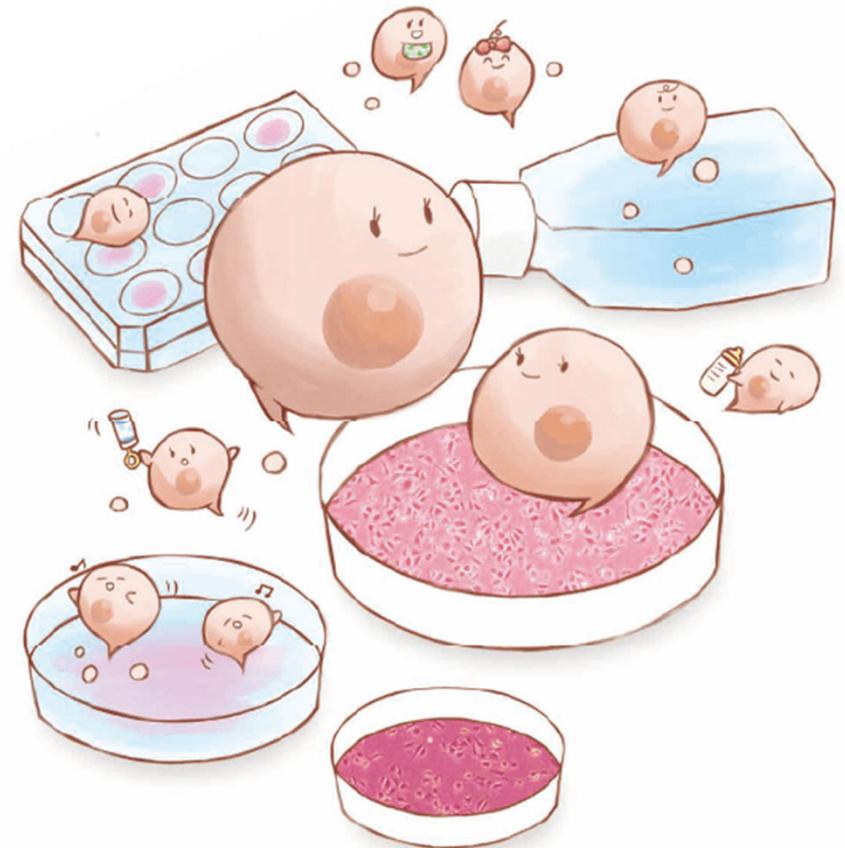


# CellSeed Inc.

## Fiscal 2021 Earnings Results Presentation



- **Company Profile**
- Financial summary FY 12/2021
- Progress of each business

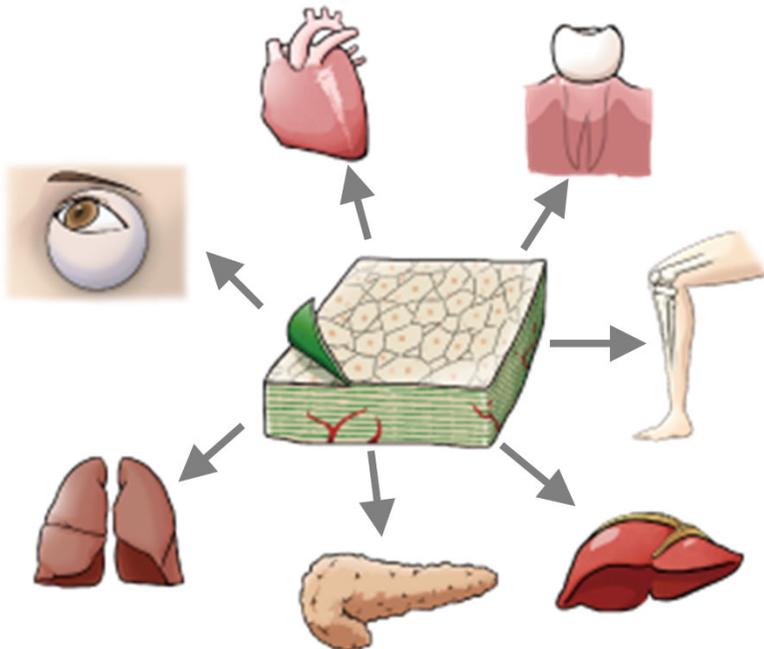
# CellSeed Inc. Corporate Information

Established May, 2001  
Core competence Cell Sheet Engineering based on Temperature Responsive Polymers  
Listed JASDAQ (7776) in 2010

