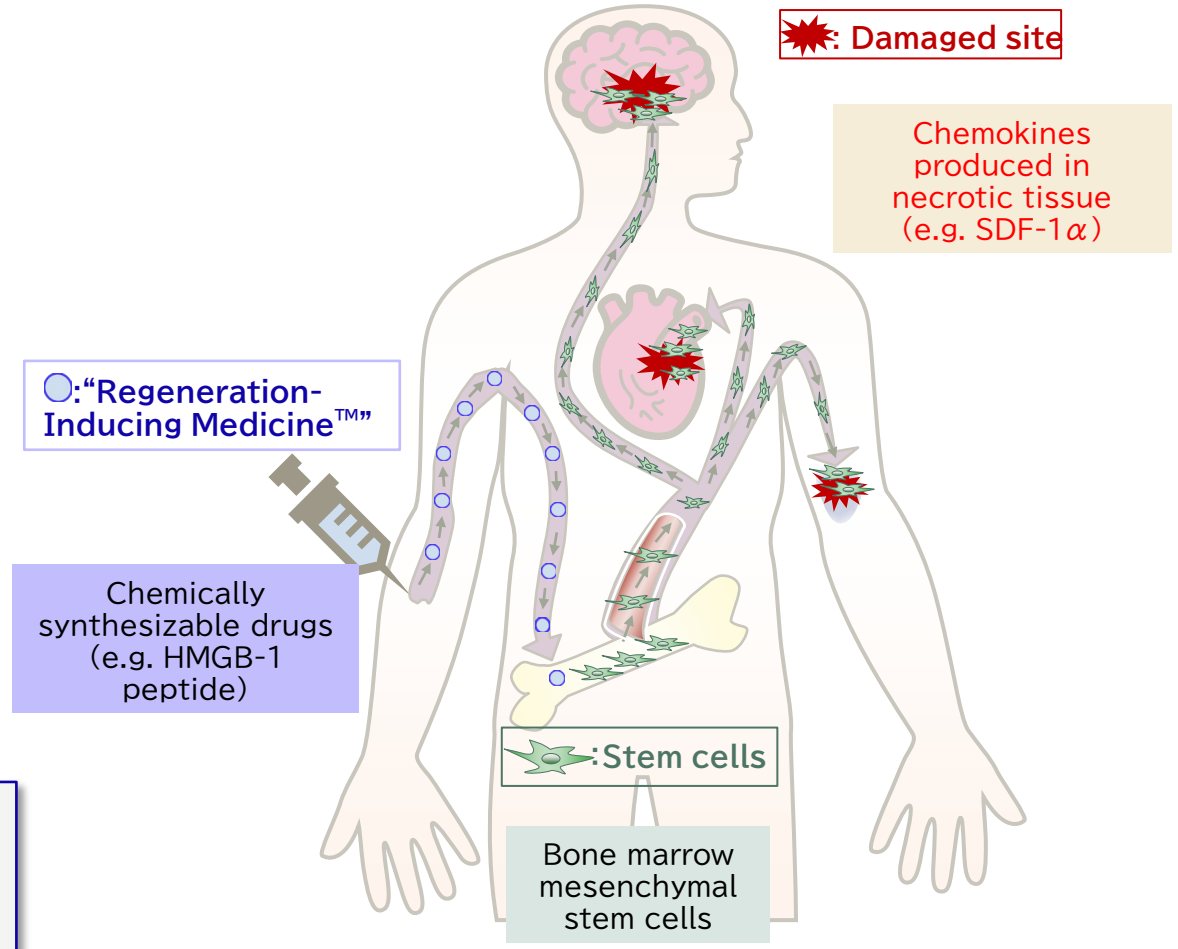
**Bone marrow mesenchymal stem cells mobilized into the peripheral blood stream induce the tissue regeneration.**

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**



# 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

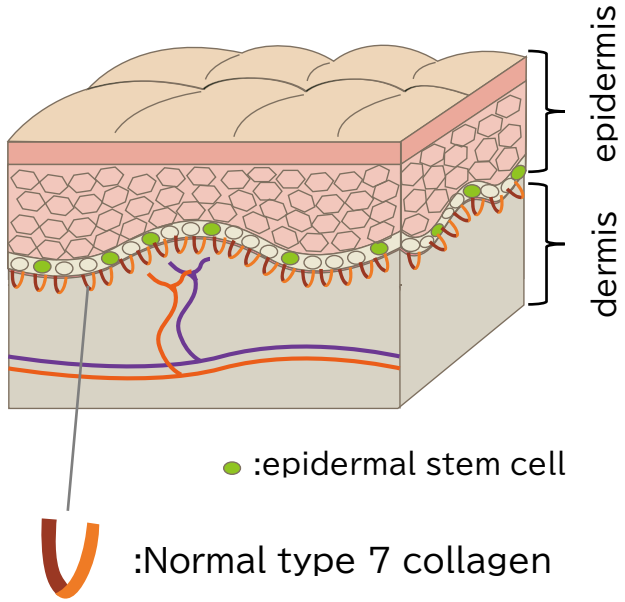
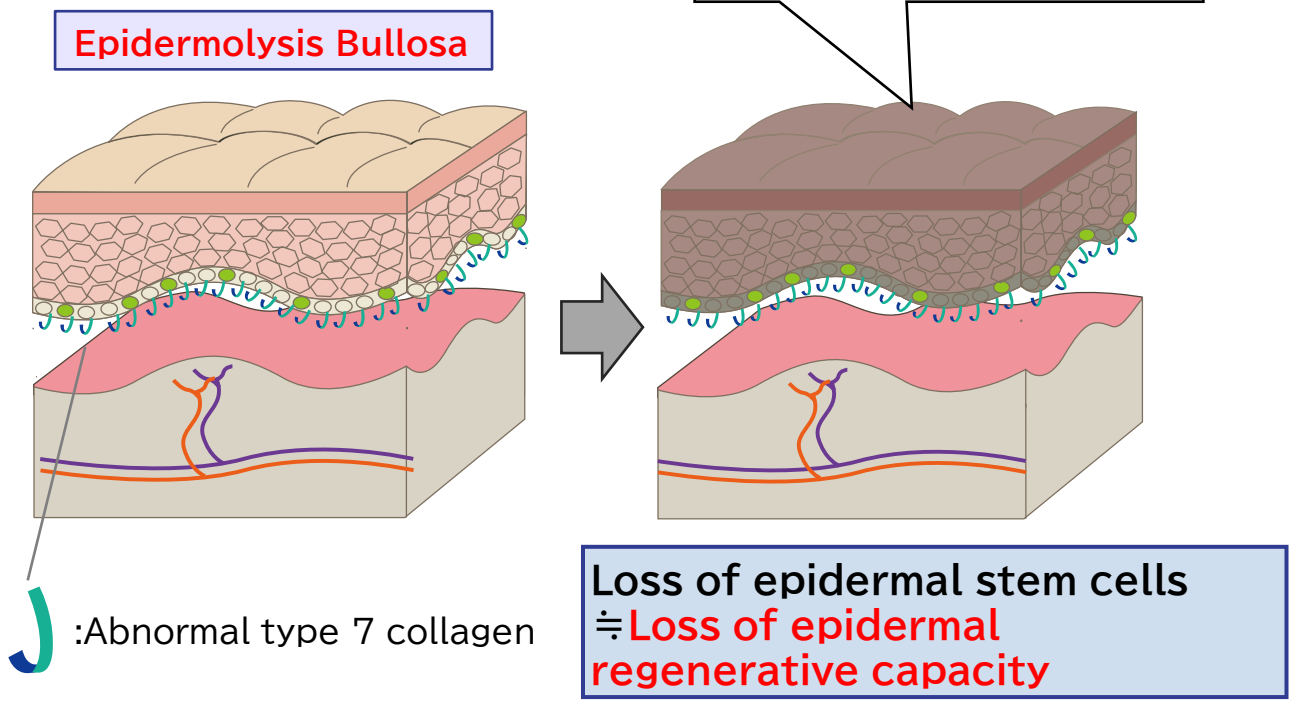
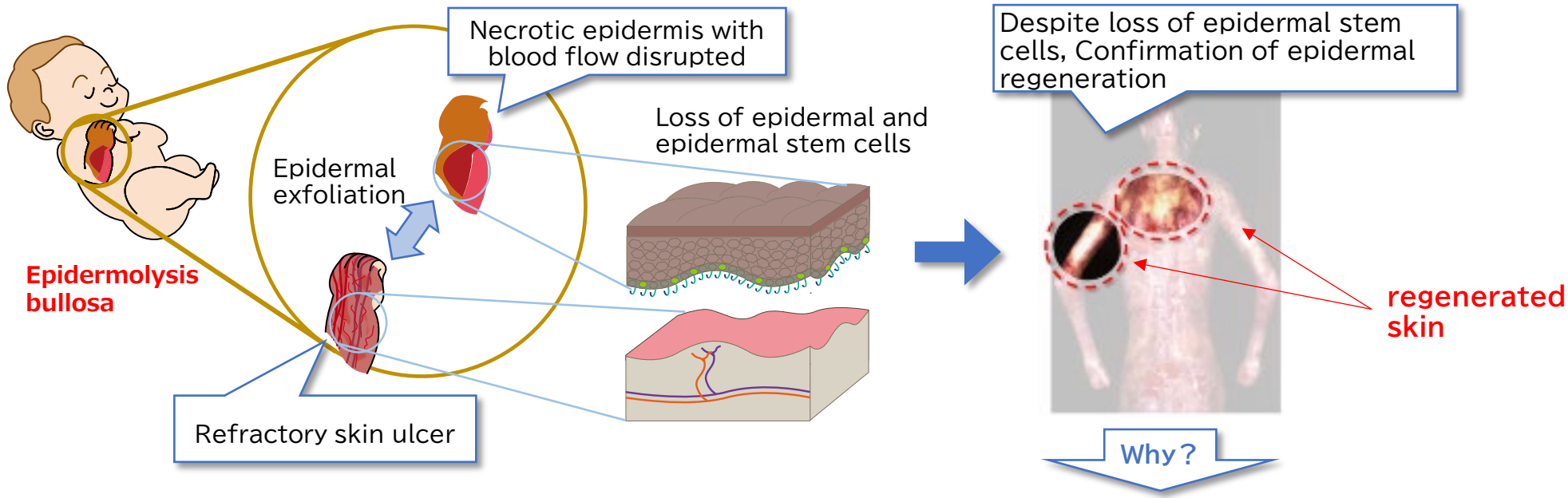


