Company Presentation

May-June 2023

Cuorips, Inc.

Company outline

Name of the firm	Cuorips, Inc.
Date of incorporation	March, 2017
Accounting year-end	March
CEO	Takayuki Kusanagi
Head office	Chuou-ku Tokyo, Japan
Research and manufacturing sites	Osaka Lab Suita City Osaka Senri Research Center/Manfacturing Plan t （CLiC-1） Minoo City Osaka
Our business line	Development and commercialization of iPS derived Cardiomyocite Patches and CDMO business
No of board of directors	9
No. of employees	44 (as of February 2023)

What is a human iPSC derived cardiomyoc y te patch ?

Human iPSC derived cardiomyocyte Patch is a regenerative therapy for patients with severe heart failures. These patients have tried all available internal medicine with limited results. Our product targets these patients. These patches are made from differentiation of iPSC cells into cardiomyoc y te on a large scale and creating them in a patch form using our proprietary technology. Through joint research with Osaka University's Department of Future Medicine Division of Health Science (Dr. Sawa) and Kyoto University's iPSC Research Institute (Prof. Yamanaka), we seek to commercialize these products. By placing these patches onto the surface of the heart suffering from ischemia, abundant supply of cytokine is released from these patches into the myocardium. These cytokine will improve the blood circulation and hence the heart function will recover. In addition, cardiomyocyte contained in the patches will expand and contract simultaneously with the patients' heart muscle and will assist recovery of the heart function.

We are conducting clinical trials in Japan, evaluating its safety and efficacy.

Investment Summary

Global Front-runner in commercialization of iPSC related products by linking R&D of Academia and Pharmaceutical Companies

1 Wide range of Network, Knowledge and Experience of Our CTO Dr. Sawa who is a global authority in cardiovascular surgery

Dr. Sawa created an appropriate Clinical trial design in the commercialization of iPSC derived cardiomyocyte patches. Close contact with influential hospitals and doctors. Strong relationship with global famous research institutes, enabling the firm to create global network of research and abundant number of partner firms.

2 Worlds' most advanced clinical trials in iPSC cells

All transplants necessary for the clinical trials have been completed. Accumulating safety and efficacy data.

3 Manufacturing sites for commercialization

The company has manufacturing sites, a must for expansion of regenerative therapeutic products.

4 Growth potential not limited to iPSC-derived cardiomyocyte patches

Possesses other pipelines other than iPSC derived cardiomyocyte patches

Achievements of Dr. Sawa, and the company and brief history of regenerative therapy

Under the leadership of our CTO Dr. Sawa (Prof. Emeritus Osaka University), we have made significant progress in the field of curing heart failures using iPSC.

2000	Osaka University started research with Tokyo Women's University using patches for regenerative therapy of heart failures.
2006	Dr. Yamanaka of Kyoto University succeeds in creating iPSC.
2007	Started research using patches from myoblasts Dr. Yamanaka succeeds in creating human iPSC.
2008	Osaka Univ. started joint research with Kyoto Univ. Receives iPSC from Kyoto Univ. Succeeds in differentiation from human iPSC to cardiomyocyte cells.
2012	Confirms efficacy using large animals (pigs) and releases research papers. Starts clinical trials to severe heart failure patients using myoblast patches.
2013	Receives grant from AMED
2015	Receives clinical grade cell lines from Kyoto Univ. Starts discussions with PMDA regarding manufacturing and non-clinical safety tests (※Receives approval for myoblast heart sheets (Terumo's product) from the PMDA)
2016	Creates master cell bank for clinical grade iPSC
2017	Starts clinical research of iPSC derived cardiomyocyte patches to severe heart failures
2019	Files an application of investigator led clinical trials using iPSC derived cardiomyocyte patches
2020	Started the above trials to the first patient

Saving patients through combination of best science and practice

No. of heart surgery over 1,000

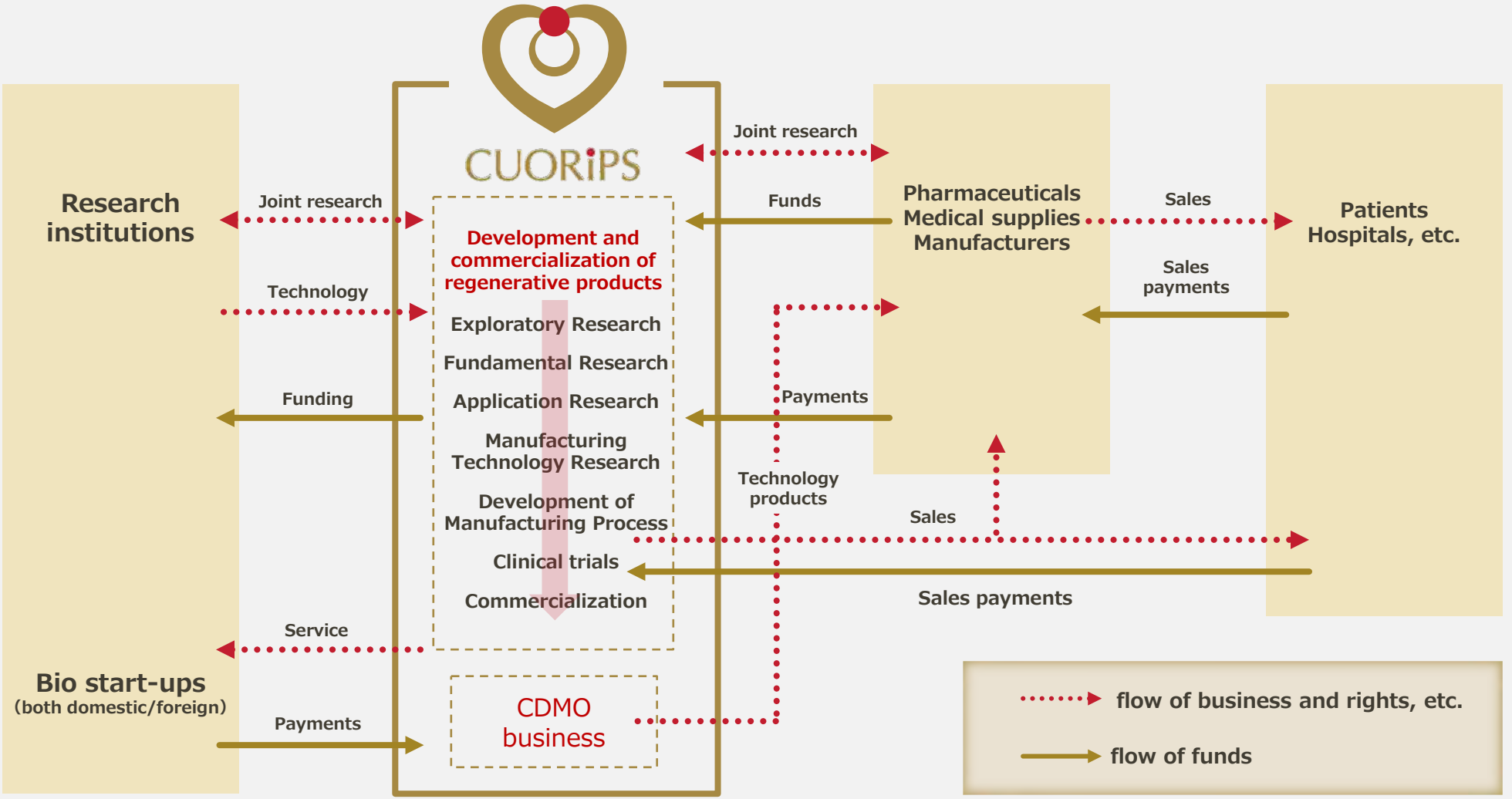
Heart transplants over 100

No. of VADs over 400

Business Model

Our business model

We have established close relationship with academia and pharmaceutical companies.