## Business

### Regenerative Medical Products Business

- Commercialization of Cell Sheet Therapies



### Regenerative Medicine Supporting Business

- Intelligent Culture Ware as Research Tools



UpCell®

- Contract Manufacturing Services • Consulting

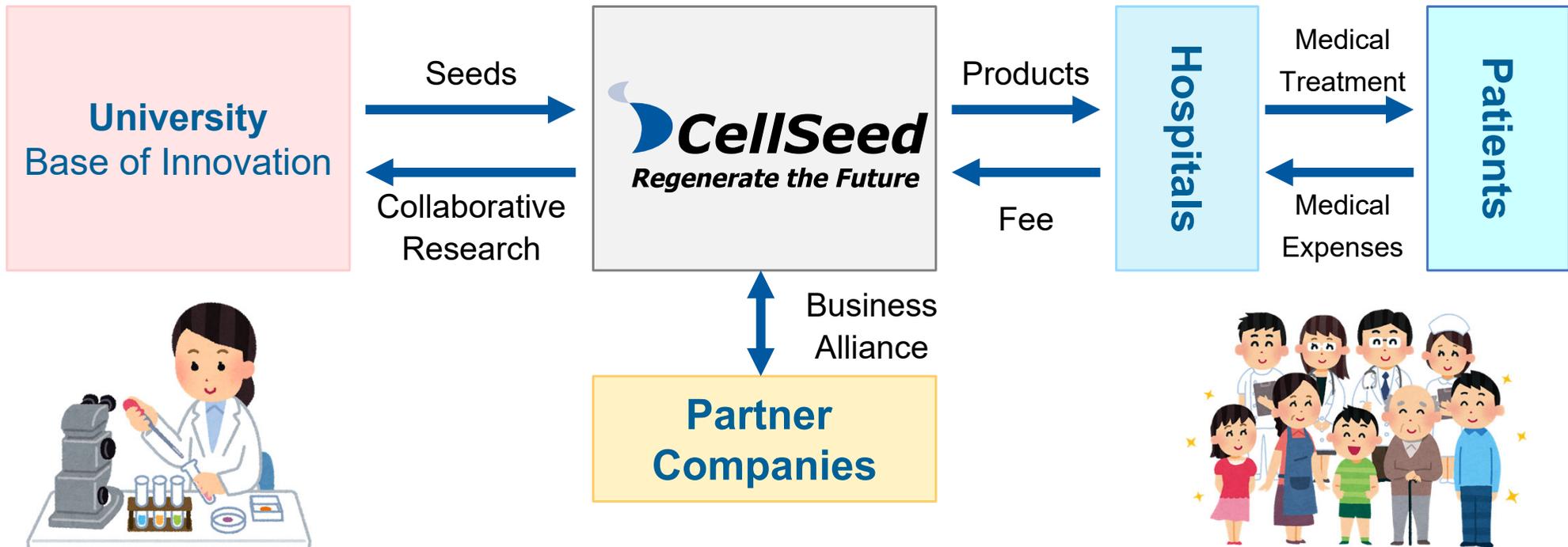


CPC

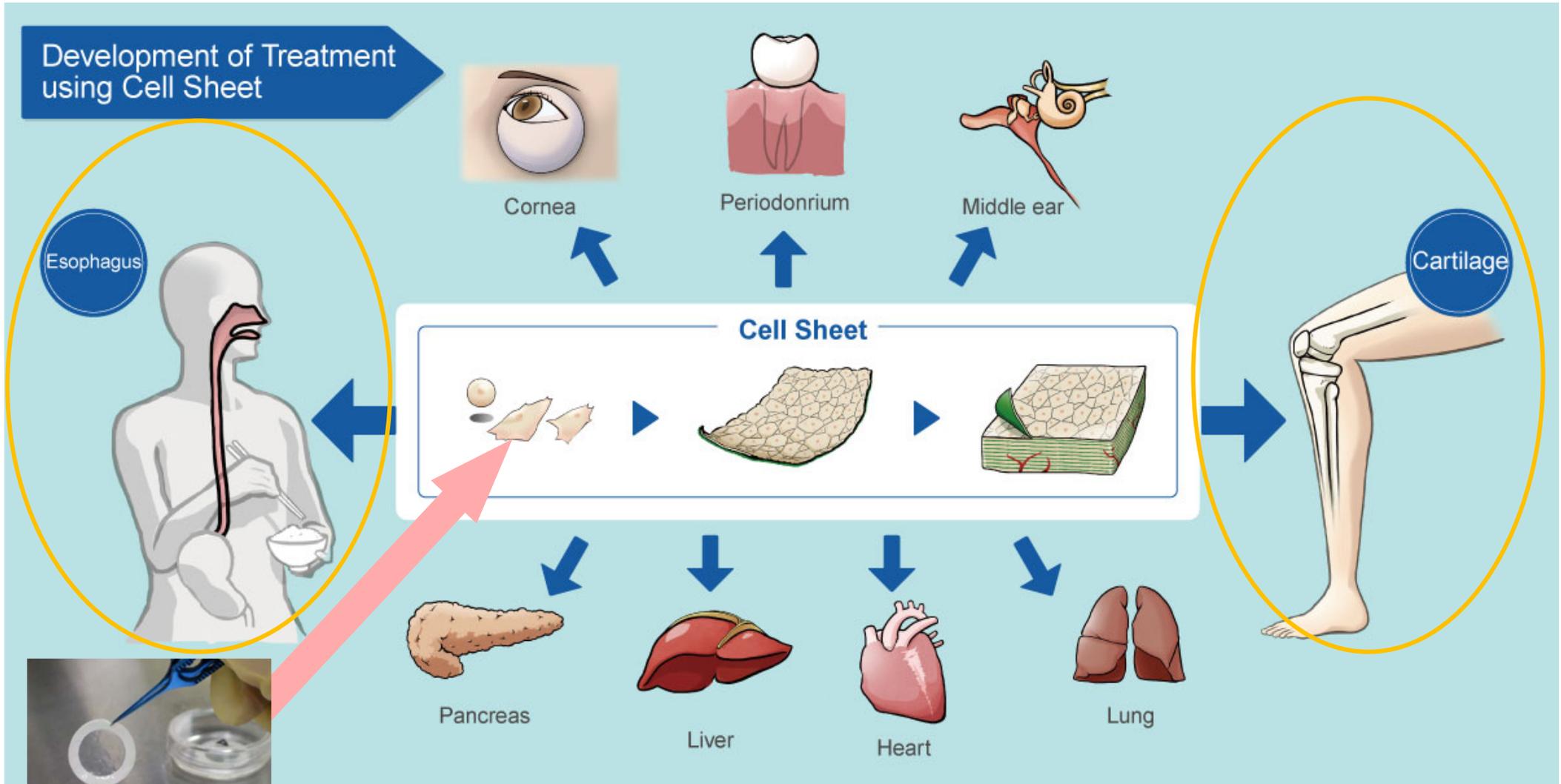
# Our Business Model

## Mission

We take the initiative of contributing to global health care in the valuable and innovative field of regenerative medicine.