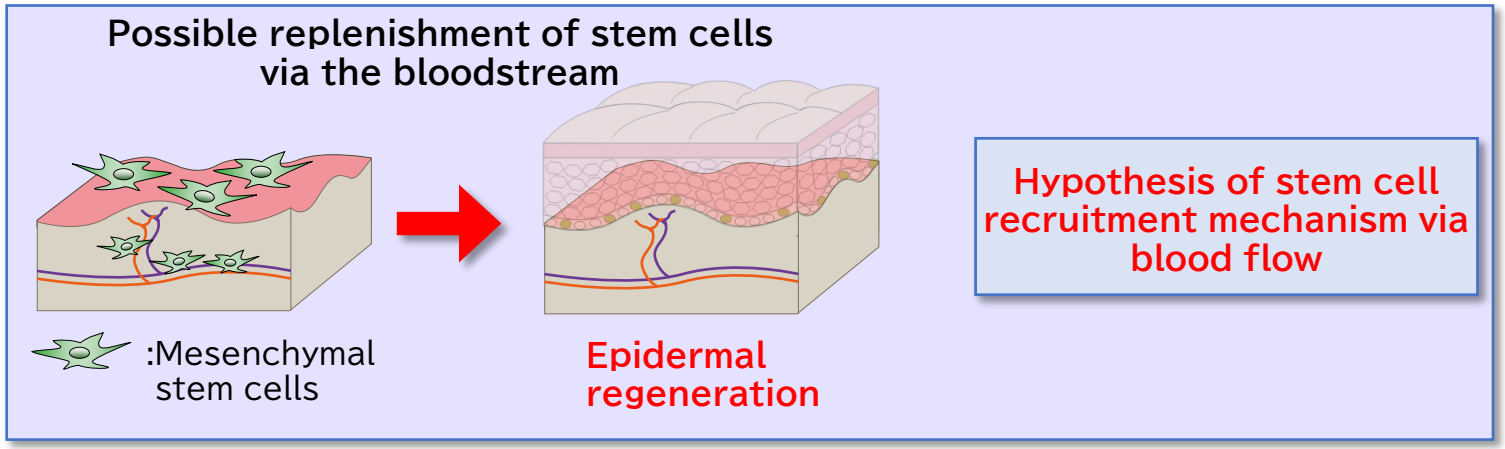

Fig. B



# 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.**

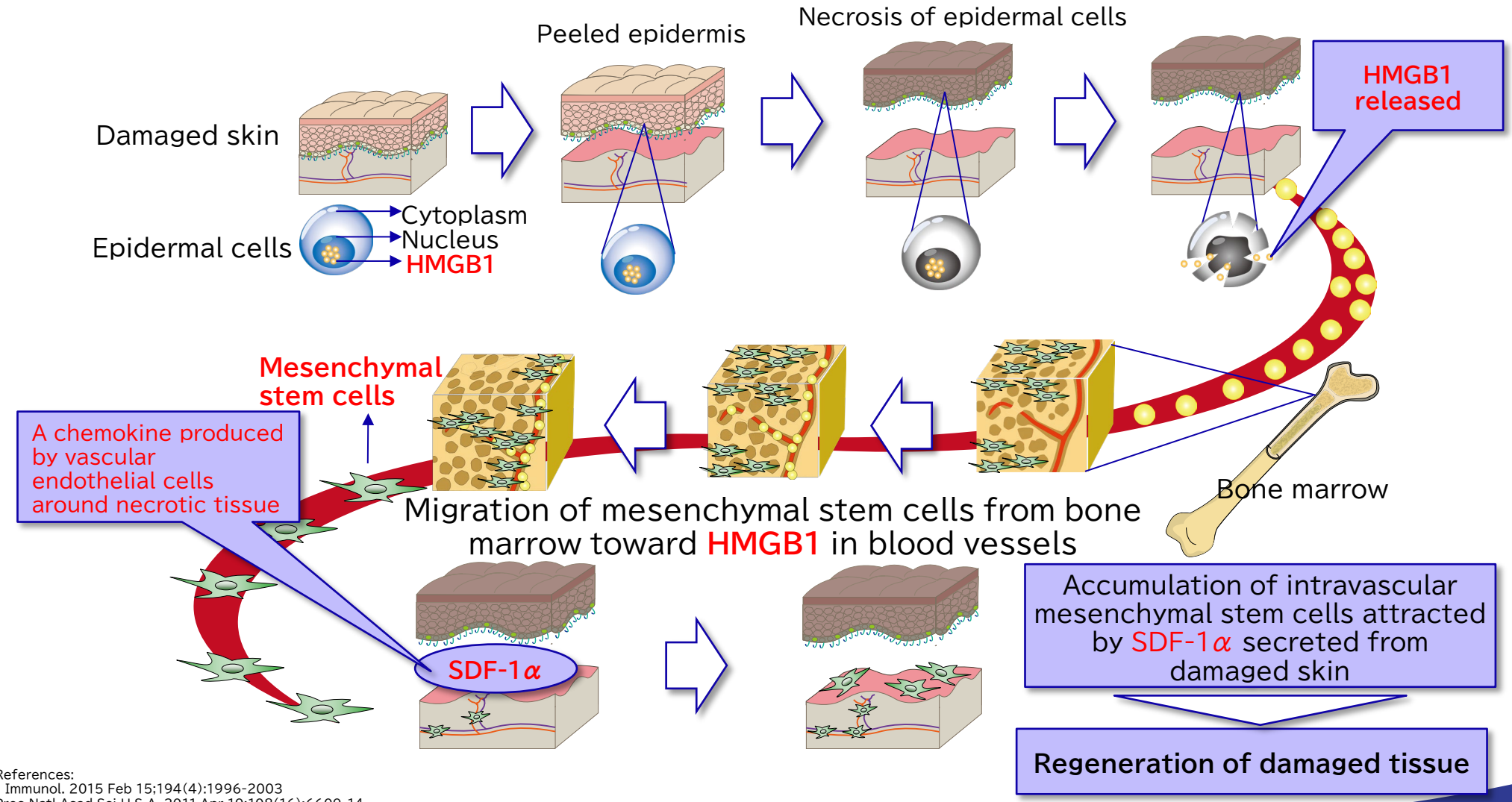



References:
*"Igaku-no-ayumi"* Vol.265 No.5 463-468;2018
Skin Diseases :41(1);7-12,2019
Photo courtesy of Osaka University

# Discovery of in-vivo mechanism inducing tissue regeneration

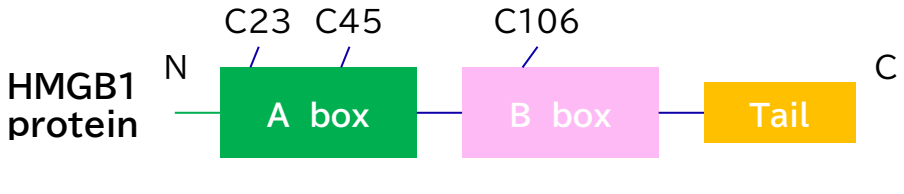
## Discovery of crosstalk mechanism between damaged skin and bone marrow mesenchymal stem cells via necrotic tissue-derived factor




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

# HMGB1 peptide drugs with improved safety

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

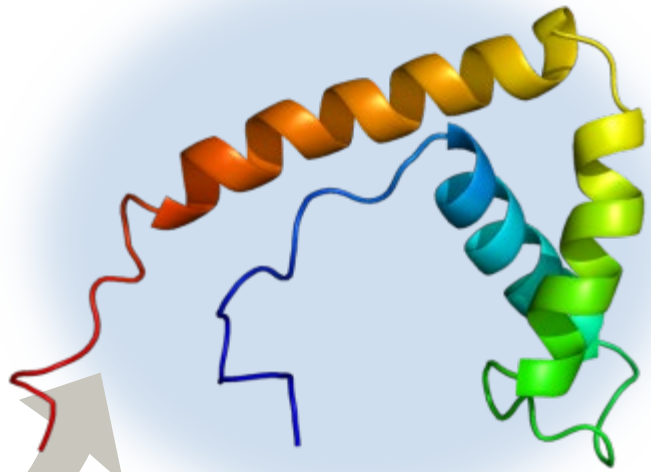



- An Important in vivo molecule that activate tissue regeneration

Prof. Katsuto Tamai
Osaka University

**Identifying the function of protein domains**

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



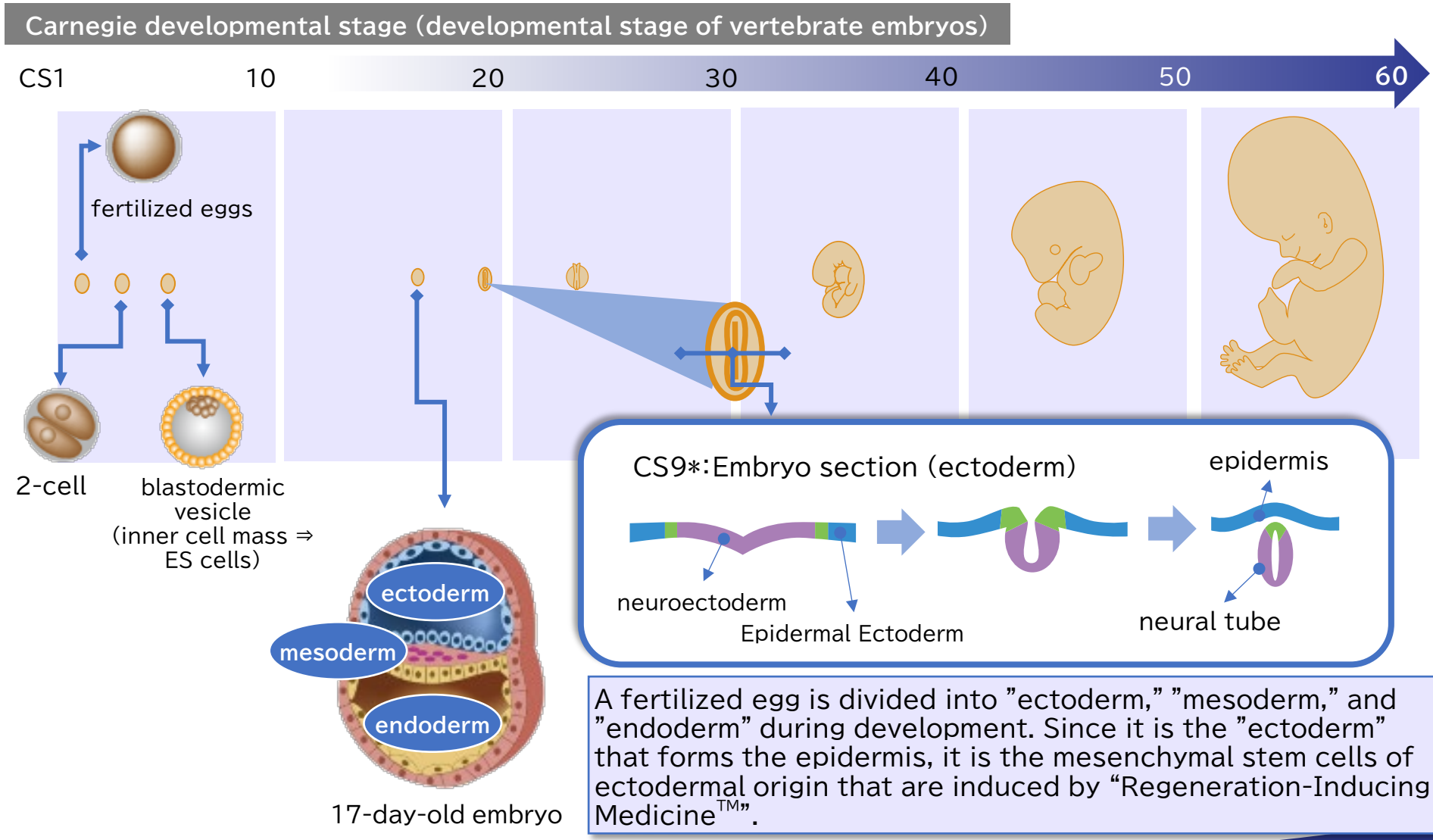
HMGB1 peptide drug excluding the domains causing side effects in HMGB1 protein

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

# 3 Advantages of “Regeneration-Inducing Medicine™”

# Advantages of “Regeneration-Inducing Medicine™”

## Epidermis formation during human development



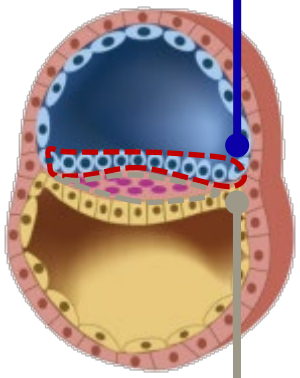

A fertilized egg is divided into ”ectoderm,” ”mesoderm,” and ”endoderm” during development. Since it is the ”ectoderm” that forms the epidermis, it is the mesenchymal stem cells of ectodermal origin that are induced by “Regeneration-Inducing Medicine™”.

# 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)

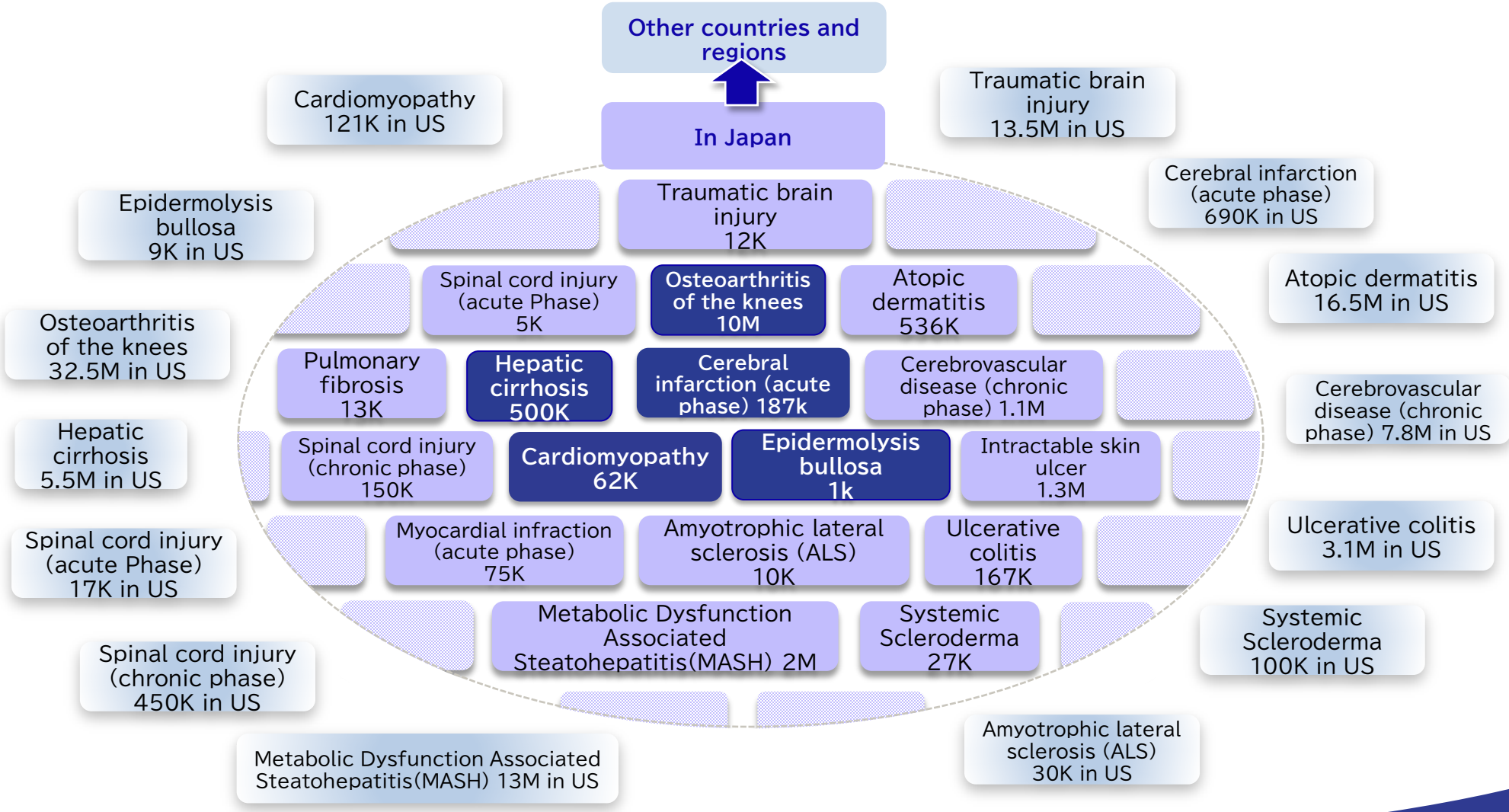
Differen-tiation

| | | |
|---|---|---|
| Bone | Cartilage | Fat |
| Blood vessels | Dermis | Muscle |
| Ligament | Heart | Others |