Our ultimate profit profile

Through stable cash generating business such as CDMO, etc., we want to limit downside risk and provide huge upside from marketing of innovative new products

Proprietary research model

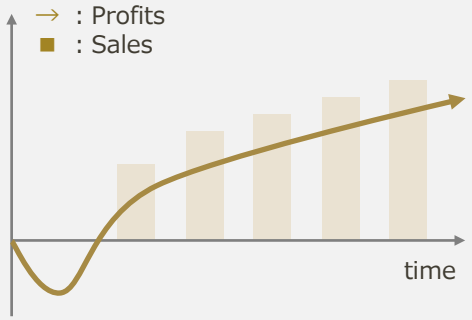
◎ Huge growth after government approval

△ Difficult to achieve break-even early

▼

High degree of business risk

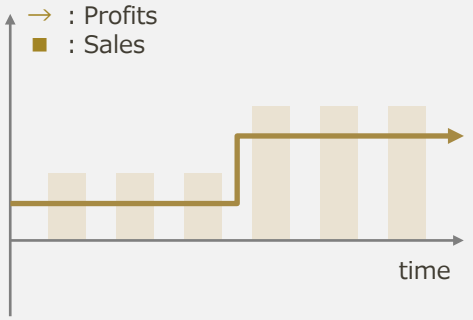
Joint research model ＋ CDMO model



◎ Break-even achieved early

△ Upside may be limited

▼



◎ Stable income

△ Upside limited

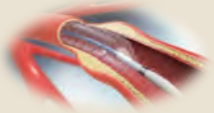
▼

By combining the two profit profile
We can realize stable cashflow early

Cuorips' hybrid platform model

Our business portfolio

Diverse set of pipeline and products

	Product	Details
Cell therapies	iPS Cardiomyocyte Patches 	• **Cardiomyocyte patches for severe heart failures** • **Indication** ＜ICM＞Ischemic Cardiomyopathy： Severe cardiomyopathy caused by a narrowing of the coronary arteries which supply blood to the heart ＜DCM＞Dilated Cardiomyopathy: heart muscle disease that causes the heart chambers (usually the left ventricles) to become thin, stretch and grow larger. No cure except heart transplants
	Catheters 	• **Providing cell therapies using catheter delivery to heart failure patients** (can be used by cardiovascular internal doctors) • **Indication** Acute myocardial infarction, coronary occlusion, chronic total occlusion
Others	Regeneration inducing factor s (YS series)	• **Repair of injured organs and tissues using prostaglandin induced regenerative factors** • May be applicable to different organs（kidney、liver、lungs, etc.）
CDMO		• **Innovative manufacturing site with research lab（CLiC-1）** • CDMO to bio-ventures and consulting services to start-ups

Current status of our pipelines

Clinical transplants for our 1st indication, Ischemic Cardiomyopathy has been completed

	Name	Indication	Research	Non-clinical	Clinical trials	Current status	Partners
Cell therapies	iPSC derived Cardiomyocyte patches	1st Pipeline (ICM)				Cohort B Completed	Osaka Univ. Dai-Ichi Sankyo
		2nd Pipeline (DCM)				Investigator led clinical trials to begin at Osaka Univ. this year	Osaka Univ. Dai-Ichi Sankyo
		Global ICM				Preparation for joint research program	U.S. institution
	Catheters	AMI CTO				Joint research and development with Asahi Intecc	Asahi Intec
Others	Regeneration inducing factors	Liver Cirrhosis NASH ASO, etc.				Pre-Clinical trials	NA

※Clinical trials for ICM cardiomyocyte patches are made of two stages Cohort A and B. As of March 2023, all trials under Cohort A and B is completed.

CLiC-1(Cuorips Labo-integrated Cell Processing Facility for Advanced Therapy-1st)

Manufacturing site combined with research lab. Construction through unique architecture and our unique concept. Unlike most bio-start ups, we have our own manufacturing site, which is one key source for our differentiation strategy.

Our pipeline

We can manufacture our own pipeline at CLiC-1
We are considering other business using this facility

CDMO operation

We can provide CDMO services to other Bio-start ups at CLiC-1

We can provide one-stop service ranging from manufacturing process development, actual production and quality control of regenerative therapeutic products and other cell products. We will also provide CDMO and consulting services.

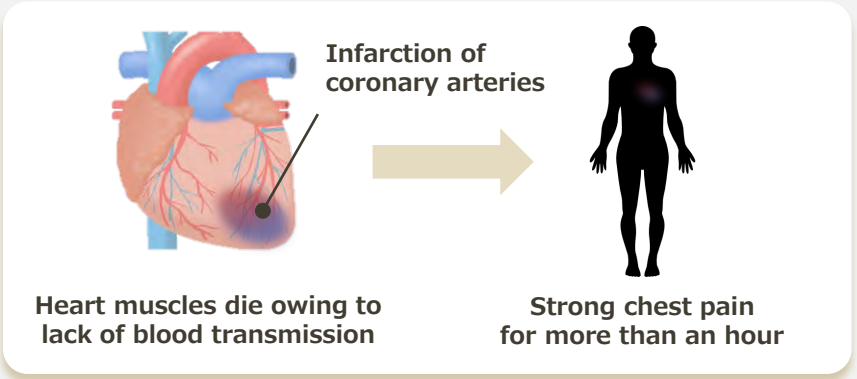
Cell therapies
(iPSC Cardiomyocyte patches)

Indication of our products

Indication of our iPSC derived Cardiomyocyte patches: ICM (ischemic cardiomyopathy)
DCM (dilated cardiomyopathy)

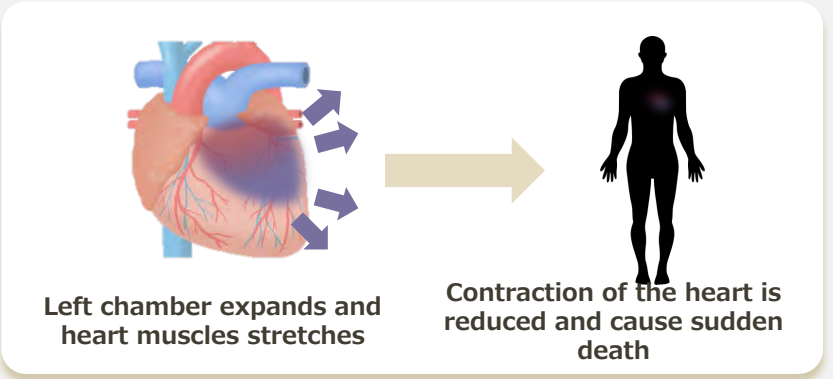
Ischemic cardiomyopathy (ICM)

severe cardiomyopathy caused by a narrowing of the coronary arteries which supply blood to the heart



Dilated cardiomyopathy (DCM)

heart muscle disease that causes the heart chambers (usually the left ventricles) to stretch, become thin and grow larger.



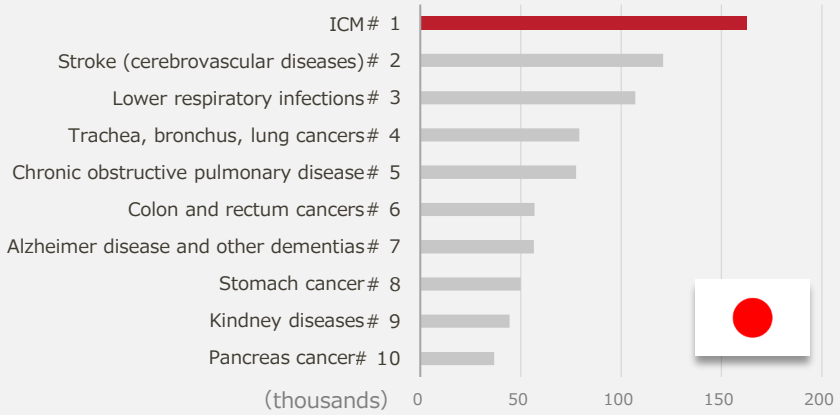
Our 1st indication
Clinical trials
Last patient's operation completed