# Development of Treatment Using Cell Sheet Engineering



- Company Profile
- Financial summary FY 12/2021
- Progress of each business

# Financial summary FY 12/2021

	FY2021 Consolidated (January 2021 - December 2021)			FY2020 Consolidated (January 2020 – December 2020)
	Amount (Millions of Yen)	Change (Millions of Yen)	Change from Previous Period (%)	Amount (Millions of Yen)
<b>Net sales</b>	161	-37	18.9	199
<b>Operating profit</b>	-864	-145	—	-719
<b>Ordinary profit</b>	-887	-142	—	-744
<b>Profit attributable to owners of parent</b>	-914	-130	—	-783

- Started supplying devices to new markets that develop preventive and therapeutic methods for infectious diseases such as COVID-19.
- Newly established and began operation of development/manufacturing facilities to meet expanding demand for devices.
- Sales of devices reached record highs due to growing overseas demand that continued from last year.
- Adopted allogeneic chondrocyte cell sheets as a subsidy project of AMED.
- Continuing from last year, we have been entrusted with the manufacture of advanced medicine B (autologous cartilage cell sheets) from Tokai University.

# Issuance of the 22nd stock acquisition rights (including a provision for exercise price revision) by third-party allotment

<b>Allocation date</b>	January 5, 2022
<b>Number of stock acquisition rights issued</b>	44,000
<b>Exercised by</b>	Barclays Bank PLC
<b>Amount of funds procured</b>	854,919,800 yen (approx. amount of deduction taken)
<b>Exercise period</b>	January 6, 2022 to January 5, 2023
<b>Use of funds</b>	R&D funds, funds for operation of development/manufacturing facilities for devices, working capital

- Company Profile
- Financial summary FY 12/2021
- Progress of each business

Temperature-responsive cell cultureware invented by Professor Okano of Tokyo Women's Medical University in 1989 can detach cells just by lowering its temperature. This feature enabled us to collect intact cell sheets for the first time in the world. As temperature-responsive cell cultureware are sold all around the world, many researchers are actively researching and developing treatment methods using cell sheets.



UpCell®



HydroCell®

1989	Professor Okano of Tokyo Women's Medical University invented temperature-responsive cell cultureware.
2004	Released RepCell® and HydroCell®
2007	Released UpCell®.
2010	Released cellZscope®.
2011	Released ThermoPlate®.
2015	The regenerative medicine product Heart Sheet (Terumo Corporation) approved. (UpCell® was adopted as its component)
2017	Released HydroCell® flasks.
2019	Overseas sales via Thermo Fisher Scientific increased 200% from the previous year.
2020	The sales of devices exceeded 100 million yen for the first time.
2021	<ul style="list-style-type: none"> <li>Reached an agreement for extending the period of the sales contract with Thermo Fisher Scientific until 2025.</li> <li>Established facilities for developing and manufacturing cell cultureware.</li> </ul>
2022	Plan to start sales of the new product UpCell® flasks

## *UpCell®*

This cultureware maintains the physiological activity of cells and retains a high level of antigen proteins on the cell surface while serving as a cell culture dish for the recovery of the cell sheet.



## *RepCell®*

In addition to the same characteristics as those of UpCell®, this cultureware allows for the recovery of cells in a single cell or small colonies using the surface grid wall.



## *HydroCell®*

Using proprietary technology, nano-surface design, super-hydrophilic polymers are fixed to the surface of this cultureware, which forms spheroids of iPS cells and cancer cells.



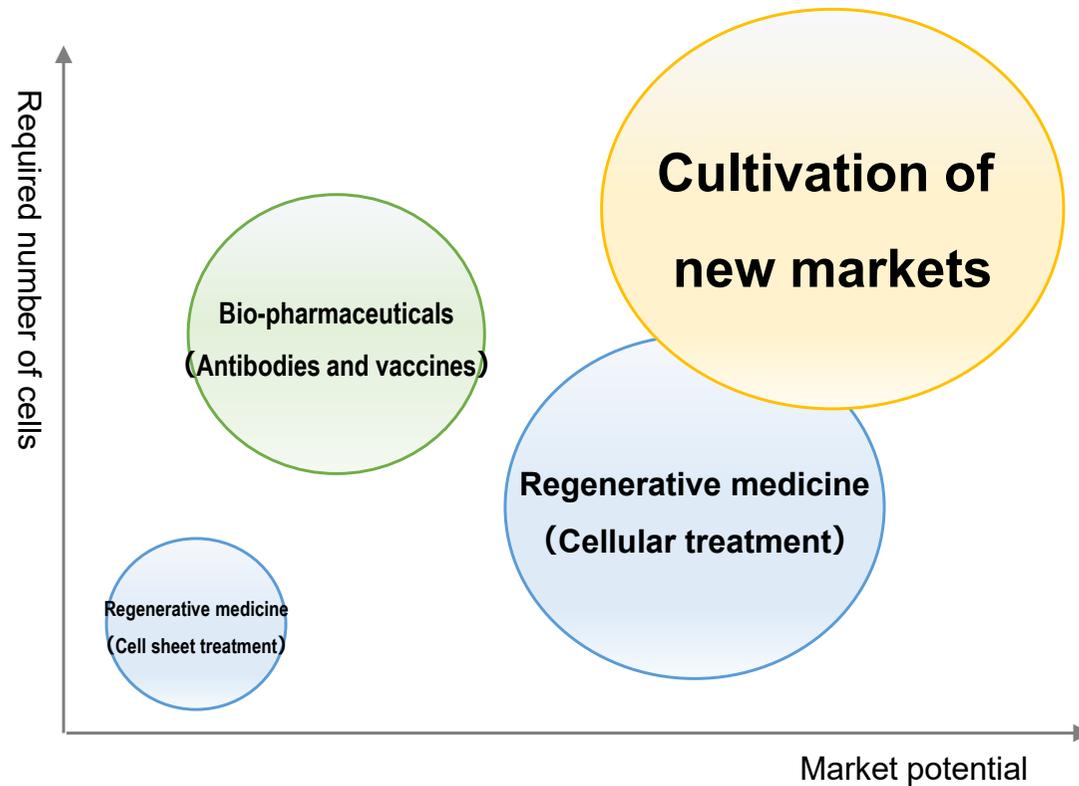
## cellZscope

This is a type of cultureware that is most suitable for research into the effect of drugs and poisons for the evaluation of cell layer barrier functions.