# Expanding Indications and Markets(Number of patients)

## Targeting all areas where mesenchymal stem cell therapy can be effective

:Clinical trial on going

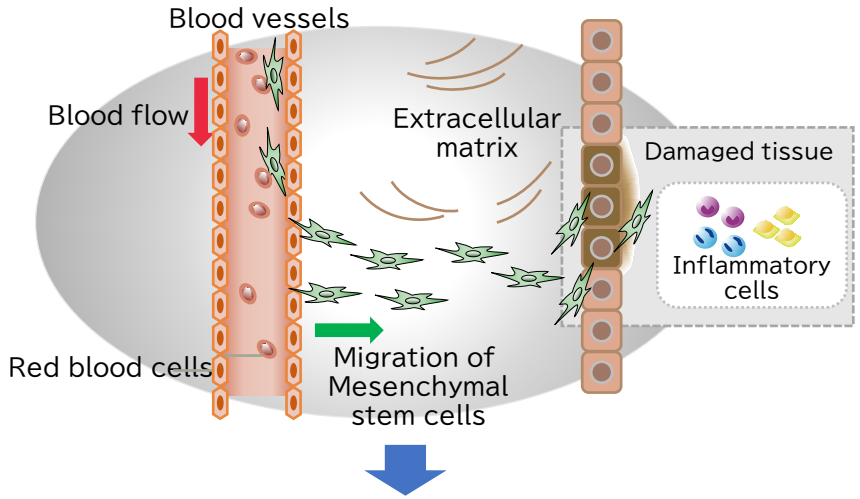


# Functions of mesenchymal stem cells

## In-vivo mesenchymal stem cells have 5 distinctive capabilities

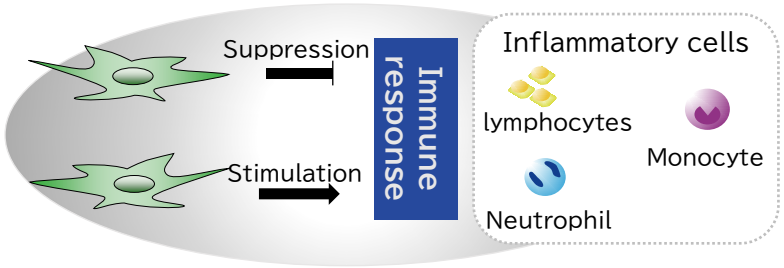
### 1. Cell migration ability

Mesenchymal stem cells migrate to damaged tissue via the bloodstream



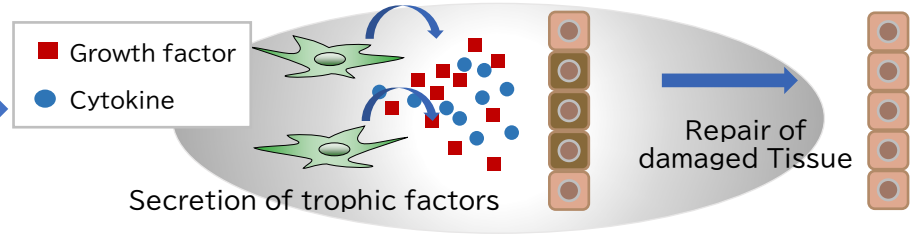

### 2. Immunomodulatory ability

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



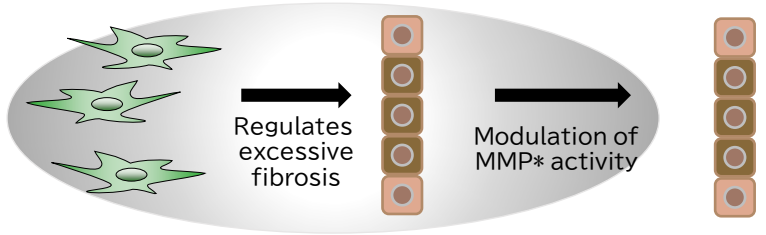

### 3. Trophic factor secretion ability

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



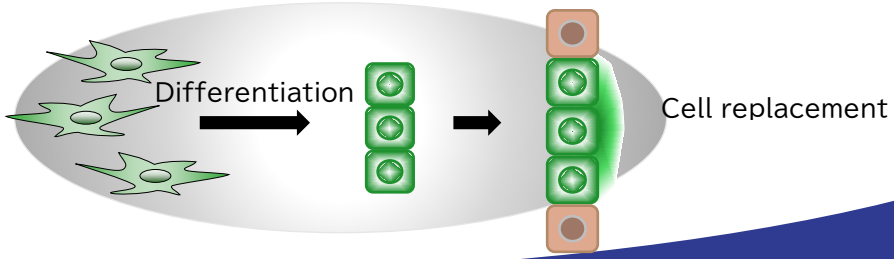

### 4. Fibrosis regulation ability

Regulates and inhibits excessive fibrosis of damaged tissue




### 5. Tissue regeneration ability

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

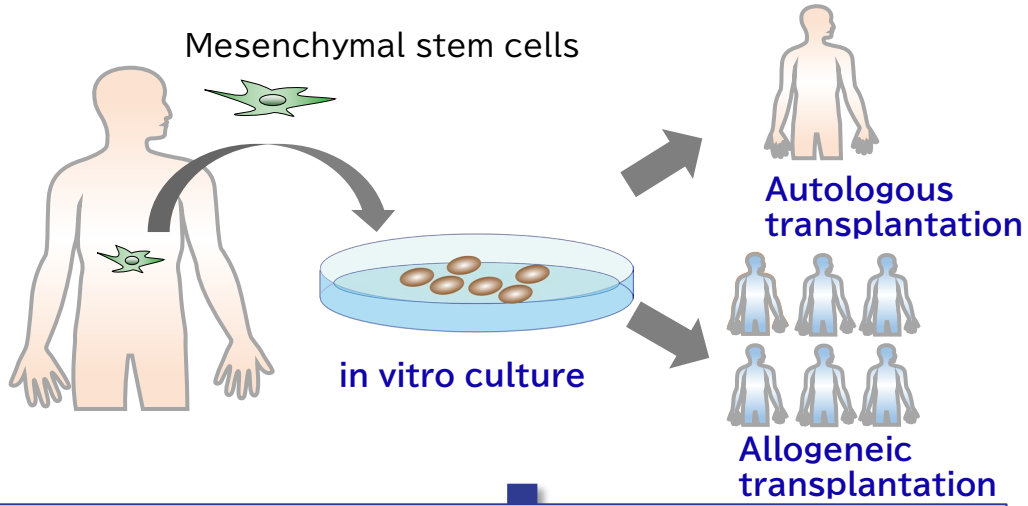



* MMP:Matrix metalloproteases

# In vitro culture reduces the functions of MSCs

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

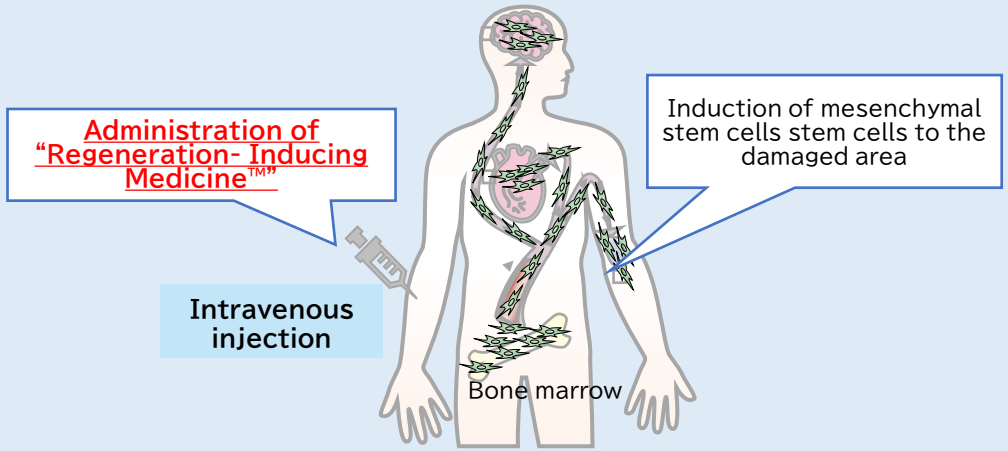
## Manufacturing process of conventional cellular medicine




**Mesenchymal stem cells lose their functions during in vitro culture**

Source: Stem Cell Research & Therapy2018,9:131


## Induction of MSC in “Regeneration-Inducing Medicine™”




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


**“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.

# 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 | Manufacturing |
| --- | --- |
| ■ Need to be frozen from CPC and other manufacturing facilities and transported with thorough quality control | ■ Need for mass culture with uniformity in cell properties<br>■ In the case of Allogeneic transplantation, the need for mass production while keeping costs down |

**These problems do not occur in “Regeneration-Inducing Medicine™”**

→ Product Transportation Advantages

→ Manufacturing Advantages

**Potential for global development “Regeneration-Inducing Medicine™”**

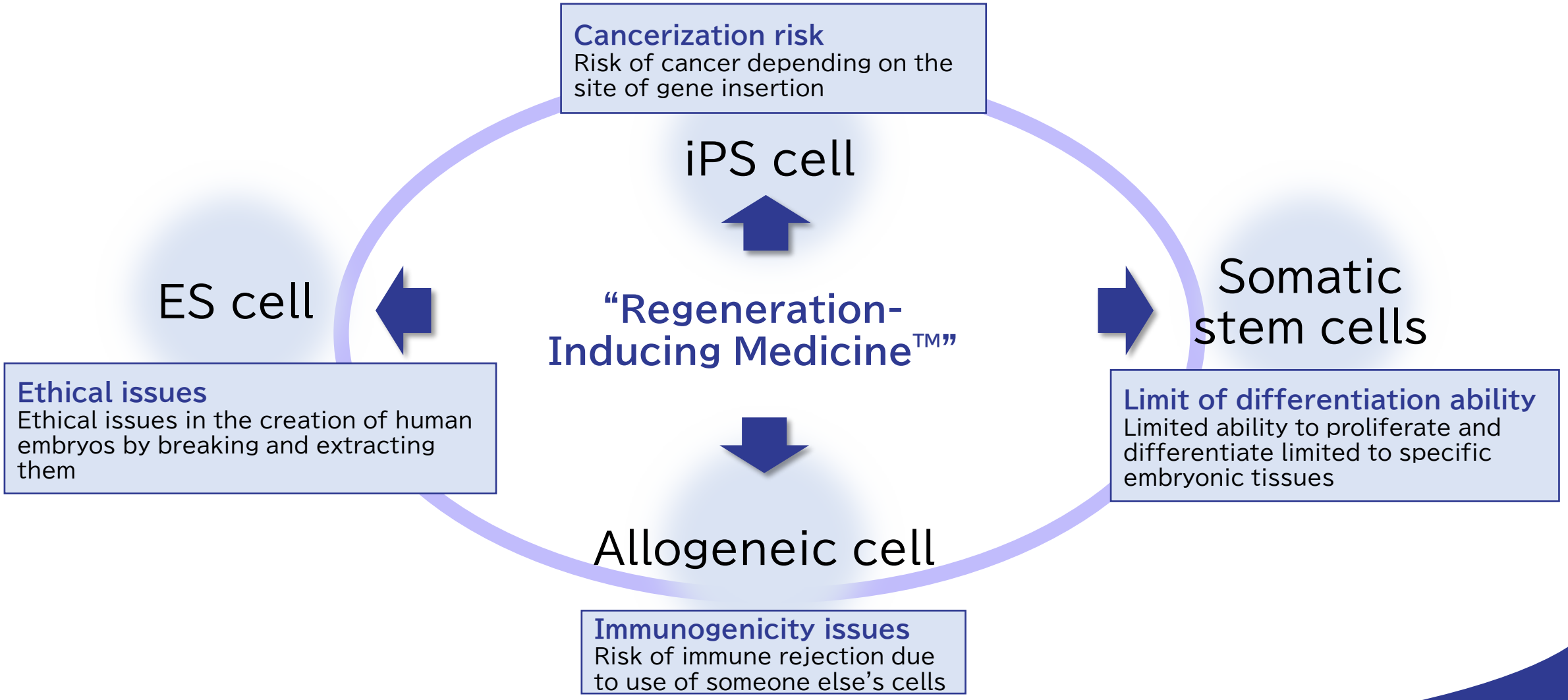
# Summary of advantages of “Regeneration-Inducing Medicine™”

