

CellSeed Inc.

Fiscal 2019

Earnings Results Presentation



Contents

- Company Profile
- Financial Summary FY12/2019
- Mid-term Business Plan Fiscal Year 2020 to Fiscal Year 2022

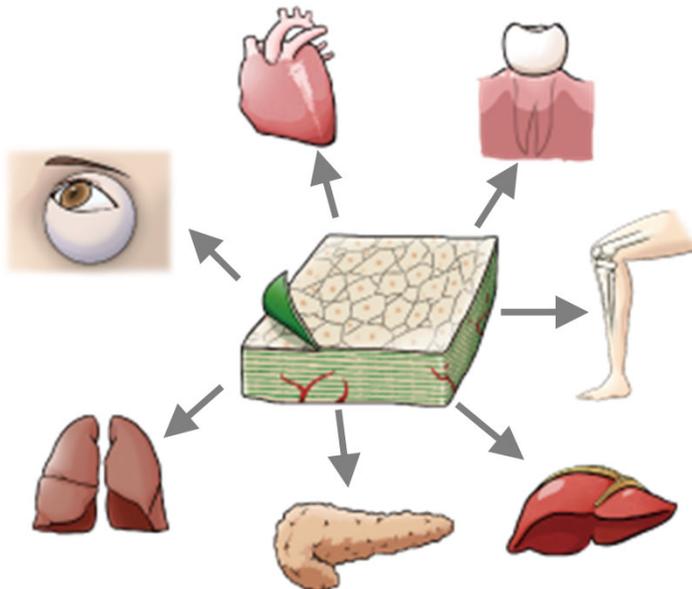