# Cultivation of new markets for cell cultureware

Recently, the production of bio-pharmaceutical products using mass-cultured cells, the immunotherapy using cells, and initiatives for solving food and environmental issues have been active. In the generally used cell collection technology, proteolytic enzymes are used, so cells are damaged when collected. Accordingly, it is difficult to keep the intrinsic functions and components of cells intact. However, by using our products, it is possible to collect cells without damaging them and utilize all functions and components of cells as they are. Therefore, our products are attracting attention, because they are expected to improve industrial efficiency and effectiveness in new markets.



Temperature-responsive cell cultureware

**Reference info: Forecast for the global market of regenerative medicine 2025/2030/2035** (100 million yen)  
 Tissue transplantation (cell sheets); 812/895/885  
 Cell transplantation (cell therapy); 13,476/24,695/36,033  
**Source:** Survey on the market of regenerative medicine and gene therapy in fiscal 2019  
 Arthur D. Little Japan Final Report, P144

**Reference info: Forecast for sales of bio-pharmaceutical products 2020** (100 million yen)  
 2020; 300,000  
**Source:** Issues in the bio-pharmaceutical industry and suggestions for further development  
 Japan Pharmaceutical Manufacturers Association, Office of Pharmaceutical Industry Research, Research Paper, No.71, P8

# Provision of consistent quality and services

Cellseed has acquired and currently maintain the following certifications in order to provide consistent quality and services.

- **Maintenance of ISO9001 certification**



- **Date of registration**  
January 6, 2020
- **Scope of registration**
  - Design and manufacturing control of cell cultureware
  - Sales of special cell monitoring devices and measuring instruments

- **Permission to manufacture specific processed cells**



- **Date of registration**  
March 13, 2017
- **Facility No.**  
FA3160008

- **Maintenance of ISO13485 certification**



- **Date of registration**  
September 18, 2017
- **Scope of registration**  
Design and manufacture of delivery system for sterile epithelial cell sheets

- **Manufacturing of Regenerative Medicine Products**



- **Date of registration**  
October 1, 2018
- Contract manufacturing is possible for all specific processed cells



## Aomi Cell Cultureware Innovation Center

Time 24 Building, 4-32,  
Aomi 2-chome, Koto-ku, Tokyo



Telecom Center Sta.

## Head Office

15F (East Wing) Telecom Center Building  
2-5-10, Aomi, Koto-ku, Tokyo

## Cell Processing Facility

Telecom Center Building 6F  
Total Floor Area 763 m<sup>2</sup>

(Facility Number:FA3160008)

Cell control room



Cell control room



# New development and manufacturing facility



<b>Name of facility</b>	Aomi Cell Cultureware Innovation Center
<b>Scope of the business</b>	Development and manufacturing of the flask products



Equipment product  
warehouse



Equipment analysis room

# 1

## Development of Manufacturing Methods and Contract Manufacturing for Cell Sheet Products

- Development of cell sheet manufacturing methods
- Contract manufacturing of cell sheet products
- Quality testing of cell sheets, etc.



# 2

## Facility Management and Application Support

- Support for preparing and submitting applications
- Support for document creation/consulting
- Support for operation and maintenance of facilities equipment/management system, etc.



# 3

## Training of Cell Culturing Technicians

- Cell sheet culturing training
- Cell sheet harvesting training, etc.



For the regenerative medicine service, we obtained the permission to manufacture specific processed cells (facility No. FA3160008) in March 2017 and the permission to manufacture products for regenerative medicine in October 2018 and have undertaken various projects so far. We will continue the commissioned production of cell sheets, while giving top priority to quality.

## ■ Autologous cartilage cell sheets

- Tokai University entrusted us with the manufacturing of autologous cartilage cell sheets, as the university started advanced medicine B with these sheets.

## ■ Cell sheets for treating liver disease

- Conclusion of a contract for the transfer of technologies for clinical trials and manufacturing of cell sheets for treating liver disease with KanonCure in Nov. 2020.

## ■ Periodontal ligament cell sheets

- The first project for commissioned manufacturing of cell sheets for clinical trials led by medical doctors

## ■ Pediatric autologous epithelium cell sheet

- For children after surgery for congenital esophageal atresia



\*The above are the projects that can be disclosed.

The 2nd Forum on Cell Sheet Engineering Innovation Forum was held online on November 1, 2021 with participation from many people throughout Japan.

Through the forum, we created an environment where participants could interact online and have lively discussions in an atmosphere similar to an actual poster session. Scenes from the forum can be viewed on YouTube. <https://youtu.be/LCsfq9KSB3Q>



- **Date and Time**

Monday, Nov. 1, 2021 1:00p.m. – 5:30 p.m.