“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 |

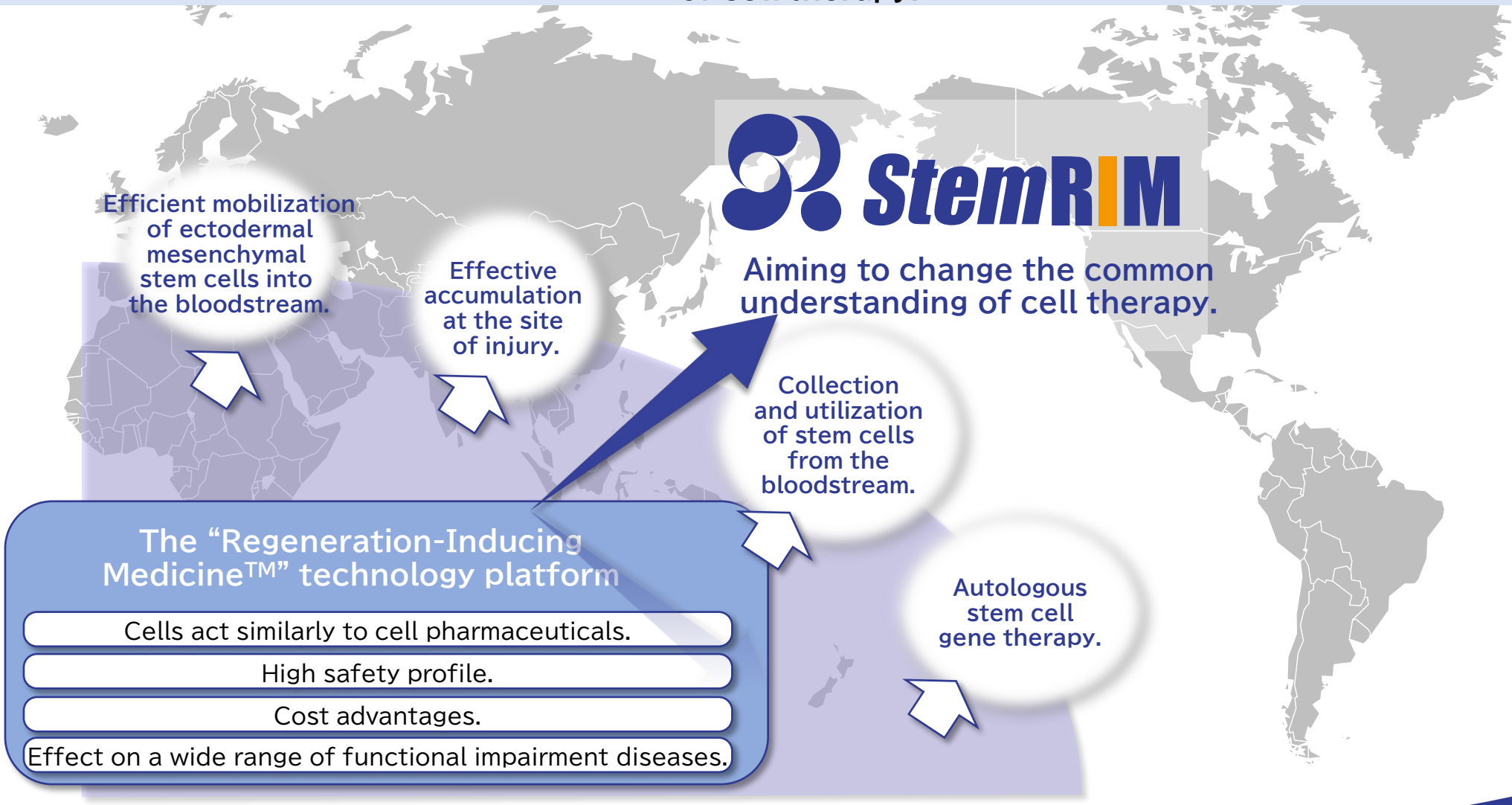
# Summary of advantages of “Regeneration-Inducing Medicine™”

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



# 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

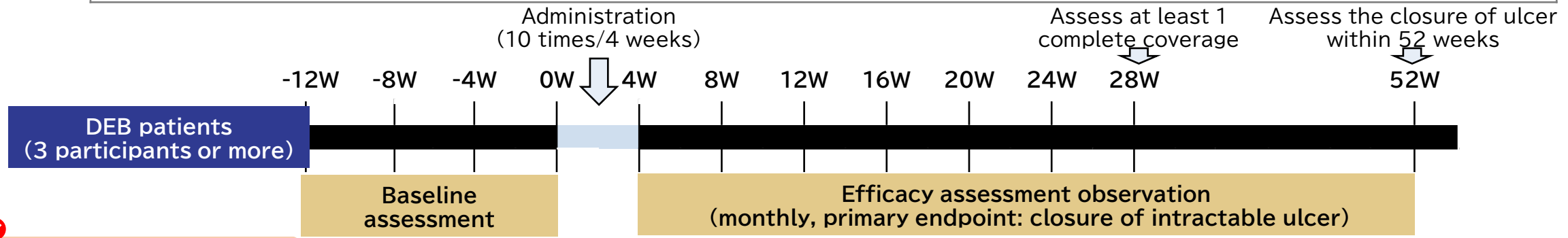
# Overview of Development Pipeline

| Project code | Development candidate | Indication | Investi-gator | Status | Development Stage | Out-license partner |
|---|---|---|---|---|---|---|
| PJ1 -01 | Redasemtide (HMGB1 cell mobilization domain peptides) | Epidermolysis bullosa | Shionogi & Co., Ltd. | Additional P2 Study **Ongoing** | Research / Pre-clinical / Phase 1 study / Phase 2 study / Phase 3 study: * | 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** | UPDATE; Start of physician-initiated phase 2 study | |
| 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 | ND | - |
| PJ5 | SR-GT1 (Stem cell gene therapy) | Epidermolysis bullosa | In-house (partnership is planned) | Under preparation for clinical trial | P1/P2 study; None | - |

* Application for approval is planed after Additional Phase2.

# 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: More than 3 participants |
| **Regimen** | 30-minute intravenous infusion once a day, total 10 times/4 weeks<br>[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 |




**Orphan Drug Designation**

In May 2023, the Ministry of Health, Labour and Welfare (MHLW) designated Redasemtide as an Orphan Drug (Orphan Drug) for the treatment of nutritionally impaired epidermolysis bullosa. The Ministry of Health, Labour and Welfare (MHLW) made certain evaluations on the possibility of the drug being effective for nutritionally impaired epidermolysis bullosa and the appropriateness of its development plan. The drug is expected to receive an early approval by shortening the review period by becoming eligible for the priority review system.Translated with DeepL.com (free version)

**Status**

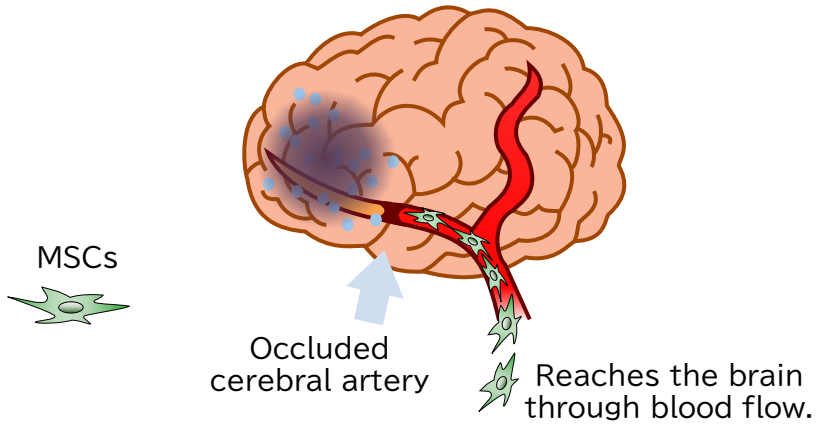
**February 2023: Initiated the administration to the first patient**

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

# PJ1-02:Redasemtide(Acute Ischemic Stroke)

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

## Acute Ischemic Stroke

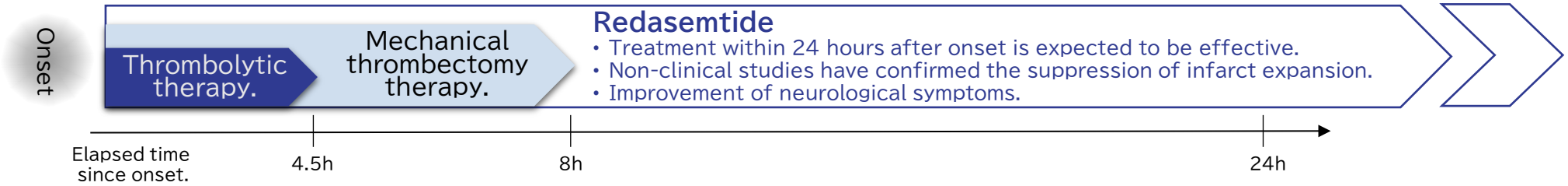



**Market Size in Japan**

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.



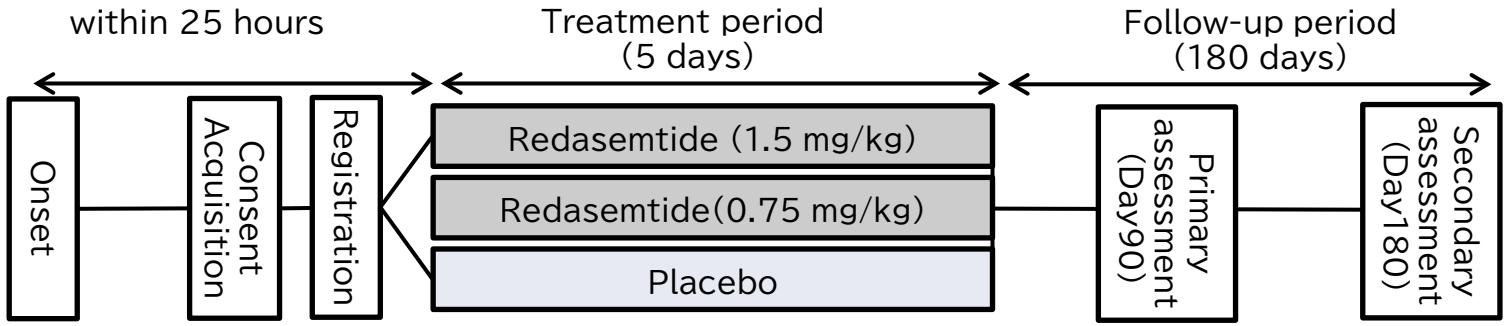

**Onset to 4.5 hours**
Thrombolytic therapy (t-PA intravenous therapy): A treatment method that dissolves clots and restores blood flow by administering a thrombolytic agent (t-PA).

**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.

# 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<br>・Baseline NIHSS score* between 8 and 22<br>・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**<br>**・Redasemtide (0.75 mg/kg) group**<br>**・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.** |