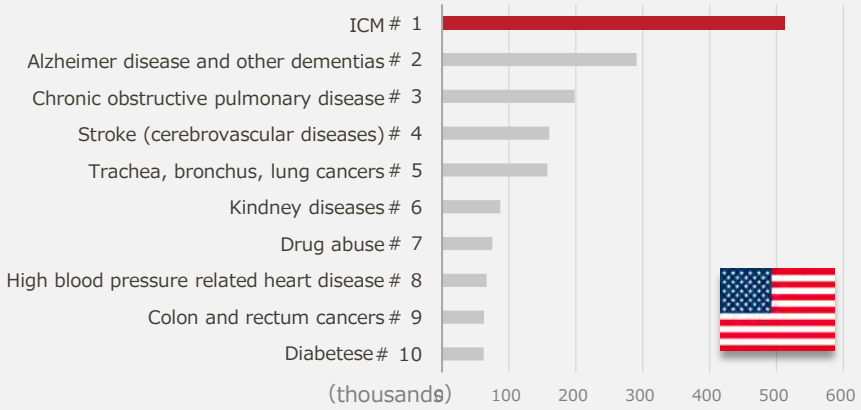
Our 2nd indication
Non-clinical research completed
Planning of clinical trials underway

Status quo of heart failures and estimate of number of patients

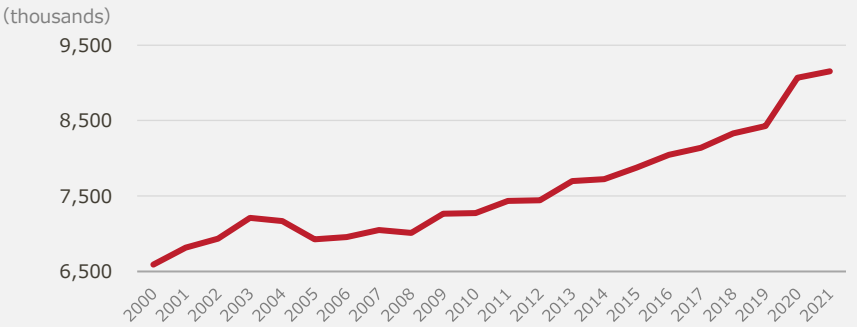
Both Japan and the U.S., ICM is the number one cause of death
The number of deaths caused by ICM is increasing globally.

Cause of death ranking (2019) [1]





Number of worldwide deaths owing to ICM[2]



No. of heart failure patients and our target market[3-5]

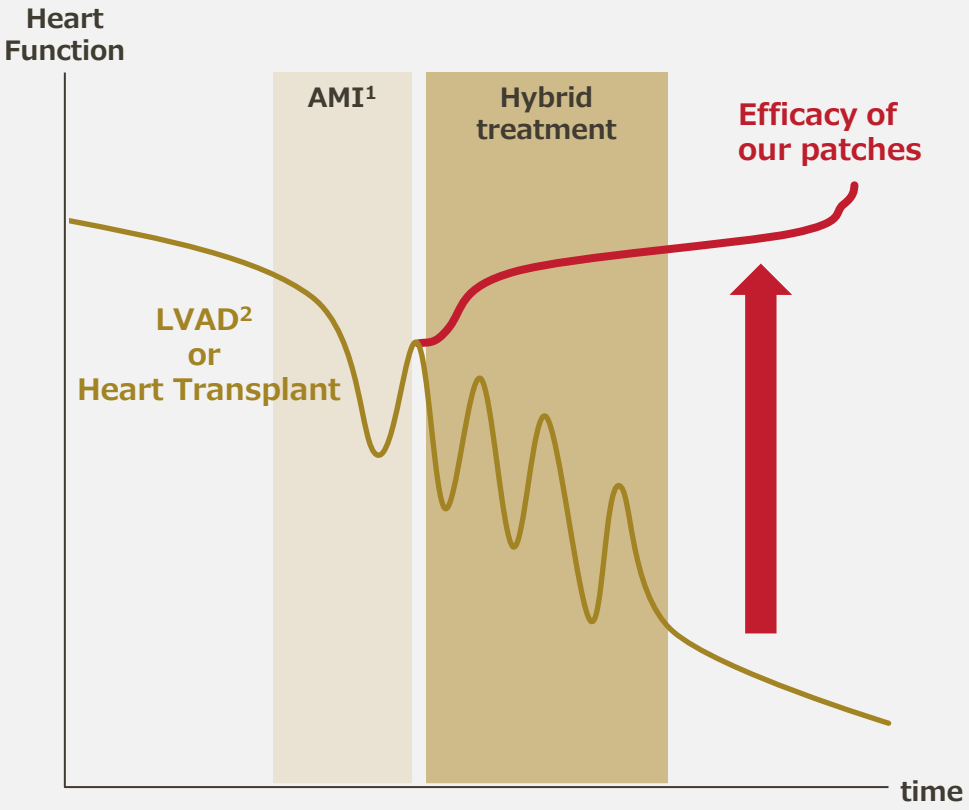
Country	Patients	NYHA class III (25%)	NYHA class IV (5%)
Japan	1.3M	325,000	65,000
U.S.A.	6M	1,500,000	300,000
World wide	26M	**6,500,000**	**1,300,000**

1. WHO
2. Calculated using number of patients per 100,000 released by Euromonitor and the number of population released bu U.N.
3. https://world-heart-federation.org/resource/heart-failure-infographic/
4. Global Public Health Burden of Heart Failure, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5494150/
5. Leslie W. Miller, Left Ventricular Assist Devices Are Underutilized, Circulation. 2011;123:1552–1558, https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.110.958991

Expected Efficacy and Merits of our iPSC derived cardiomyocyte patches

The product can provide different merits to patients, hospitals, government, etc.

①Improvement of patients' QOL



②No need of heart donors

Through our therapies, we can avoid patients from hear transplants or LVADs. The treatment can save patients from lack of heart donors

✓ Registered heart transplants applicants as of June-end 2022 : 921
✓ Number of heart transplants in 2021 : 59 cases (source : Japan organs transplant network)

→ Extremely long waiting time for available organs

③Reduction of Cost

Significant cost savings from our product

(vis-à-vis LVAD)
✓ LVAD Cost 19million yen (about $150,000)
✓ Maintenance fee 5.4 million yen/year (about $40,000)

→ If we assume patient wearing LVAD for 5 years, total cost is 46 million yen (about $350,000)

1. AMI : Acute Myocardial Infarction。Myocardial necrosis resulting from acute obstruction of a coronary artery
2. LVAD : Left Ventricular Assist Device A mechanical pump that is implanted in patients with severe heart failure

Example of the World's first implant of iPSC derived cardiomyocyte patches

After successful production of the above patch, in Jan. 2020, research group led by our Sawa CTO has successfully transplanted to the 1st clinical trial patient.

Osaka University conducts world's first heart operation using iPS regenerative therapy in the cardiovascular area.

Group led by Prof. Sawa of Osaka Univ. announced the first transplant of cardiomyocyte patches derived from iPS cells on the 27th to a patient with severe heart failure. **The operation was conducted as Investigator-led clinical trials, and the results thus far have been quite good. The group will transplant to total of 10 patients within 3 years and will conduct research regarding its safety and efficacy.** Regenerative therapy using iPS cells have already begun in the area of eye but the first in a vital organ such as the heart which is critical in saving life of a human being. Everybody is keen on its efficacy.

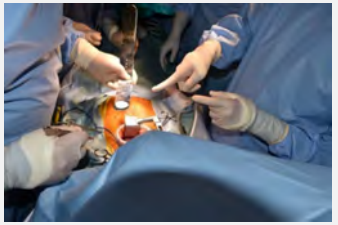
Investigator led clinical trials have begun in Dec. 2019, and the first operation was conducted in January at Osaka University Hospital to severe heart failure patient. No further details have been released.