- **Participant**

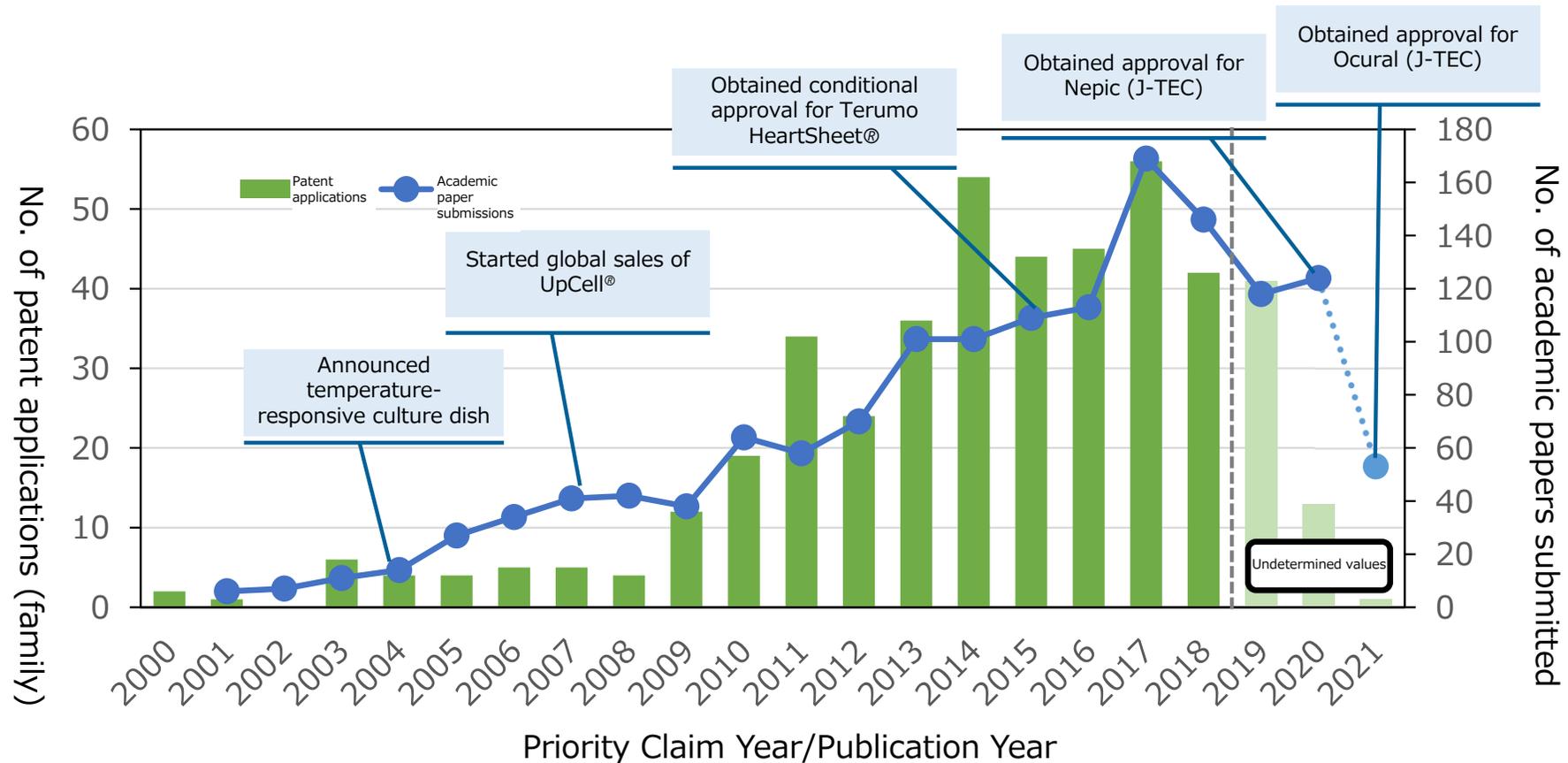
Audience : 118 / Poster presenter : 30

- **Speakers**

- **Tatsuya Shimizu, Ph.D., M.D.**  
Professor, Tokyo Women's Medical University, Director, Institute of Advanced BioMedical Engineering and Science
- **Yuji Miyahara, Ph D.**  
Professor, Tokyo Medical and Dental University
- **Ryoichi Sakiyama Associate Professor**  
Associate Professor, Osaka Institute of Technology Department of Biomedical Engineering
- **Kohji Nishida, Ph D.**  
Professor, Graduate School of Medicine / Faculty of Medicine, Osaka University



# Annual changes in the number of patent applications and submitted academic papers related to cell sheet engineering



- For this graph, we analyzed patent applications by the priority claim year
- Since there is a maximum grace period of one year from the priority claim to application and a maximum time difference of 1.5 years from application to publication, applications are treated as undetermined for 2.5 years from the time of that screening is implemented.

- Cell sheet engineering is one of the few technologies in the life science fields for which Japan has a leading position in patent applications and academic papers
- After starting global sales for UpCell®, patent applications and academic papers are increasing

- **Theme**

Research on "cell sheet", "temperature-responsive cell culture equipment" and peripheral technologies

- **Best Poster Award**

- Kazuyoshi YAMAZAKI (Hokkaido University)



- **Innovation award**

- Ryuichiro Tanaka (Tokyo Women's Medical University)



- **Poster presentation excellence award**

- Noriyuki OGAWA (Shinshu University)
- Kodai TAHARA (Waseda University)
- Yasushi FUCHIMOTO (International University of Health and Welfare)