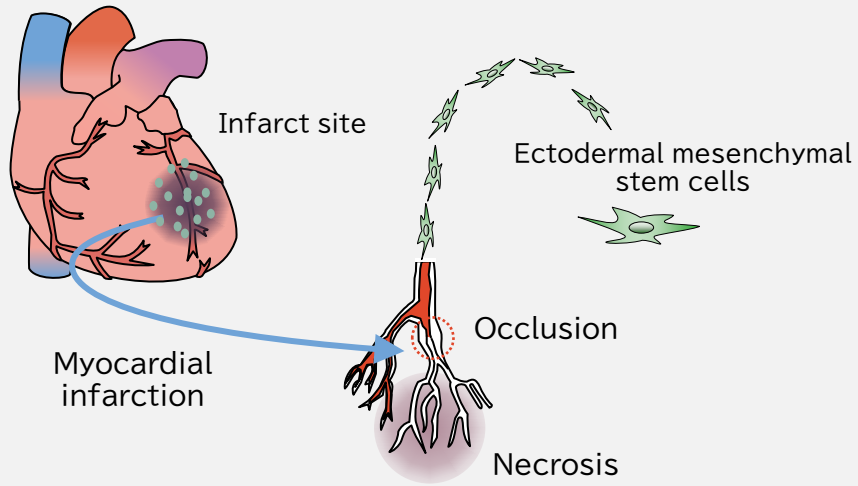

**Status**

**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

# PJ1-03:Phase 2 Clinical Trial in Ischemic Cardiomyopathy

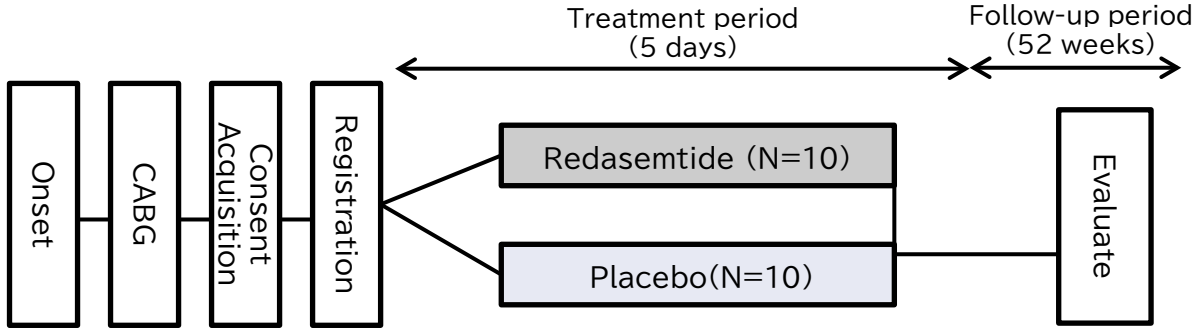
## Ischemic Cardiomyopathy




### 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<br>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**

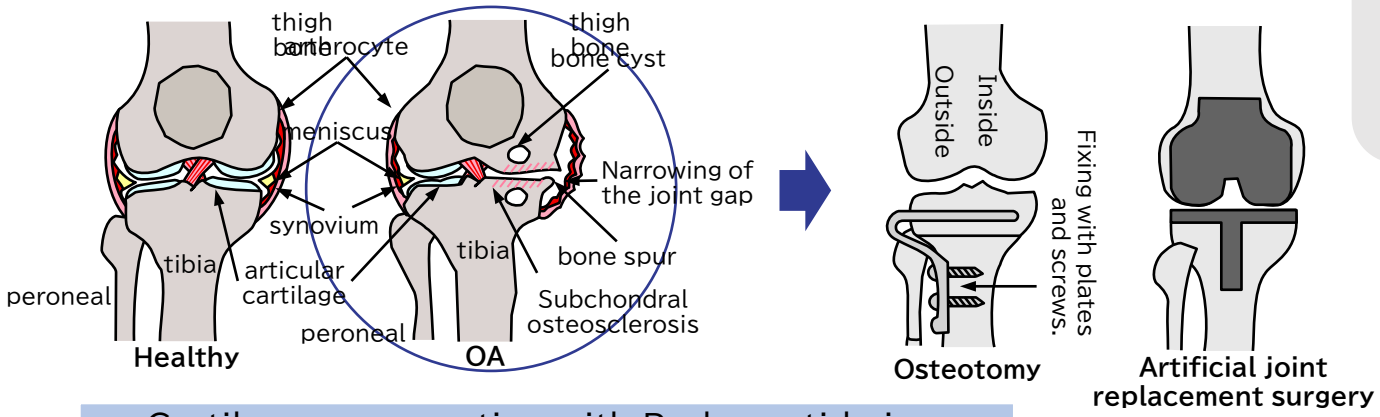
**March 2024:**
**Phase 2 Clinical Trial started in Japan**

*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).

# PJ1-04:Redasemtide(Knee Osteoarthritis)

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

## Knee Osteoarthritis(OA)



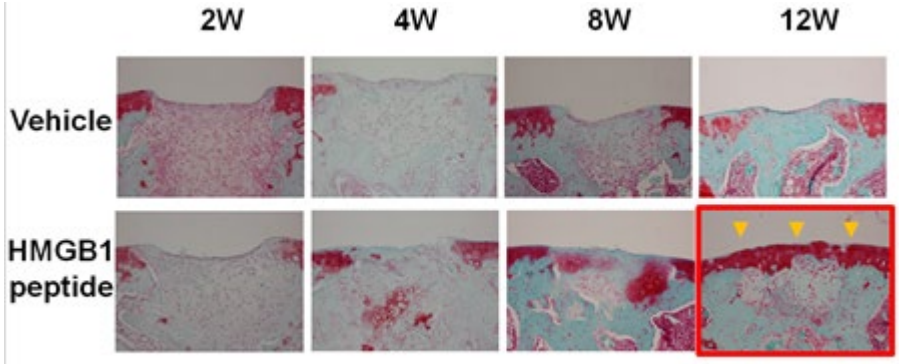

### Market size in Japan

・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 ▼)

### 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**

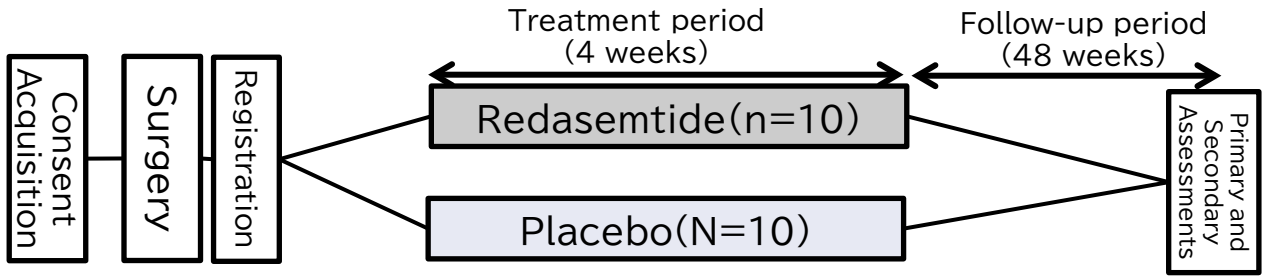
# PJ1-04:Redasemtide(Knee Osteoarthritis)

| 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<br>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**

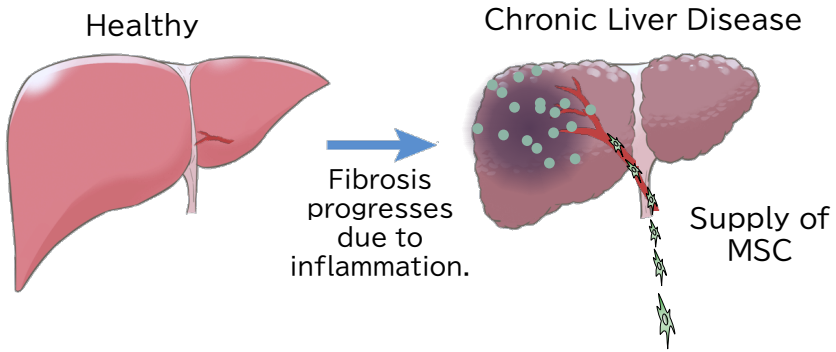
**Confirmation of the result that there are no safety issues in March 2023.**

* 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

# PJ1-05:Redasemtide(Chronic Liver Disease)

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

## Chronic Liver Disease



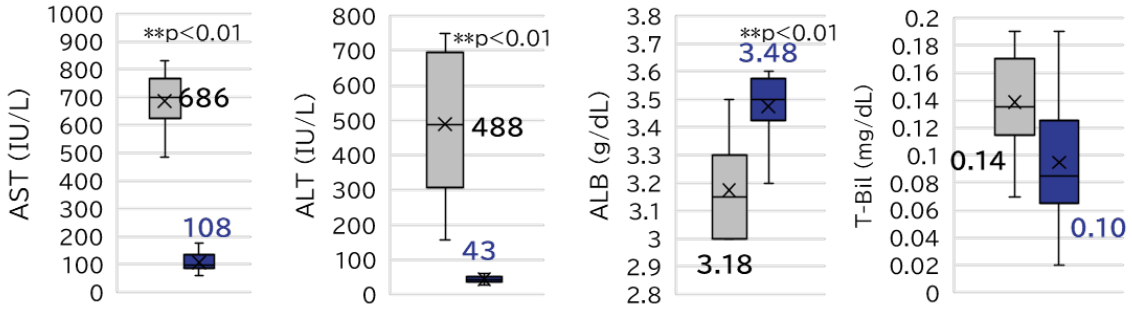

**Market size in Japan**

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

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.




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

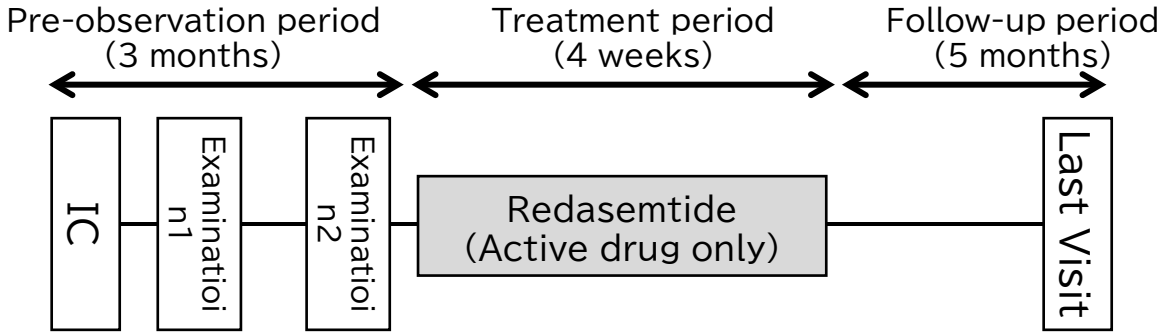
**Conventional treatment methods**

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.

# 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<br>•Cohort A: 4 times / 4 weeks [once a week]<br>•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 |




* 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

## 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.

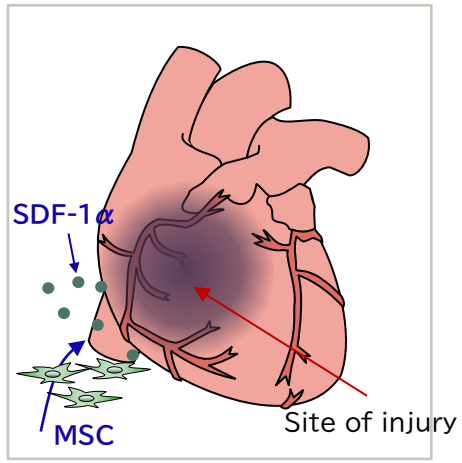
**Status**

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

# PJ3 Novel Regeneration-Inducing Peptide for Local Administration

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

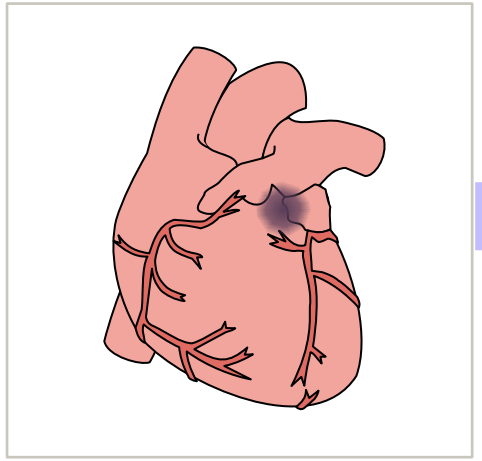
### Large injury




- SDF1-a is released, and mesenchymal stem cells mobilized in the blood accumulates at the injury

=Mechanism of action in PJ1, PJ2 is effective

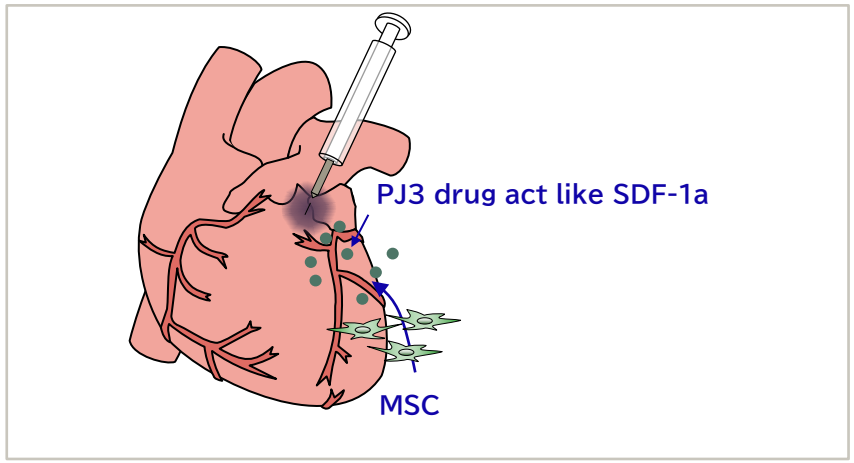
### Small injury or chronic phase



- 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 of PJ3 drug



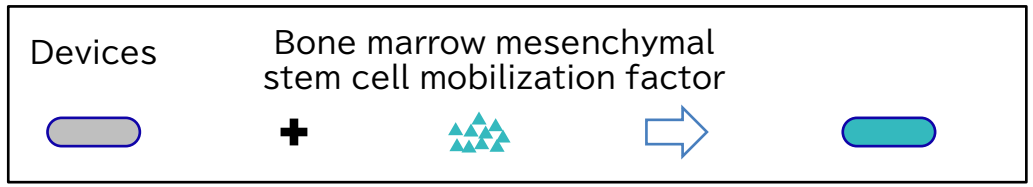

- Effective accumulation of mesenchymal stem cells at the site of injury by topical administration or intravenous injection

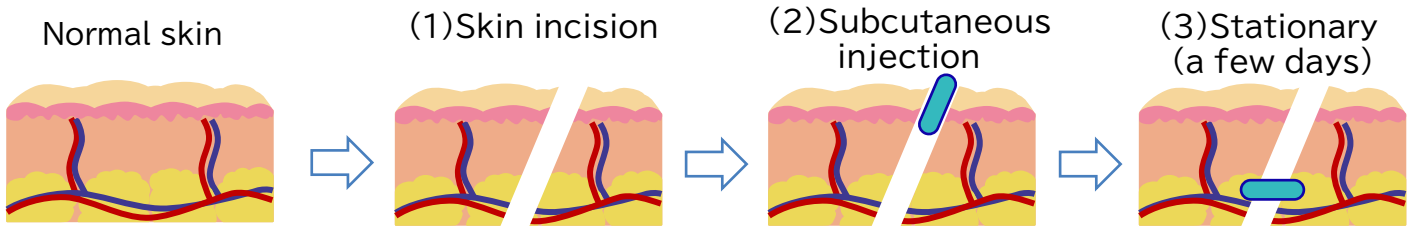
**=Maximize damage repair effect of mesenchymal stem cells**