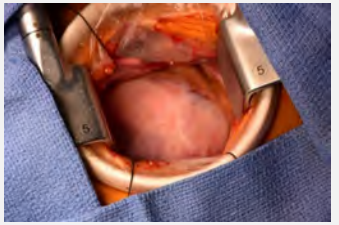
Kyoto University created the cardiomyocytes using its iPS cell stock. These cardiomyocytes have been frozen and stored. The patch was created according to the date of the operation, by defrosting the cells and forming them in a patch、During the operation, these patches were placed on to the damaged heart area. Its safety and efficacy will be observed during one year surveillance.

At present, heart transplant is the only method for solving severe heart failure. However, such donor is extremely limited and there are many cases, where a patient cannot be operated. Dr. Sawa expects that this product will turn into a competitive solution which will save so many lives. **If everything goes accordingly, a start-up venture Cuorips (Tokyo Chuo-ku) will commercialize this product.**

From Nikkei (2020/1/27)

Source : Osaka Univ.





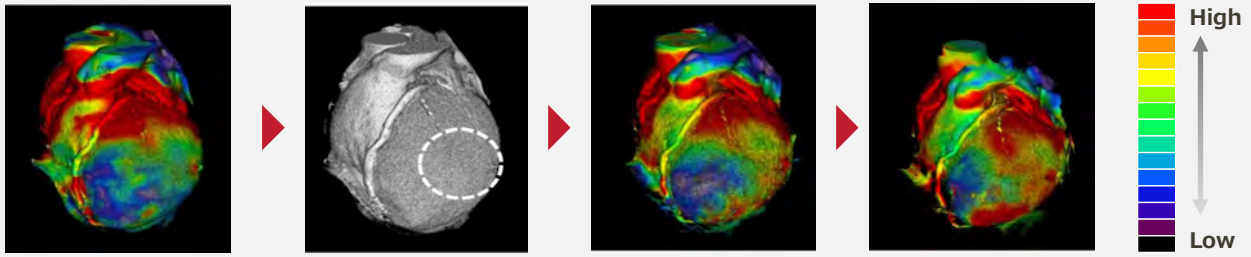
1. Investigator-led clinical trials : Clinical trilas conducted by the doctors as opposed to conventional clinical trials initiated by pharmaceutical firms. Such trials were approved owing to the 2008 revision of the Pharmaceutical Affaris Law
2. P`ictures provided by Osaka University (Jan. 20, 2020)

Efficacy of iPSC derived cardiomyocyte patches（ICM）

We have been able to observe recovery in the blood circulation and function of the heart muscles in the transplanted area.

Change in activity of the heart muscle after iPS derived cardiomyocyte patches

In the dotted area（transplant area）, the red area（area of active heart muscle movement）is increased. **Recovery in the function of heart muscles is observed.**

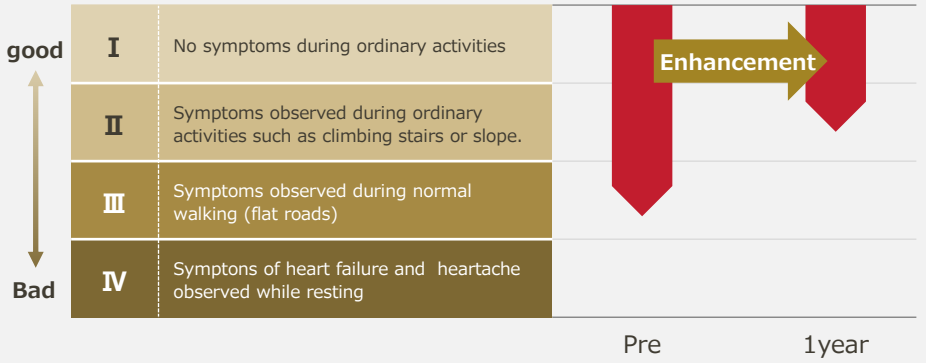


LVEF[1]

After the transplant, improvement in the LVEF is observed.

NYHA[2]

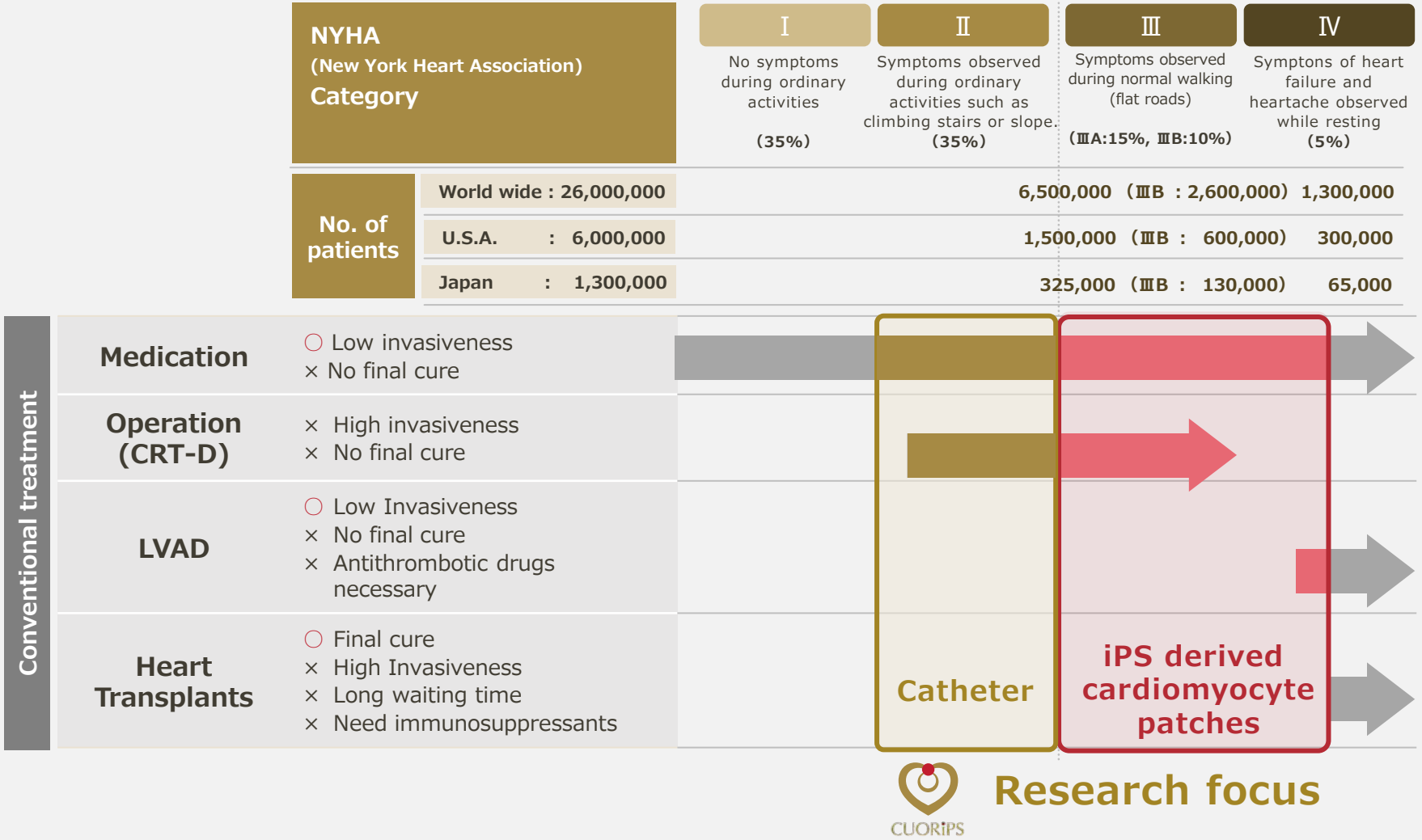
Significant one year improvement is seen in NYHA category.