## Regenerative medicine

The Act on the Safety of Regenerative Medicine

The Act on Pharmaceuticals and Medical Devices

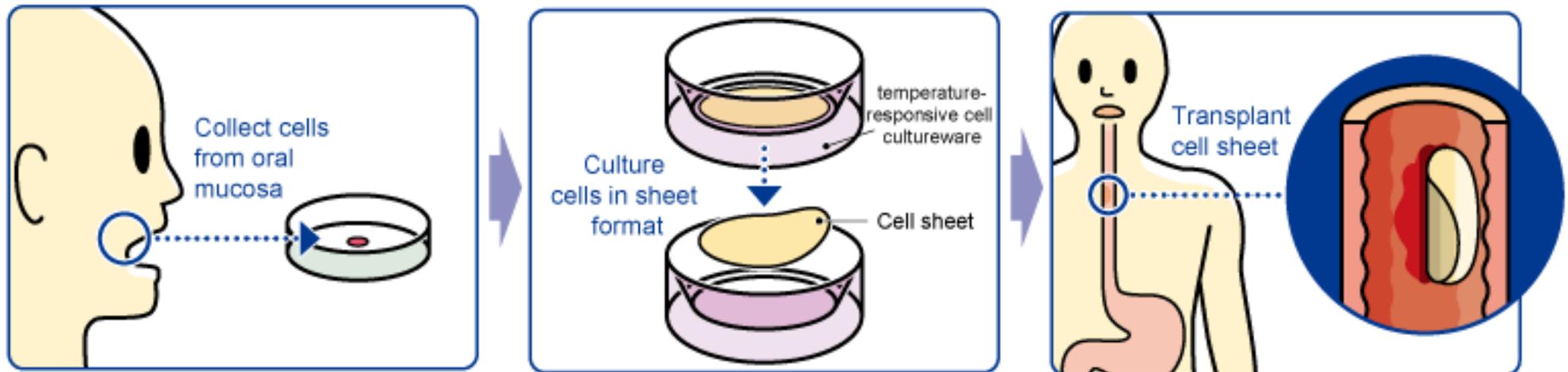
Clinical research

Self-funded medical treatment

Manufacturing and sales



- A medical treatment developed by Tokyo Women's Medical University as a regenerative treatment for esophageal cancer (to heal esophageal wound and prevent stricture)
- Cell sheet is on a temperature-responsive cell culture ware and then transplanted into the ulcerated area in the esophagus after endoscopic surgery for esophageal cancer



## Tokyo Women's Medical University

### ● Clinical Research at Universities

2008 – 2014 <Japan>

Tokyo Women's Medical Univ.	10case
Tokyo Women's Medical Univ. and Nagasaki Univ.	10case

<Europe>

Karolinska University Hospital	10case
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Basic Development Agreement

### ● Clinical Trials sponsored by CellSeed

"SAKIGAKE Designation" in Feb. 2017

Japan



2017.4 Business alliance agreement signed with Taiwan's MetaTech(AP) Inc.

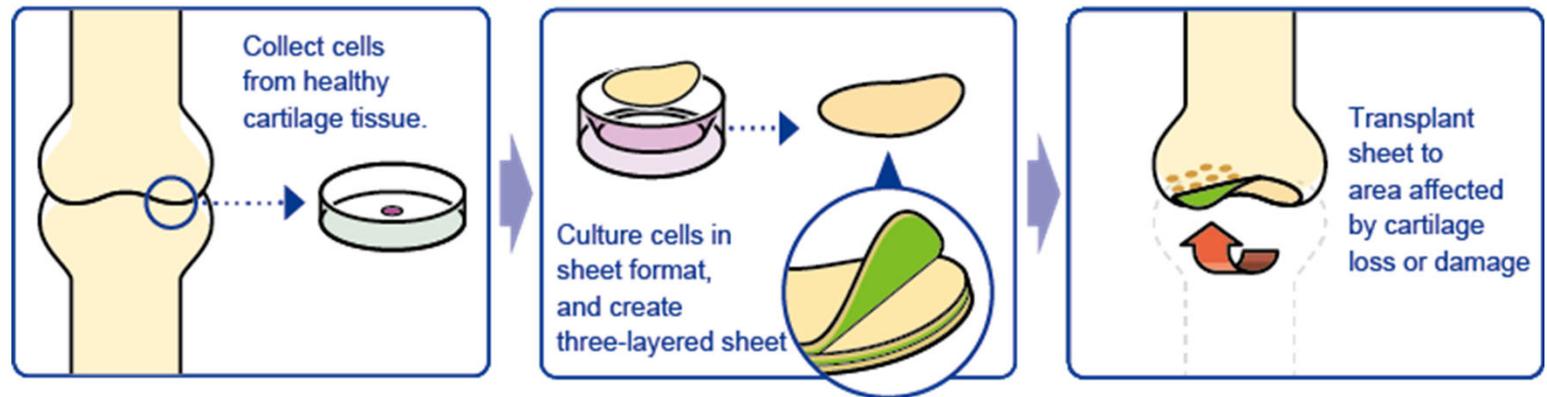
Taiwan (MetaTech) Europe (Sweden)

- 2016 Apr. Submitted a notification of clinical trial plan
- 2019 Mar. Completed the clinical trial in Japan
- 2020 Oct. Additional clinical trial plan notification submitted
- 2021 Feb. First medical case recorded