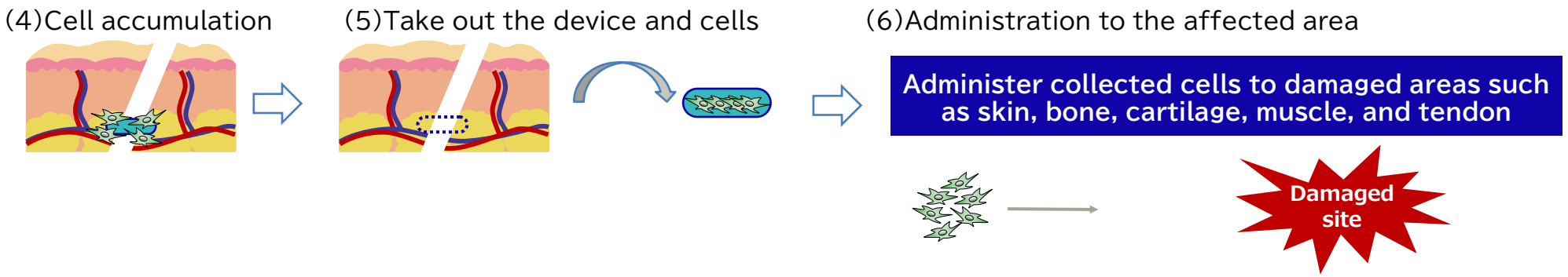
- ✓ Multiple candidate proteins have been identified so far
- ✓ Confirmed good results in animal experiments
- ✓ Currently, the most suitable indication is being selected through multiple animal model experiments

# PJ4 Autologous cell collection device for treatment

## Developing devices to collect mesenchymal stem cells mobilized in vivo



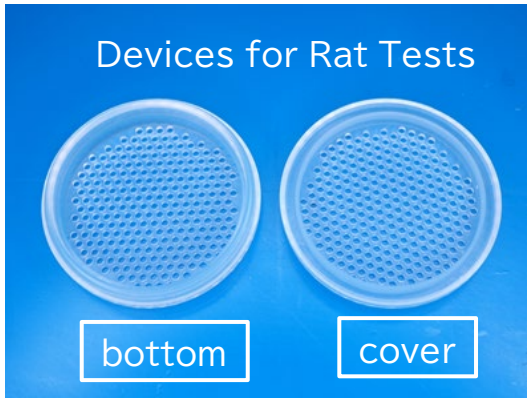




- ✓ Animal testing confirms that the device has good stem cell recovery capability
- ✓ The most suitable indication is being selected through experiments with several disease model animals
- ✓ Conducting non-clinical trials needed to start clinical trials

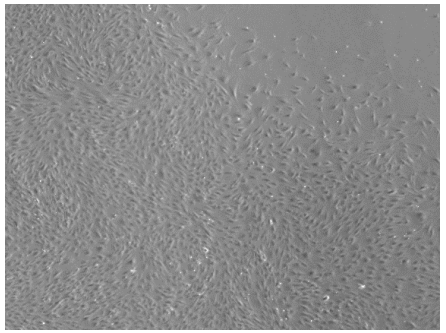
# PJ4 Autologous cell collection device for treatment

## Confirmation of mesenchymal stem cell harvesting in a rat model



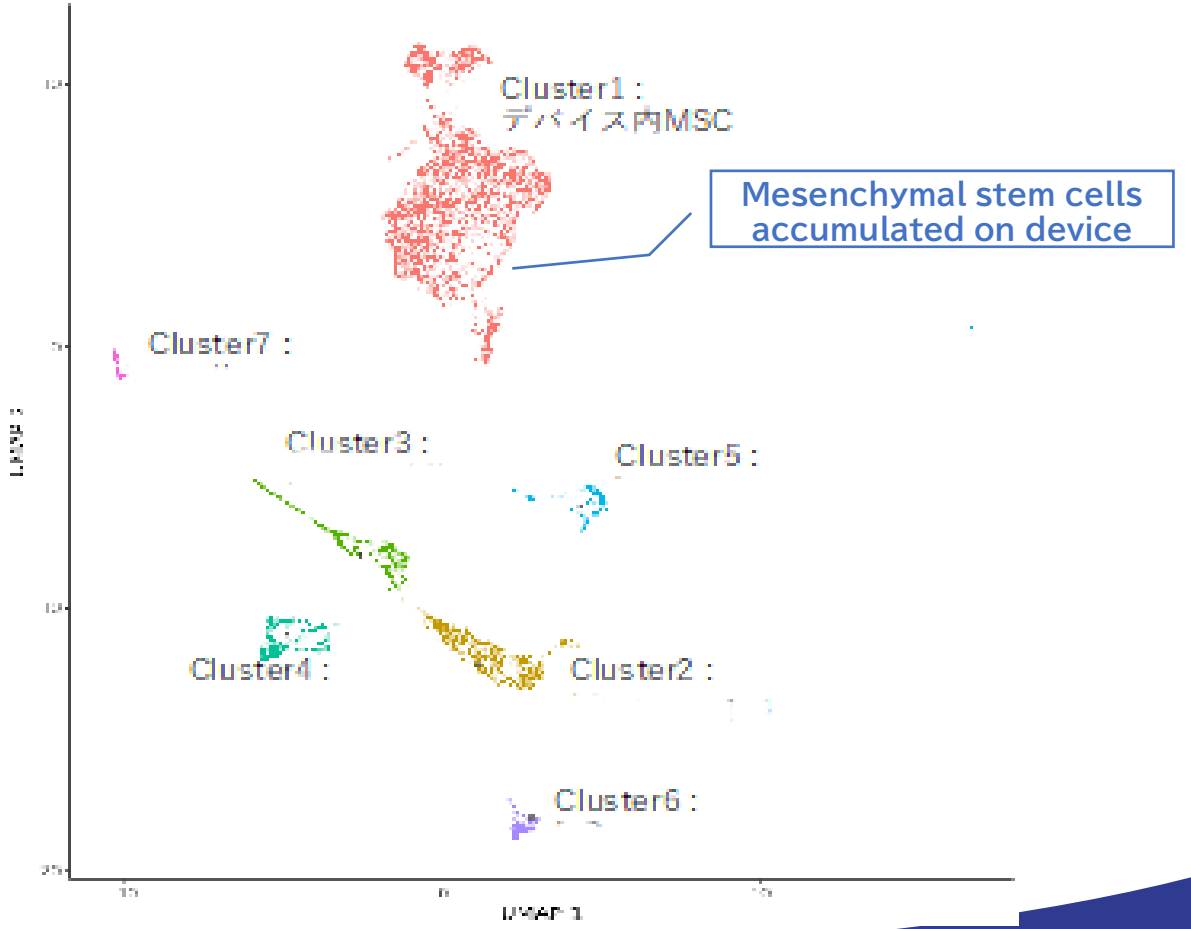

**Devices after cell harvesting**

Aggregated cell mass



Confirmation of the presence of MSC-like cells by culture of accumulated cells

**Single-cell transcriptome analysis by next-generation sequencers for cells accumulated on the device**

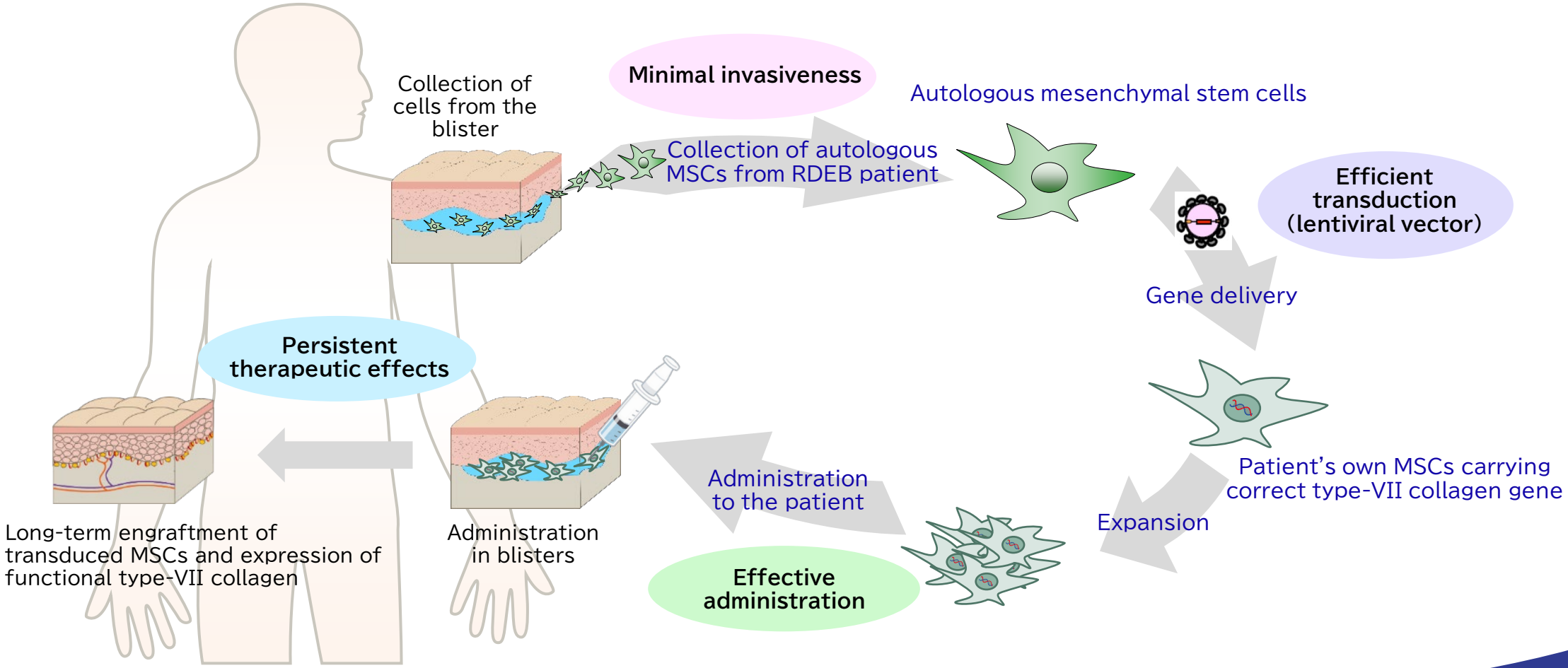


# PJ5 Stem cell gene therapy

## 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.



# PJ5 Stem cell gene therapy

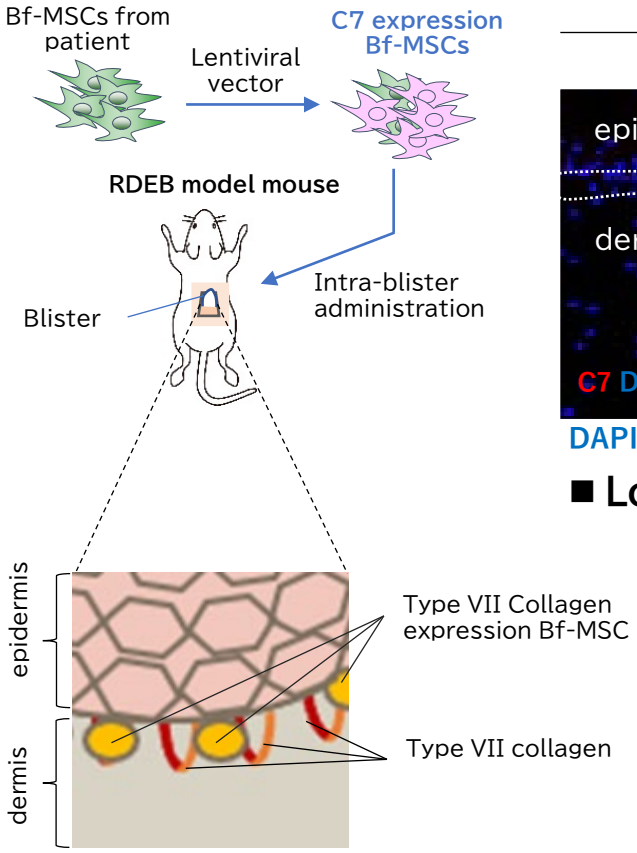
**Ex vivo gene therapy with minimal invasiveness, high efficacy, and persistent effect**
**This therapy employs a novel method of isolating Bf-MSCs from a patient, efficient delivery of functional type VII collagen gene to the cells, and novel administration method to the patient with minimal invasiveness.**

| Company | Brand, Generic or Code name | *in/ex vivo* | Target cell | Formulation | Administration route | Comparison with StemRIM | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 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 |