1. LVEF : Left Ventricular Ejection Fraction. Measurement of the percentage of blood leaving the heart each time it squeezes.
2. Severity of the heart failure defined by NYHA : New York Heart Association

Target segment and comparison with other current available treatment

iPSC derived cardiomyocyte patches are geared toward patients with no other treatment until the symptom worsens to a stage requiring heart transplants.
Catheters with less intervention will target wide range of segment



Advantages of iPSC derived cardiomyocyte patches

Significant difference in lead time for cultivation and processing.
Significant cost reduction owing to mass production

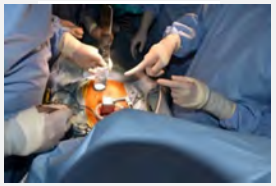
iPSC derived cardiomyocyte patches

Our plant

Patch production

Less invasive owing to iPS cells

Patches can be delivered Under normal temperature on a timely basis



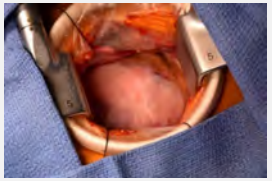
Hospitals

Patch transplant

No additional facilities necessary at each hospital

Significant reduction in lead time of cultivation and processing

Autologous cells



Cells obtained from each patient

Myoblast cells obtained from each patient
High degree of invasiveness

Cultivation necessary

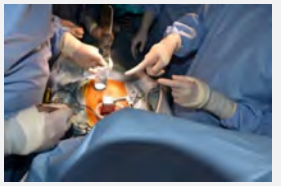
Cultivation Plant

Cultivation

Must collect myoblast cells from the patient before operation.
Must cultivate the cells at each hospital for 3 months.
Difficult for emergency operation.

Hospitals

Proeess into patches



Hospitals

Transplant of patches

Each hospital must have CPC.
Number of hospitals limited

Benefits of iPSC cardiomyocyte patches

Compared with existing product using autologous myoblast cells, significant improvement is attained

	Myoblast patches	iPS derived cardiomyocyte patches
Invasiveness before transplant	**High** Must collect myoblast cells from the patient	**Nil** No invasiveness since allogenic cells
Timely action	**Impossible** 3 months necessary to cultivate the cells collected from the patient	**Possible** No cultivation necessary. Can deiiver the patches under normal temperature on a timely basis
Number of hospitals which can offer our treatment	**Limited** Must have CPC	**Limitless** No special facility necessary

Significant improvement in feasibility of treatment

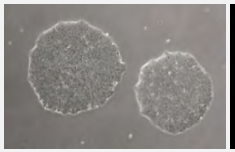
Manufacturing process of iPSC derived cardiomyocyte patches

In regenerative cell therapy, manufacturing process is vital.
We have established a manufacturing process for commercialization including removal of undifferentiated cells.

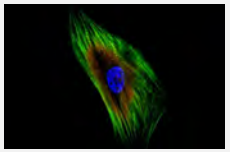
Manufacturing process of iPS derived cardiomyocyte patches

Master/working cell bank → **Cultivation** → **Storage** → **iPS derived cardiomyocyte patches** → **Delivery** → **Clinical trials**

Cultivation of HLA homo iPS cells



cultivation 49days



differentiation 3days

Large scale differentiation into cardiomyocytes. Removal of undiffentiated cells

Freezing storage 1day

Highly efficient frozen cell storage
Cell can last more than 1.5years

Forming a patch 4days

Forming patches a c cording to opearation schedule

delivery

Pasting of the patches to the injured part

Patent
Technology of removing undifferentiated cells using CD30 (Patent in Europe and Canada)

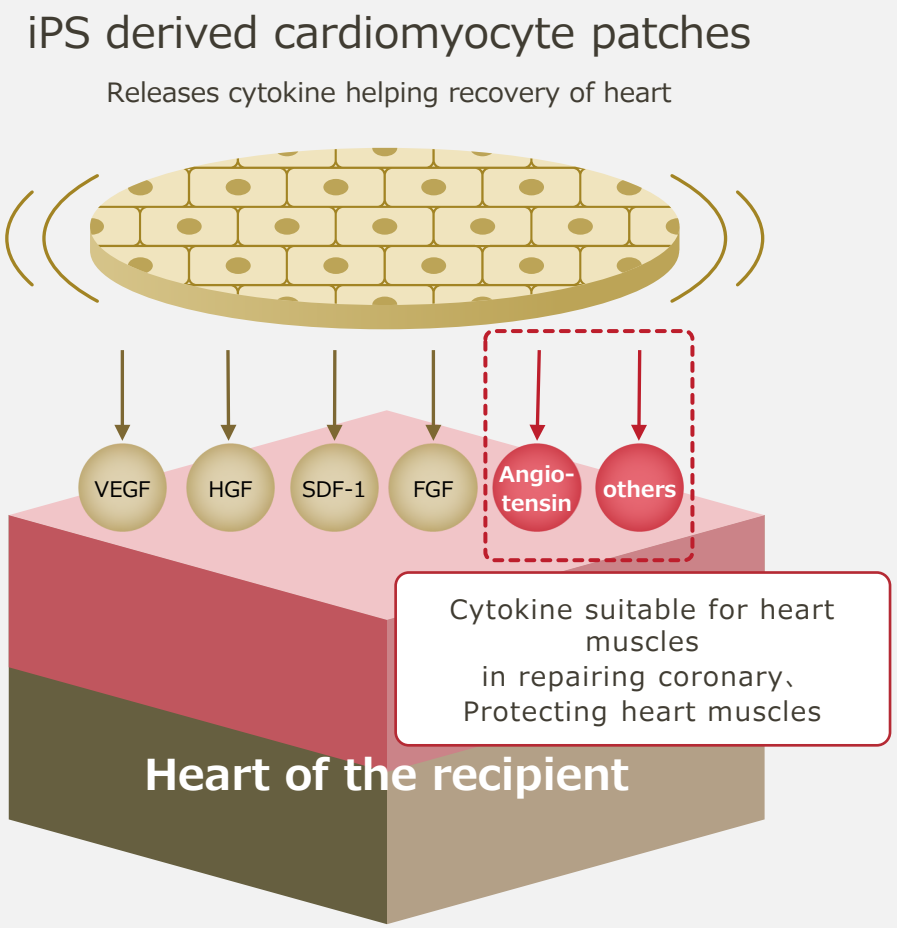
Expertise
Patch technology is owned by us only

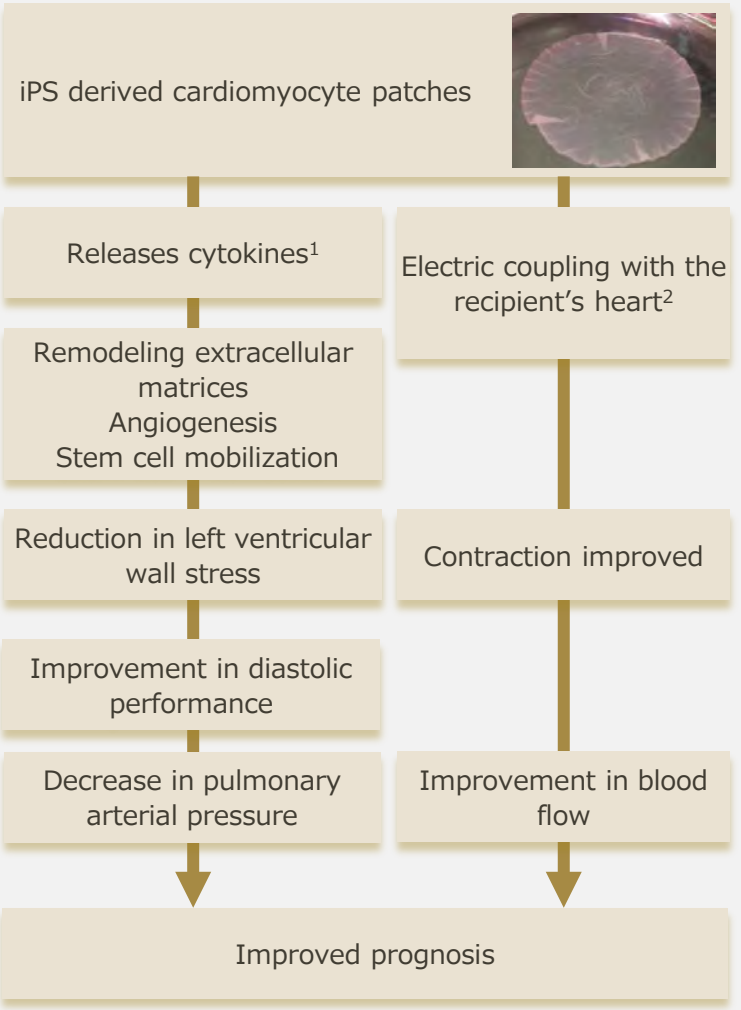
Characteristics
Can deliver under normal temperature