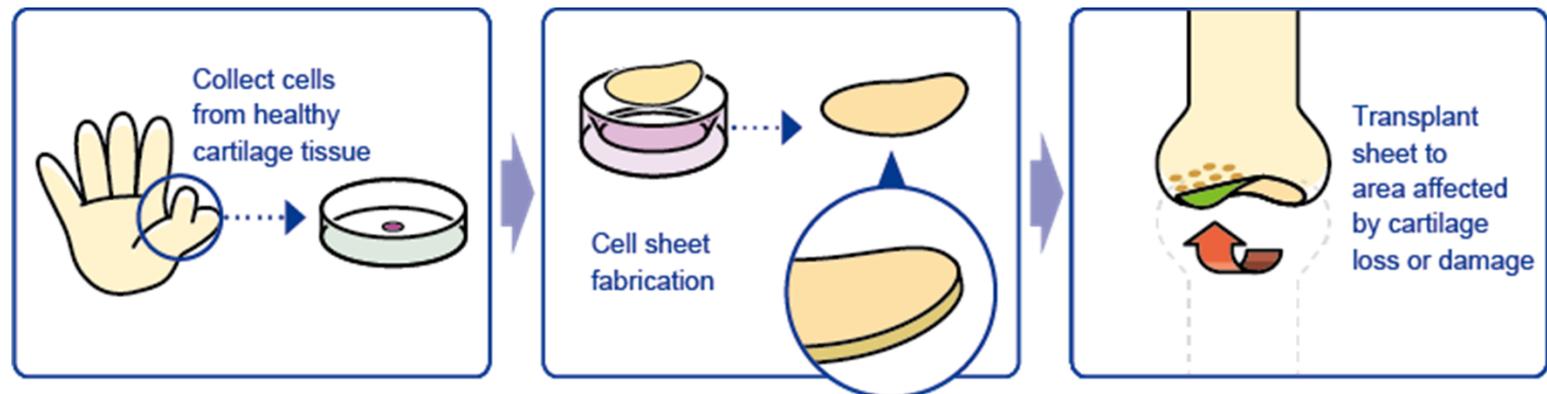
- 2016 Consulted with European Medicines Agency (EMA)
- 2017 Licensed out the product to MetaTech in Taiwan
- 2018 Submitted a notification of a clinical trial in Taiwan
- 2020 Suspended the clinical trial in Europe

- Disease characteristics
  - Causes : ageing • obesity traumatic
  - No treatment to regenerate lost cartilage is available
- In Japan, estimated number of potential patients about 30 million persons of which, about 10 million shows symptoms.

- **Autologous chondrocyte sheets**



- **Allogeneic chondrocyte sheets**



# Allogeneic chondrocyte sheets

2017  
|  
2019

Clinical Research at Tokai University  
Completed in December 2019 transplants of 10 cases

2018  
|  
2021

Adopted as the ancillary project of AMED  
Adopted as “a project for developing fundamental evaluation technologies for industrializing regenerative medicine (support for acceleration of development of regenerative medicine seeds)”;  
project period: Oct. 2018 to Mar. 2021

2020-

Acquired cartilage cell for commercial purposes  
from the National Center for Child Health and Development

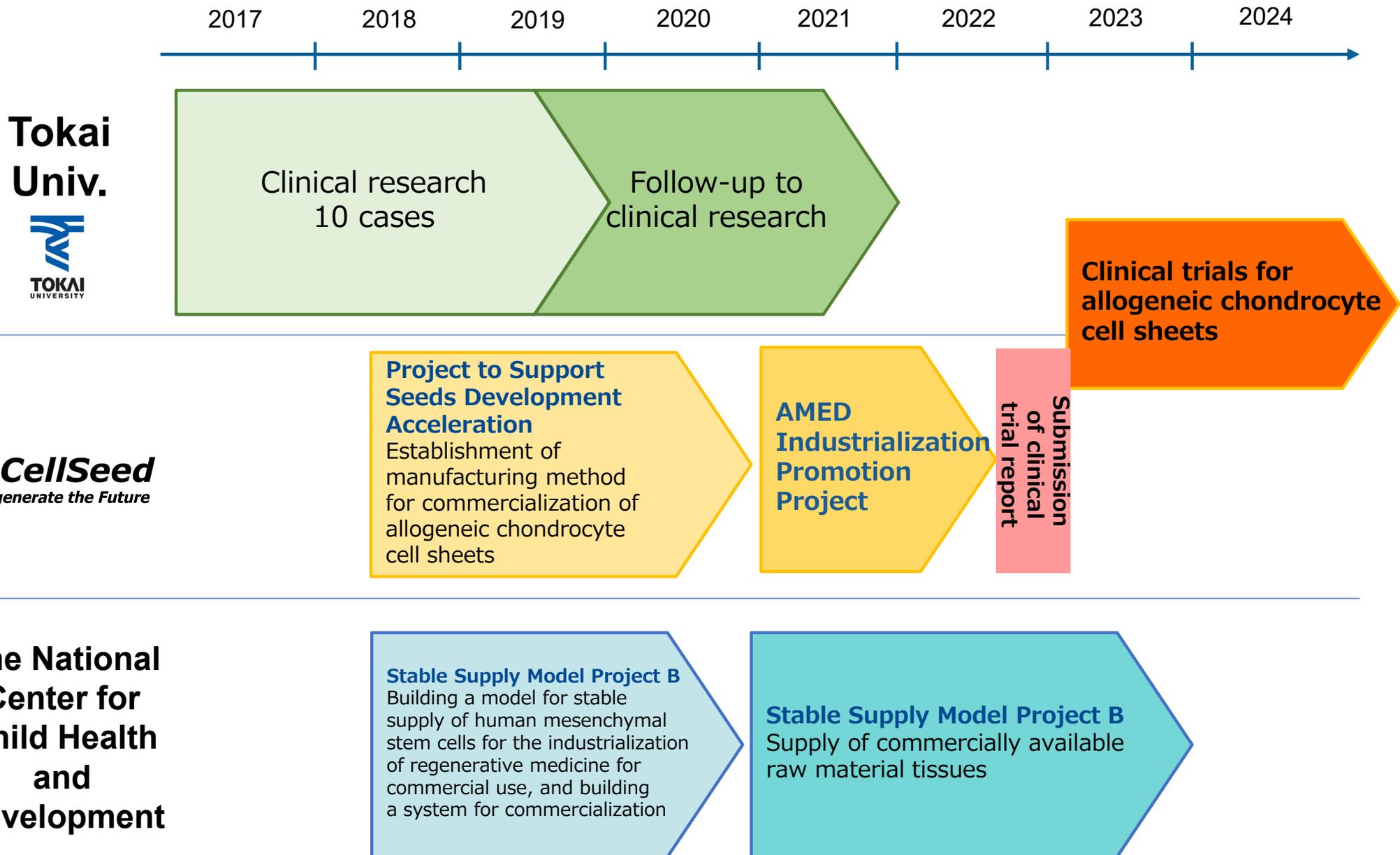
2021  
|  
2023

Adopted as the ancillary project of AMED  
Adopted as “a project for developing fundamental evaluation technologies for industrializing regenerative medicine (project for promoting the industrialization of regenerative and cell medicine and gene therapy)”;  
project period: Aug. 2021 to Mar. 2023