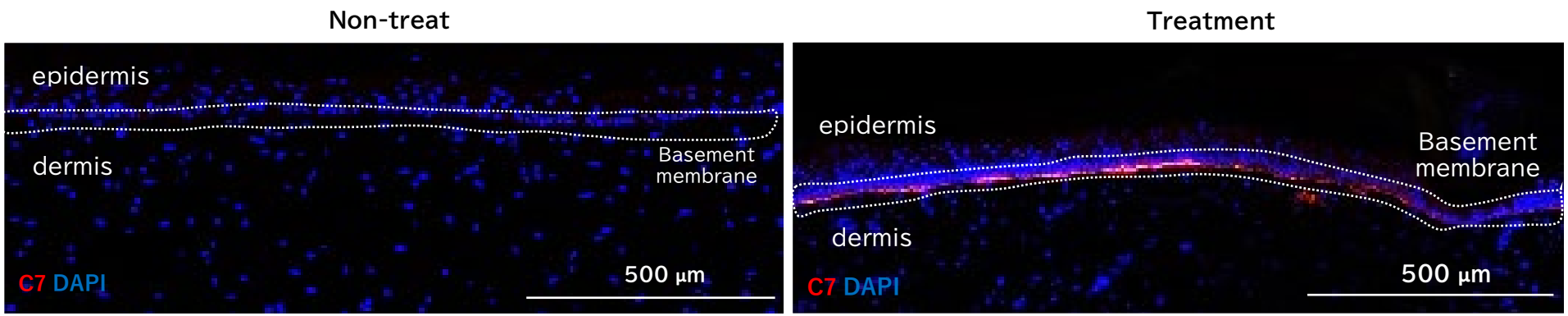
# PJ5 Stem cell gene therapy

## 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

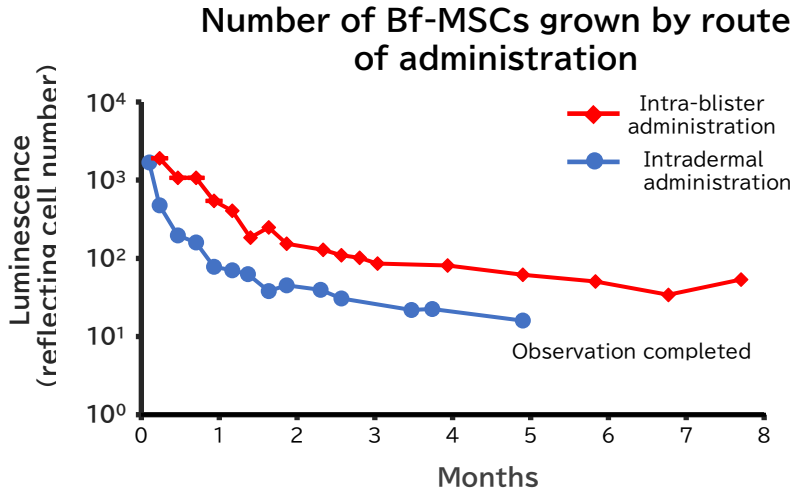



Skin tissue of RDEB model mouse after administration

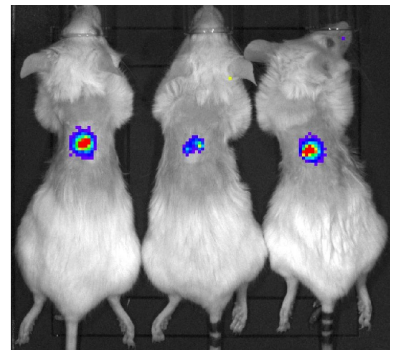



DAPI:

■ Long-lasting strong signal compared to the intradermal administration




Intra-blister (5 months)



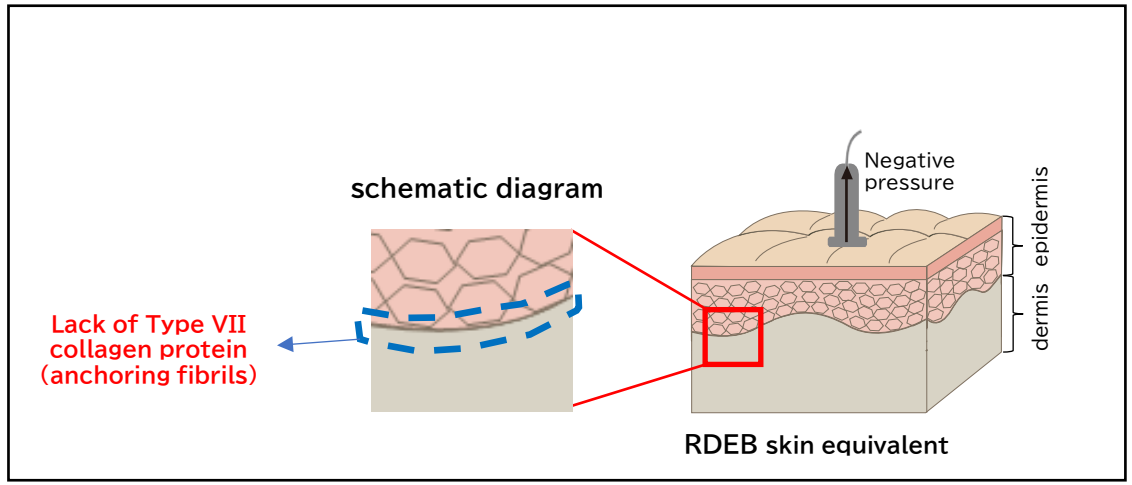
*Joint research between and Osaka University

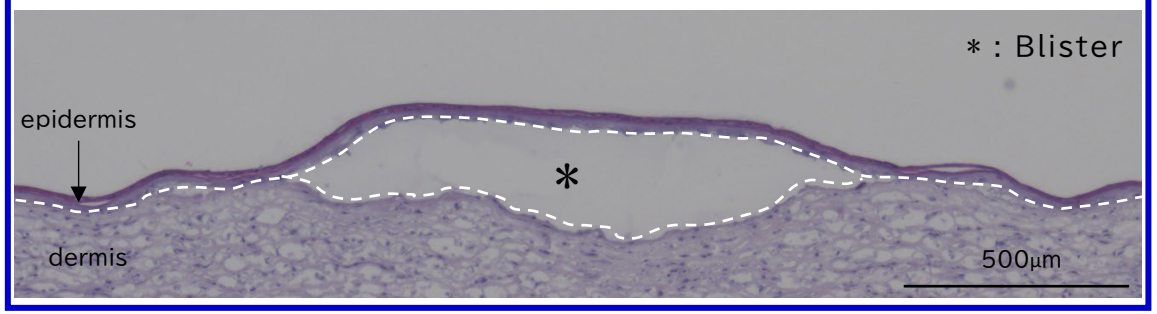
# PJ5 Stem cell gene therapy

## Therapeutic effects on RDEB skin model

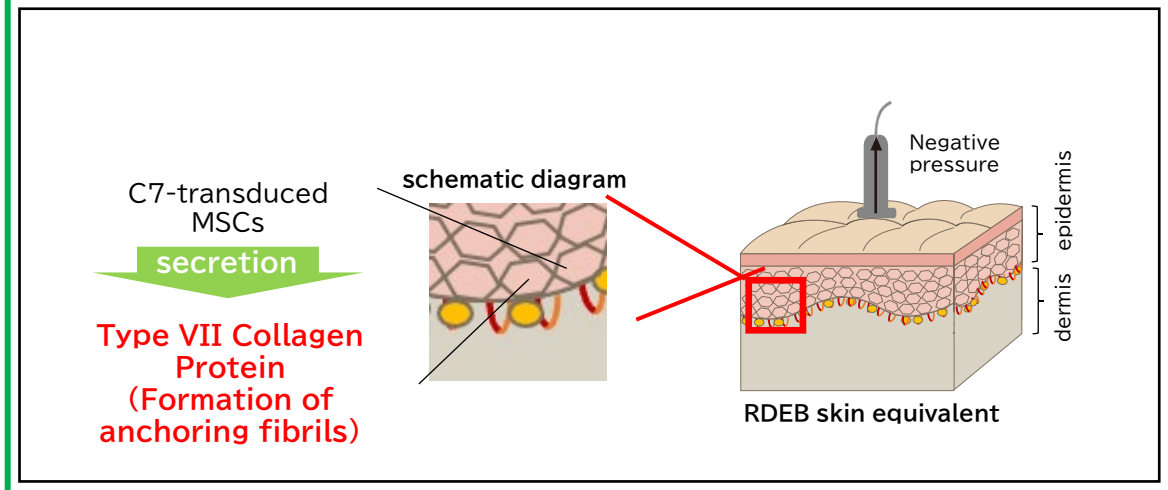
- We confirmed the effect of gene therapy using patient-derived Bf-MSCs by RDEB skin model and artificially forming blisters by suction method.

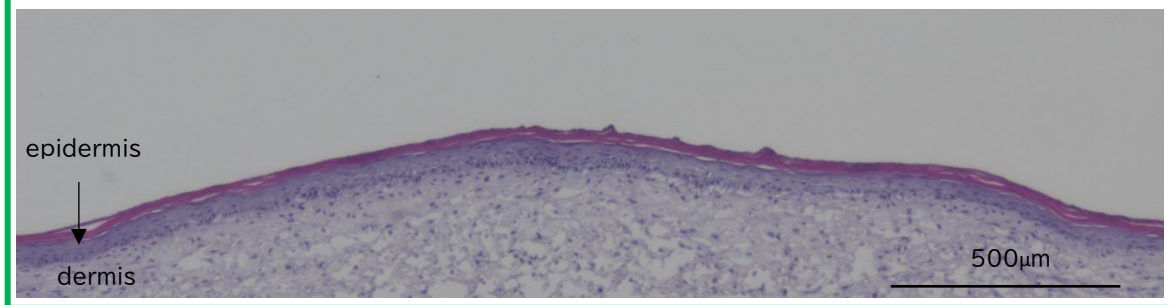
### RDEB skin equivalents




### RDEB skin equivalents with gene transduced Bf-MSC




Joint research between and Osaka University

# 5 Future Growth Strategy

# Future Growth Strategy

## Development of next-generation “Regeneration-Inducing Medicine™”

・Promote licensing activities for new compounds with significant activity in non-clinical trials.
・Expand business development activities with a global development perspective, not limited to domestic companies.

## Support for the development of Redasemtide.

・Continue support for ongoing clinical trials of Redasemtide and further advance joint research and development with Osaka University.

## Expansion of the development pipeline.

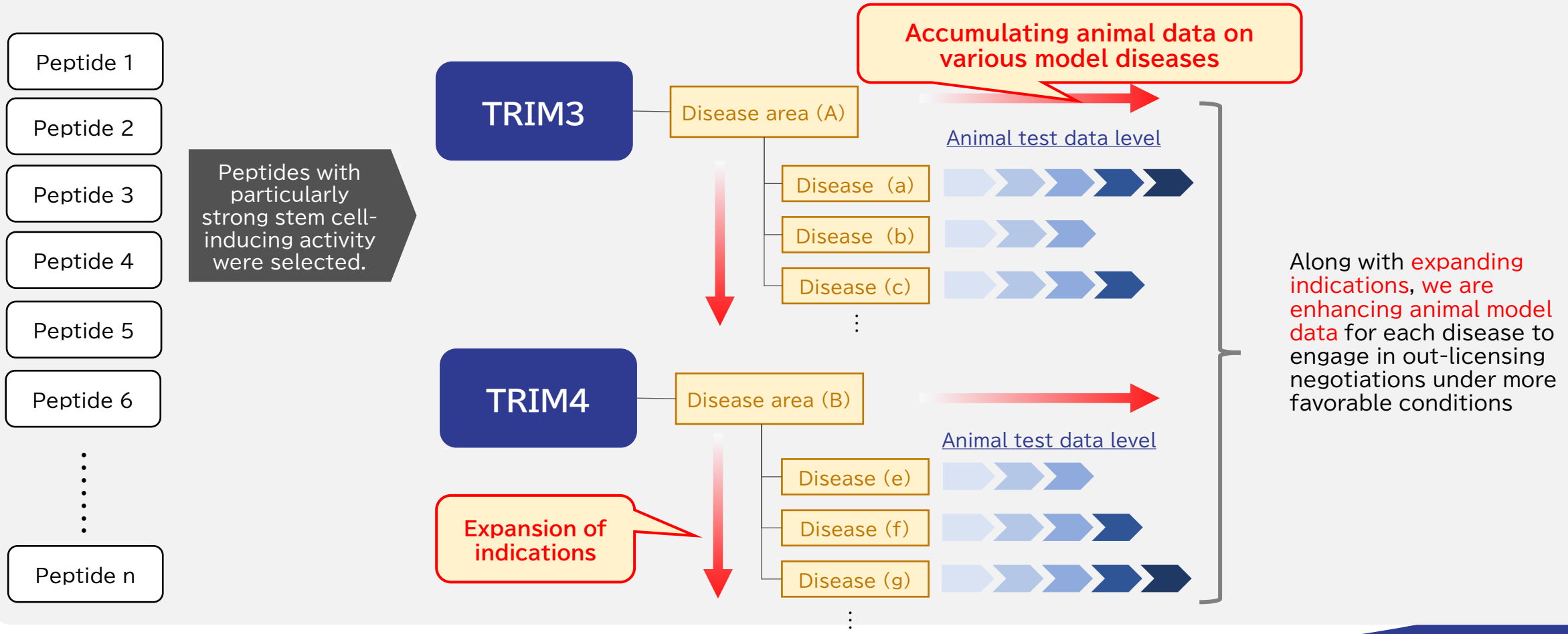
・Continue to identify multiple candidate compounds through rapid confirmation of animal efficacy and regulatory strategy planning.
・Conduct multifaceted non-clinical trials aimed at developing new “Regeneration-Inducing Medicine™” through collaborations with various universities at partnered research institutes.