Expertise
Pasting technology same as Terumo's Heart Sheet and is already established

Mechanism of iPSC derived cardiomyocyte patches

iPS derived cardiomyocyte patches secrete Cytokine which enables recovery of the heart function



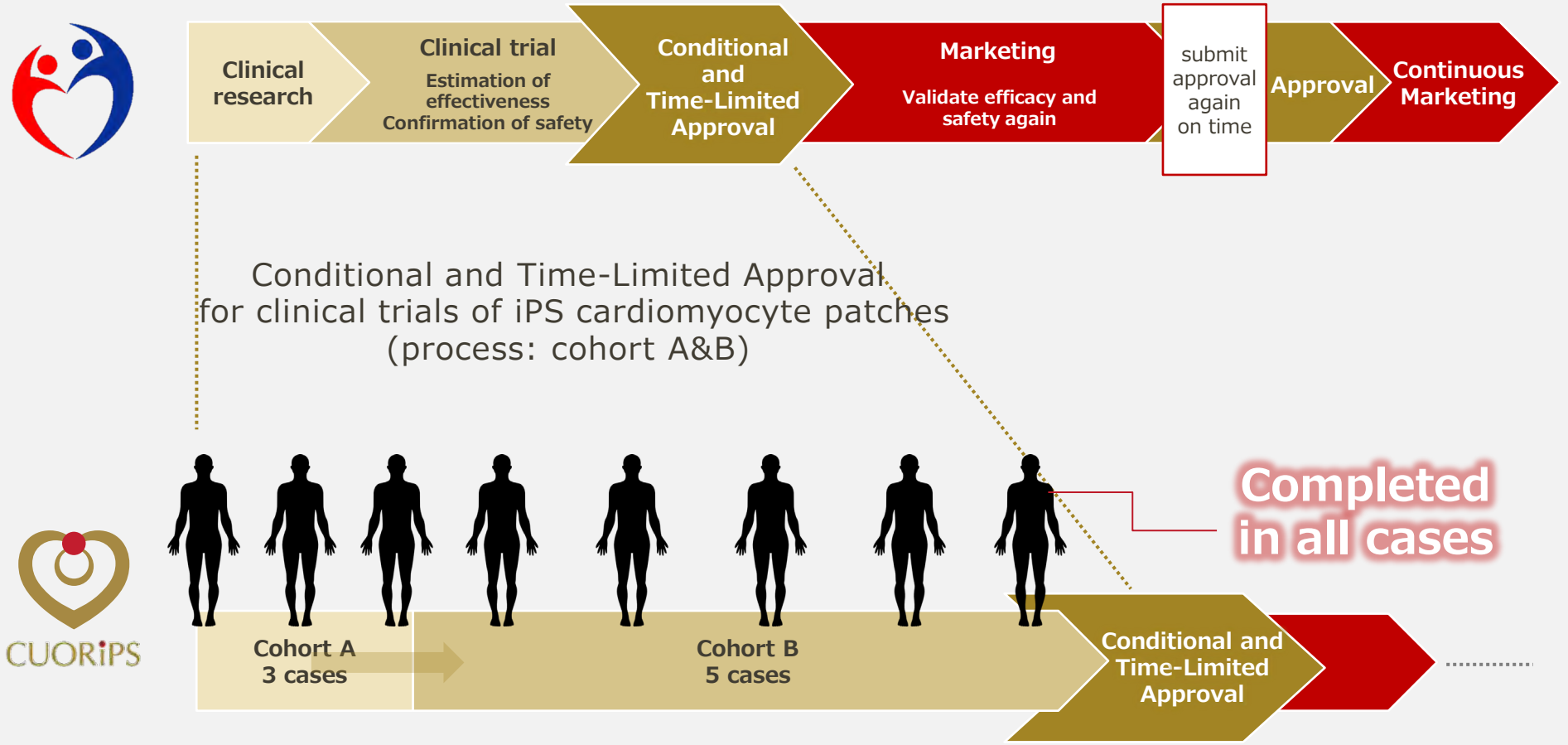


1. Cytokine : Small poroteins produced and released from cells, activating a variety of biological processes in the recipient cells.
2. Recipient heart : Host animal or patient heart in the transplantation of iPSC-derived caridomyoycte patches.

Current status of Clinical trials of Cardiomyocyte patches for ICM

Clinical trial process for conditional and time-limited approval is as follows:
As of March, 2023 all eight transplants of the clinical trial is completed.

Conditional and Time-Limited Approval



Comparison with our peers

We have made significant progress in allogenic cardiomyocyte patches vis-à-vis our peers and closest in commercialization.

		Cells	Delivery	Indication	Safety Tumorigenicity	Clinical Trials
Japan	**Cuorips**	iPSC derived cardiomyocytes	Patches	ICM	○	**All 8 cases** under the investigator led clinical trials
Japan	Company A	ditto	Direct injection into heart muscles	Severe heart failure from ischemia	Unknown	First step
Japan	Company B	ditto	Patches (Absorbs into the body)	Chronic heart failure	Unknown	Pre-clinical/Pre-IND
Japan	Company C	Autologous myoblast	Patches	Chronic heart failure	○	Approved by PMDA on a conditional basis
Overseas	Company D	iPSC derived cardiomyocytes	Patches	ICM	Unknown	Pre-clinical
Overseas	Company E	iPSC cells	Patches (absorbs into the body)	Chronic heart failure	Unknown	Pre-clinical

CUORiPS

High safety

- GMP level production
- Removal of undifferentiated iPS cells
- Effective and safe Immunosuppressants

Cell therapies
(Catheter)

Catheter: Joint Research and Development with Asahi Intecc

Development program in the area of PCI (through the percutaneous coronary intervention) geared towards not severe but mild heart failure patients

CUORiPS

Expertise in large scale cultivation and differentiation of iPS cells

Development iPS derived cells
Suitable for catheter delivery

Joint Dev. Contract

ASAHI INTECC

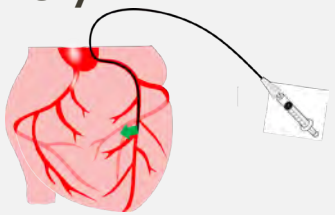
Development of special purpose catheters using sophisticated material processing technology

Establishment of wide spread new cell delivery methods

Making huge contribution to add less invasive regenerative therapies to patients suffering from heart failures