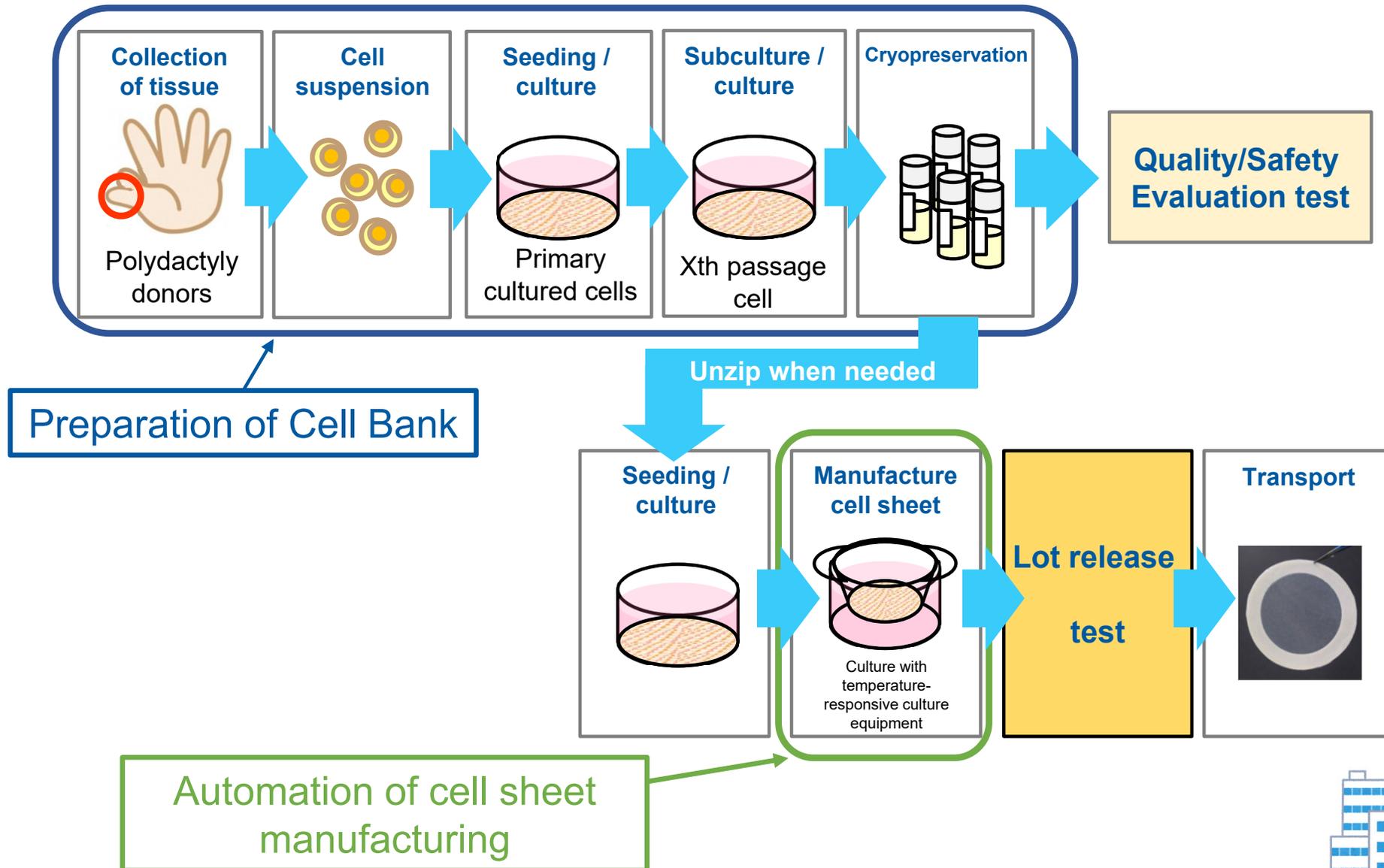
End of  
2022

**We plan to submit a clinical trial plan at the end of 2022.**

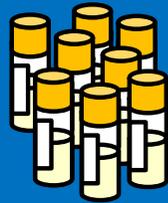
# <Allogeneic cells> Industry-academia collaboration in cartilage cell sheets



# Allogeneic chondrocyte sheets



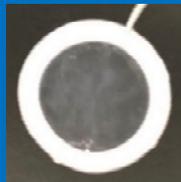
## Construction of cell bank



- Optimization of cell stock creation procedures
- Establishment of product manufacturing and quality control methods
- Non-clinical test
- Review of transport method



## Clinical trial product manufacturing Preparation for clinical trial



Receipt of commercial tissue  
Creation of stock



Creation of sheet for evaluation



Grasping the number of passages and changes in characteristics



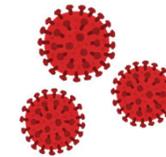
Pharmacological test  
(Heterogeneous orthotopic transplantation: Donor selection using cartilage regeneration as an index)

Non-clinical safety test

Characteristic test



Manufacturing and evaluation of cell bank



Optimization of manufacturing/quality control methods



Shipping test



Creation of protocol  
Consultation with PMDA





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