## Maximizing the potential value of “Regeneration-Inducing Medicine™”.

**Aiming to be a game-changer in the field of cell therapy.**

# 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

# 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

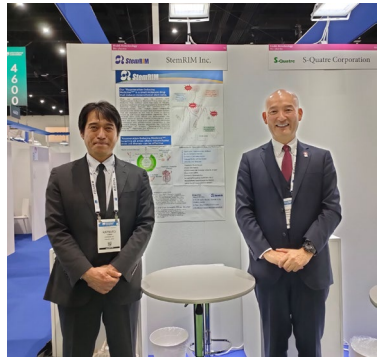
## FY 2023.7 Conference Participation

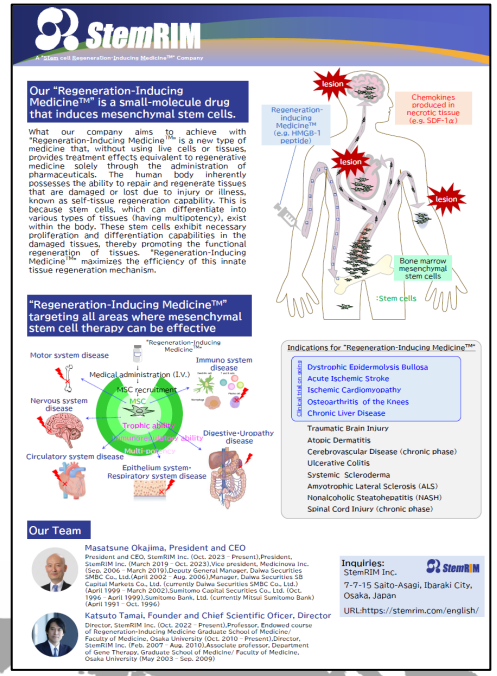
**BioJapan 2022**
2022.10.11~13 @Yokohama

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

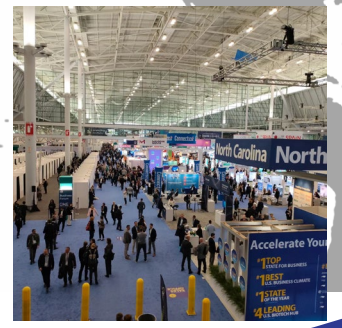
**41st Annual J.P. Morgan Healthcare Conference**
2023.1.9~12 @San Francisco, CA

**BIO International Convention 2023**
2023.6.5~8 @Boston, MA









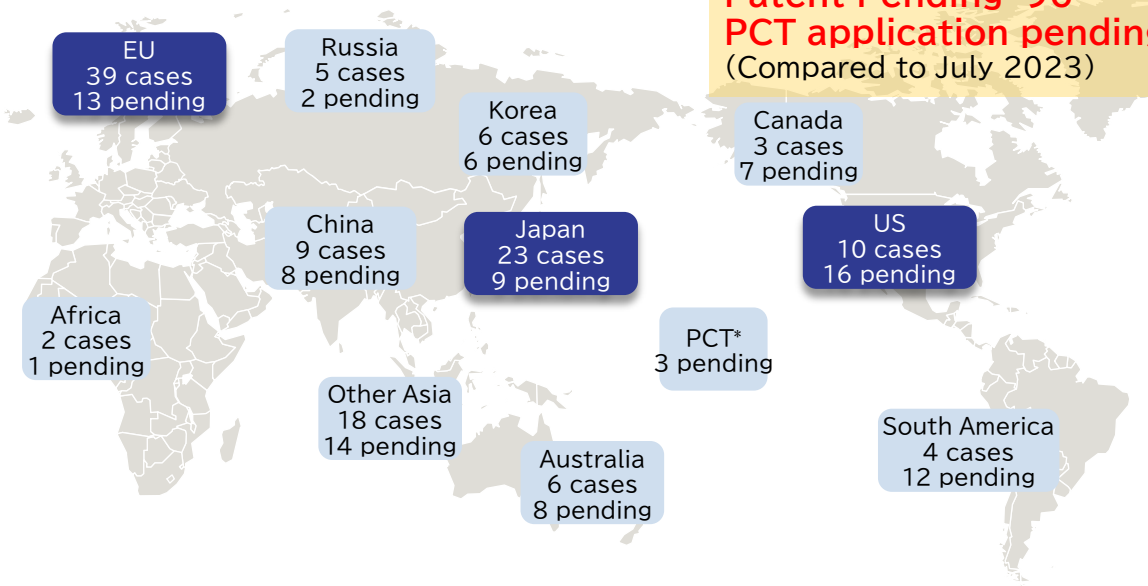

**Conducted out-licensing negotiations with several domestic and foreign pharmaceutical companies**

# IP Strategy

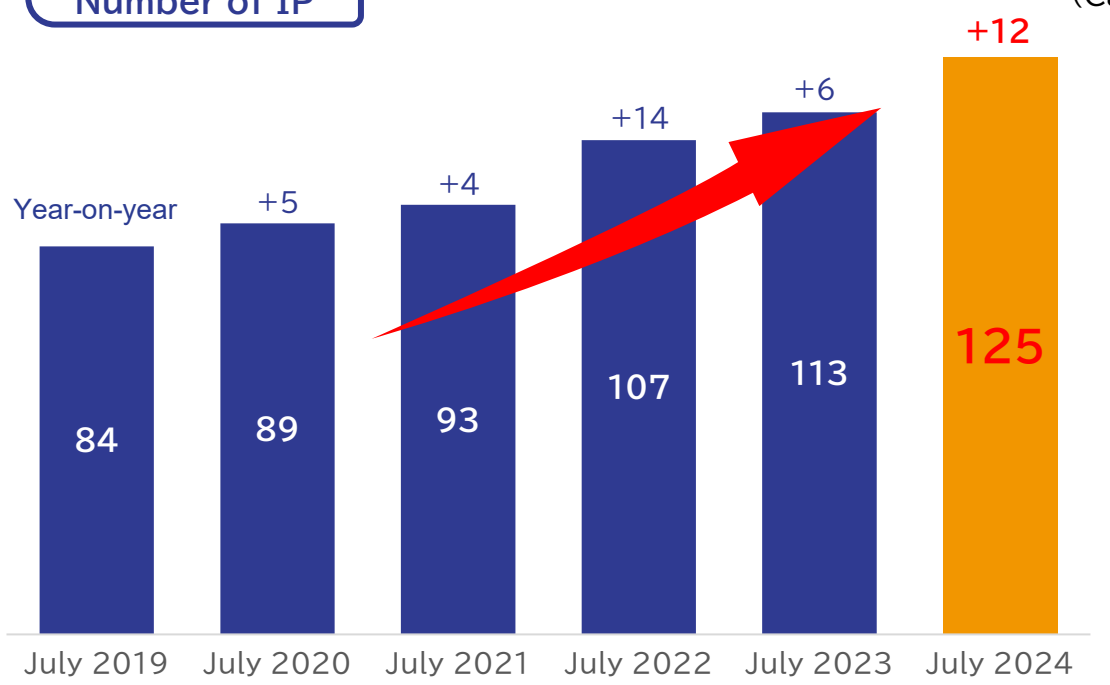
Patents related to “Regeneration-Inducing Medicine™” have been granted in various countries. We are steadily promoting the intellectual property protection of our research outcomes, paving the way for global expansion.

## 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

# 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/

# Pipeline Development Plan

**Given the long development timeline for pharmaceuticals, a pipeline development plan is formulated based on a long-term management vision.**

| Pipeline | Indication | Status | Development Schedule |
|---|---|---|---|
| PJ1 Redasemtide | Epidermolysis bullosa | Additional P2 Study Ongoing | Add. Phase 2 End → Application |
| | Acute Ischemic Stroke | Global P2b Study Ongoing | Global Phase 2b End → Global Phase 3 Start → Global Phase 3 End → Application |
| | Ischemic Cardiomyopathy | Physician-Initiated P2 Study Ongoing | Phase 2 End → Phase 3 Start (TBD*) |
| | Osteoarthritis of the knee | Physician-Initiated P2 Study Primary endpoint achieved | Phaes 2b Start (TBD*) |
| | Chronic liver disease | Physician-Initiated P2 Study Primary endpoint achieved | Phaes 2b Start (TBD*) |
| PJ2&3 TRIM3,4 | Multiple tissue damage diseases | Pre-clinical | Phase 1 Start |
| PJ4 Autologous cell collection device for treatment | Multiple tissue damage diseases | Pre-clinical | Phase 1 Start |
| PJ5 SR-GT1 (Stem cell gene therapy) | Epidermolysis bullosa | Under preparation for clinical trial | Phase 1/2 Start → Phase 1/2 End |

Current

This table represents our company's projections and does not guarantee progress as outlined.

*TBD: to be determined

# Forecast for the fiscal year ending July 2025

## Research and Development Progress for the Fiscal Year Ended July 2024

### Previous Disclosure (October 31, 2023)

**Research Progress Outlook for the Fiscal Year Ending July 2024**

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 Medicine™" following Redasemtide continue to advance.

**Cash Outflow Forecast for the Fiscal Year Ending July 2024**

| | |
|---|---|
| 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 2024**

A physician-led Phase II 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 2024**

| | |
|---|---|
| Cash Outflow for R&D | 1,266 million yen |
| Cash Outflow for General and Administrative Expenses | 263 million yen |

## Research and Development Progress Forecast for the Fiscal Year Ending July 2025

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 2025, so earnings projections are not disclosed.

**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 Medicine™" 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 |

# 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) |
|---|---|---|---|---|---|
| Stock issuance associated with new listing (August 2019) | 8,625 | Funds for establishing the "Regeneration-Inducing Medicine™" research institute and an animal testing facility | 7,195 | — | — |
| | | | (FY 2020) | — | — |
| | | Costs for promoting R&D for the existing pipeline and R&D for new pipeline development. | 1,430 | — | — |
| | | | (FY 2020) | — | — |

Change in Use of Funds Raised through Listing on November 11, 2021.

(Amount: million yen)

| | | | | | |
|---|---|---|---|---|---|
| Stock issuance associated with new listing (August 2019) | 8,625 | Funds for the establishment and maintenance of the "Regeneration-Inducing Medicine™" research institute and an animal testing facility. | 3,153 | 1,949<br>[Breakdown]<br>Establishment Costs 940<br>Maintenance Costs 1,009 | 1,204 |
| | | | (FY 2020 to FY 2030) | (FY 2020 to FY 2024) | (FY 2025 to FY 2030) |
| | | Costs for promoting R&D for the existing pipeline and R&D for new pipeline development. | 5,471 | 2,828<br>[Breakdown]<br>Outsourcing Costs 512<br>Research Material Costs 943<br>Collaborative Research Costs 1,372 | 2,642 |
| | | | (FY 2020 to FY 2026) | (FY 2020 to FY 2024) | (FY 2025 to FY 2026) |

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.

# 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.

## 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.

## 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

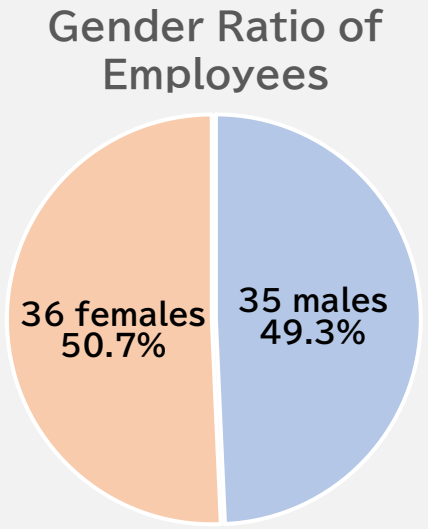
**Development of Various Systems, Including the Promotion of Paternity Leave for Men, Maternity and Childcare Leave, Leave of Absence, and Shortened Working Hours Programs**
This contributes to the promotion of women's empowerment and the strengthening of organizational capabilities.

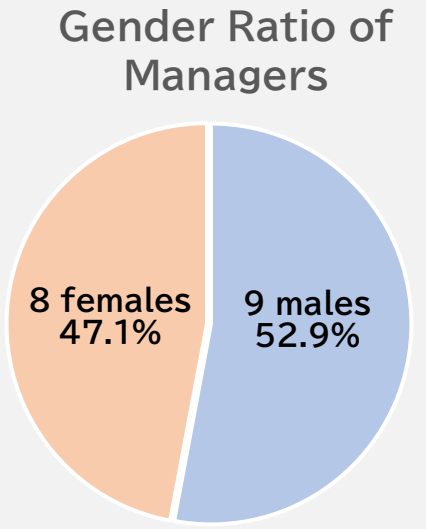
**Introduction of Online Mental Health Counseling**
This contributes to the early detection and prevention of employees' mental health issues.

### 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)



# 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 in Regeneration-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.

# 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.<br>・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.<br>・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.<br>・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.<br>・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.<br>・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

## 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)

### Katsuto Tamai, Founder, Director

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 (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

# 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<br>*In-house patent attorney and pharmacist<br>*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.<br>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. |

# Disclaimer

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*The next disclosure is scheduled for around October 2025.*