New Catheter Delivery

iPS derived new cells through catheters



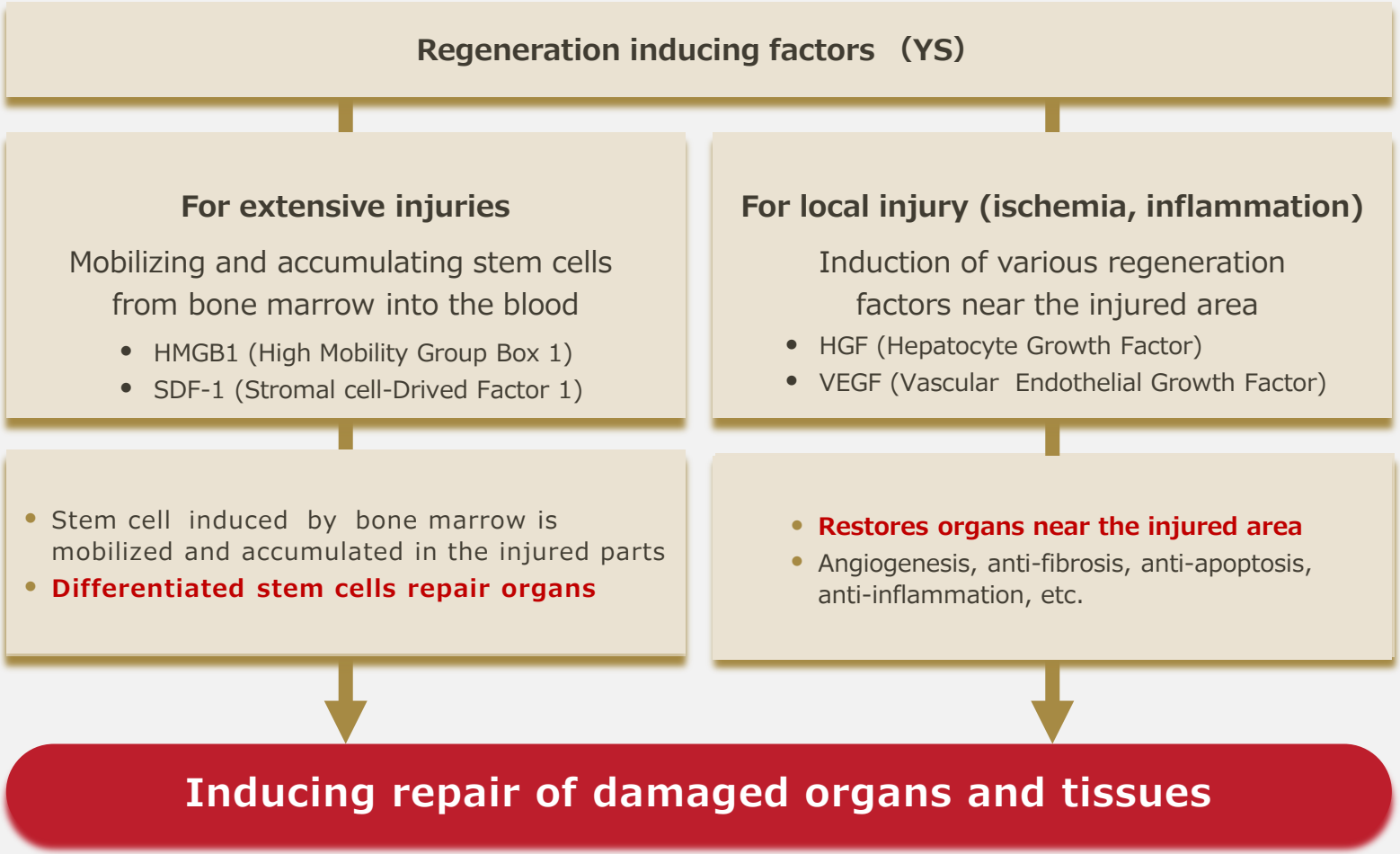
- Finding new solutions to AMI*1、CTO*2 patients (roughly 10 to 20% of PCI patients may be applicable, the number of patients are from Japanese Circulation Society)
- More involvement by cardiologists

No. of patients (est.)
20,000
Shooting for 2028 approval

Other Pipeline
(Regeneration inducing factor)

Characteristics of Regeneration inducing factors (YS)-two actions

YS can augment natural healing power which all humans originally possess.
We expect YS can induce regeneration of organs and tissues



Source:『Lind Pharma,Inc.』

CDMO business

Our CDMO business

Our one stop service of providing product development service based on our experience of commercialization of Academia research and utilizing our sophisticated manufacturing sites
Effective use of our resources and improvement in capacity utilization

Strong technology development expertise as evidenced by our iPSC derived cardiomyocyte patches

- Large scale production of homo iPSC derived cardiomyocyte cells
- Patching forming, storage and delivery technology
- Technology in removal of undifferentiated iPS cells

Manufacturing site with lab capabilities (CLiC-1)

Filing for patents

- Single manufacturing site ranging from non-clinical and clinical products
- Huge efficiency resulting from shorter period of technology transfer
- Innovative and unique architecture for large scale production

Seeds Development → **Manufacturing Process dev.** → **Non-clinical production** → **improvement of process** → **Clinical grade production** → **Cellular and Tissue-based, Cell processing products**

- **Production for regenerative products for our clients**
  - Many inquiries from many bio-start ups
  - Currently production for 3 companies
- **Consulting services for regenerative medicine**

2022/3 cumulative Sales
Yen13,913K

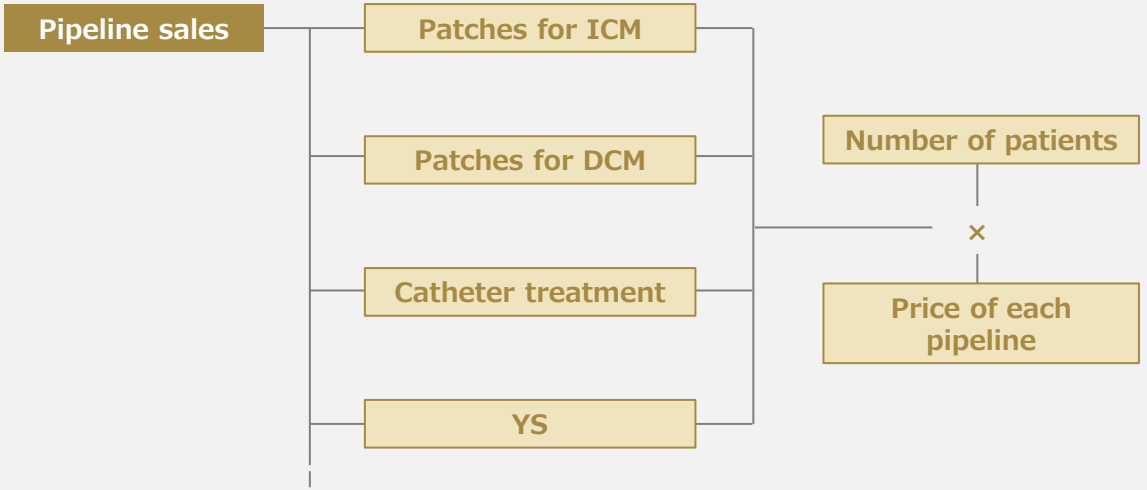
2023/3 3Q cumulative Sales
Yen13,488K

Growth strategy

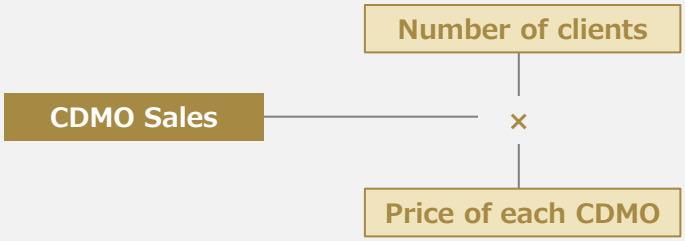
Assumptions of profits by each segment

Our profit profile is consisting of sales from each pipeline and CDMO operations
Pipeline sales are derived from multiplying expected price and expected number of patients

Breakdown of pipeline sales



Breakdown of CDMO business



As of March 2023
4 clients

Reference

Number of target patients

Japan : 5,000 per year/US : 20,000

Price of heartsheet

15 million yen+tax

Number of catheter patients

Japan : 20,000/US : 100,000

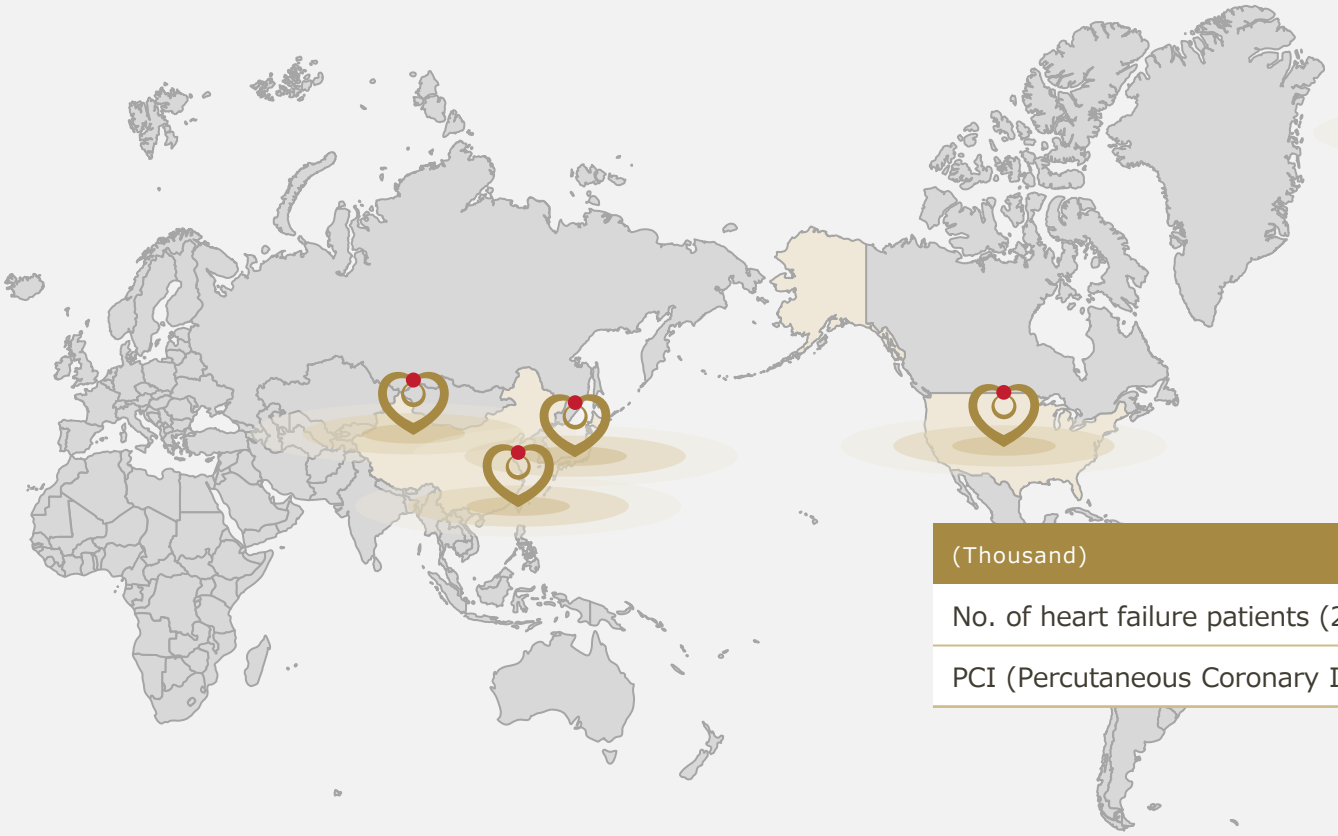
Expected price for catheter

5 million yen（+tax)

Our overseas expansion plan

Seeking global partners in the U.S., mainland China, Taiwan, etc.
We will accelerate this process, once receiving approval from the Japanese Authorities

Our potential business partners (including Japan)



: Looking for partners

(Thousand)	Japan	U.S.A
No. of heart failure patients (2017)[1]	3,714	9,623
PCI (Percutaneous Coronary Intervention) (2019)	271	413

Image of our business segment growth

Image of our revenue growth

1：Cureus「Global Epidemiology of Ischemic Heart Disease: Results from the Global Burden of Disease Study
Source: Cureus, HCUPnet ,Japanese Circulation Society

Appendix

Management Team

Strong management team consisting of science, medicine, pharmaceuticals, finance, economy, law and accounting

Takayuki Kusanagi
CEO

- 1981 Joined Industrial Bank of Japan
- CIO of YMR Asset Mgt., Director of Management Planning, Entrust Corp., etc.
- 2020/4 Our Advisor
- 2020/8 Appointed as CEO

Manabu Inoue
Vice CEO

- 1979 Joined Industrial Bank of Japan
- Head of Aetos Japan, CEO of Hotel Nikko Tokyo, etc.
- 2017 Our external Auditor
- 2020 Our COO

Yoshiki Sawa
Founder／CTO

- Pioneer of regenerative therapy in the heart area
- Awarded Medal with Purple Ribbon by the Japanese Emperor
- 2021/8 Roto Pharm Science Advisory Committee
- 2021/8 Our CTO and Board Member

Tadashi Sameshima
Board member

- 1983 Joined Terumo Corp.
- 2016 Executive officer of Heart sheet business
- 2020 Management Advisor, Terumo
- 2021 Technical advisor of Cuorips
- 2022 Our board member

Ryouhei Shimazaki
Board member

- CEO of Iapan Invest Corp.CEO of BNP Paribas Asset Management Co.
- 2020 Our board member

Tohru Sumiyoshi
Internal Auditor

- 1978 Joined IBJ
- Worked in Jakarta Branch, and Chinese subsidiary
- 2009 Joined Press Kogyo
- 2020 Internal Auditor of Cuorips

Kotaro Yamamoto
External Auditor

- 1991 awarded New York Bar
- 2020 External Auditor of Cuorips

Shinji Abe
External Auditor

- 2007 Awarded CPA
- Chief Representative of Abe Accounting Firm(Current)
- Chief Representative of Abe Shinji Tax Accountin (Current)
- 2020 External Auditor of Cuorips

BS, PL, CF

Balance Sheet

(Thousand Yen)	2021/3	2022/3	2023/3		2021/3	2022/3	2023/3
Current Assets	3,618,569	3,367,090	2,977,402	Current Liabilities	104,422	112,410	97,425
Fixed Assets	745,725	677,816	610,015	Capital	4,222,342	3,895,546	3,453,623
Total Assets	4,364,295	4,044,906	3,587,417	Total	4,364,295	4,044,906	3,587,417

P&L

(Thousand Yen)	2021/3	2022/3	2023/3
Sales	220	13,913	38,278
COGS	82	3,260	17,266
SGA	281,978	383,917	471,447
R&D*	72,616	112,805	168,152
Others	209,362	271,112	303,295
Operating Loss	△281,840	△373,264	△450,435
Recurring Loss	△295,845	△373,140	△450,418
Net Profit or Net Loss	△307,834	△375,337	△452,077

Cashflow statement

(Thousand Yen)	2020/3	2021/3	2023/3
Cashflow from operations	△282,797	△220,762	△401,612
Cashflow from investments	△670,208	△28,444	△8,968
Cashflow from financial activities	3,766,740	48,541	10,694

*SGA R&D (2021/3) : ¥ 72,616,000 = ¥ 664,840,000 (R&D expenses (2021/3)) – ¥ 592,224,000 (Joint R&D expenses received from partners)
*SGA R&D (2022/3) : ¥ 112,805,000 = ¥ 655,546,000 (R&D expenses (2022/3)) – ¥ 543,741,000 (Joint R&D expenses received from partners)
*SGA R&D (2023/3) : ¥ 168,152,000 = ¥ 648,463,000 (R&D expenses (2023/3)) – ¥ 480,310,000 (Joint R&D expenses received from partners)

Disclaimer

- This material contains forward-looking statements. These statements are based on assumptions made at the time of making such statements regarding future events and trends, and there can be no assurance that such assumptions will necessarily be accurate. Furthermore, such statements are not guarantees of future results and involve risks and uncertainties. Please note that actual results may differ materially from those projected in the forward-looking statements due to changes in the business environment and other factors.
- Factors influencing the above actual results include, but are not limited to, domestic and international economic conditions and related industry trends in our company.
- Updates to this material will be disclosed around the time when these financial results are announced.
- Information contained in this material concerning countries other than our company is derived from public information, etc. our company has not verified the accuracy, appropriateness or other aspects of such information in any way and does not guarantee such accuracy or appropriateness.
- The information contained herein is subject to change without prior notice.