CellSeed Inc. Corporate Information



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



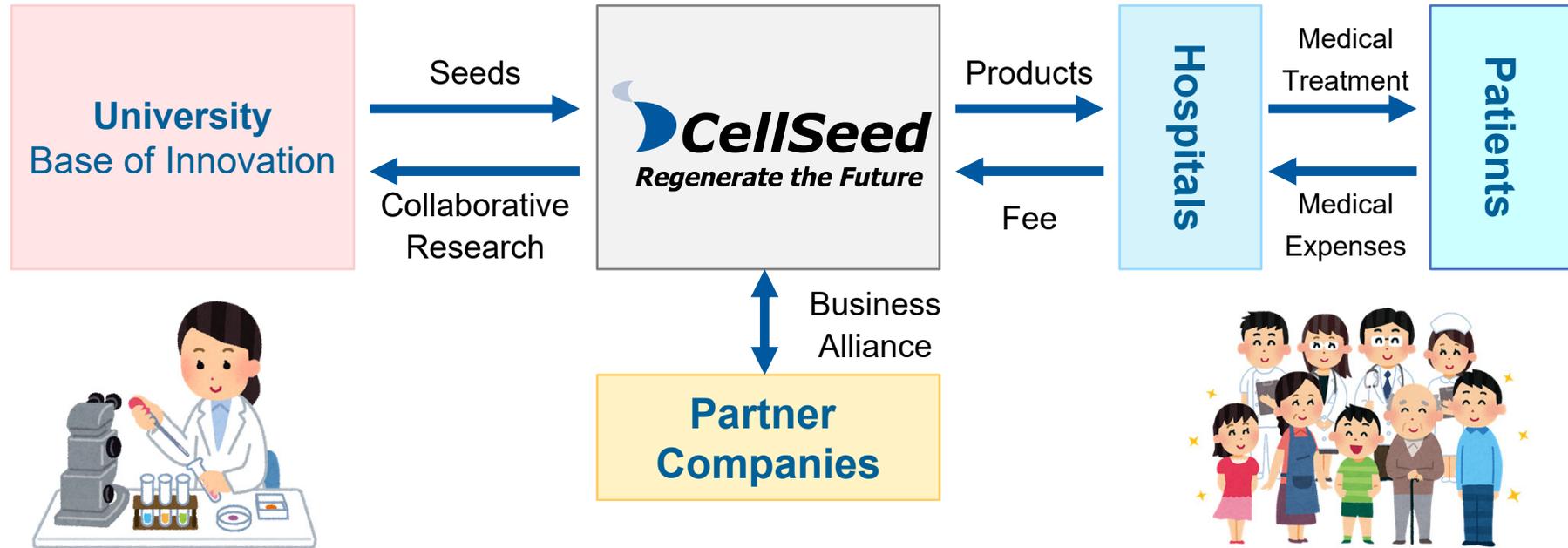
UpCell®

- Contract Manufacturing Services • Consulting



CPC

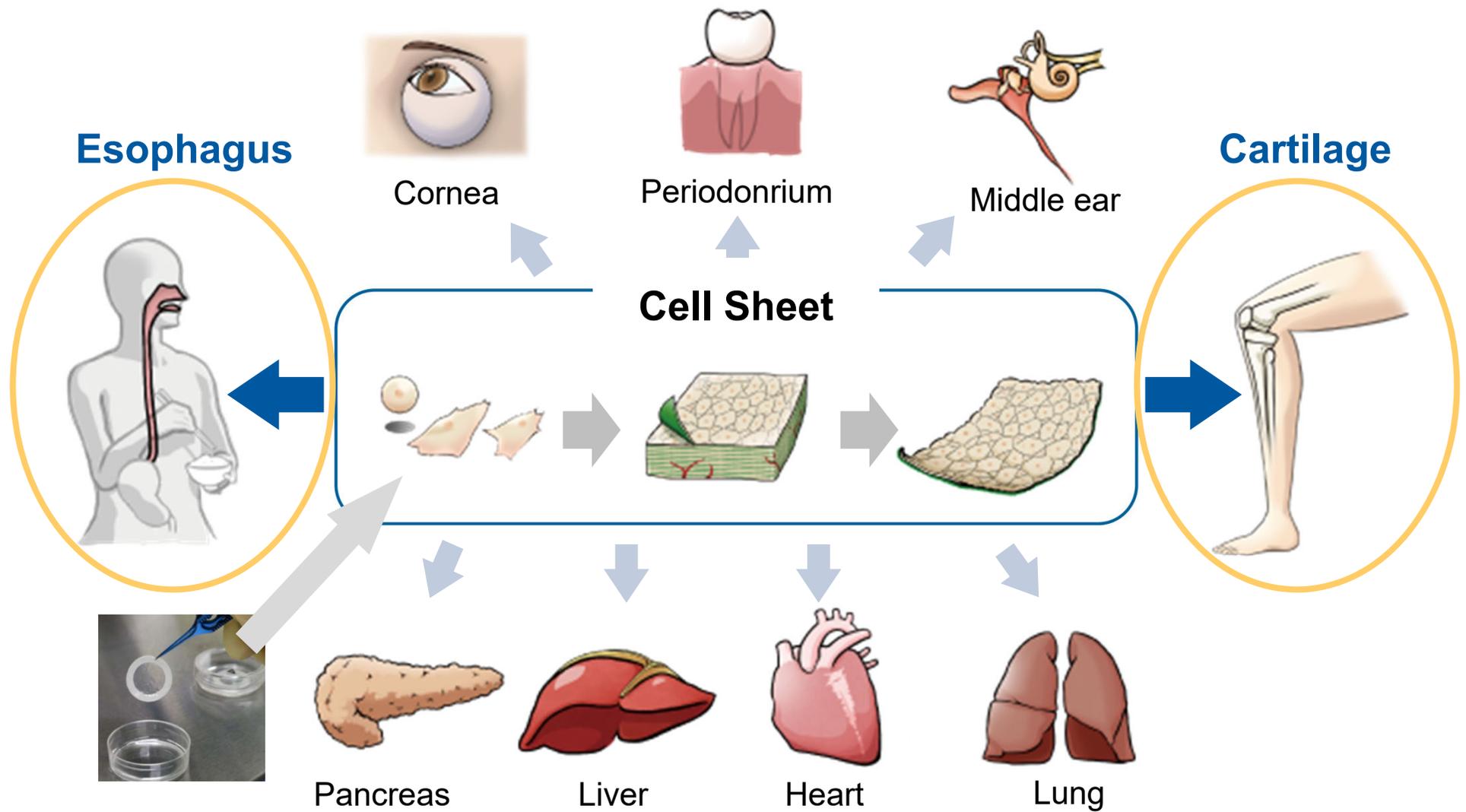
Our Business Model



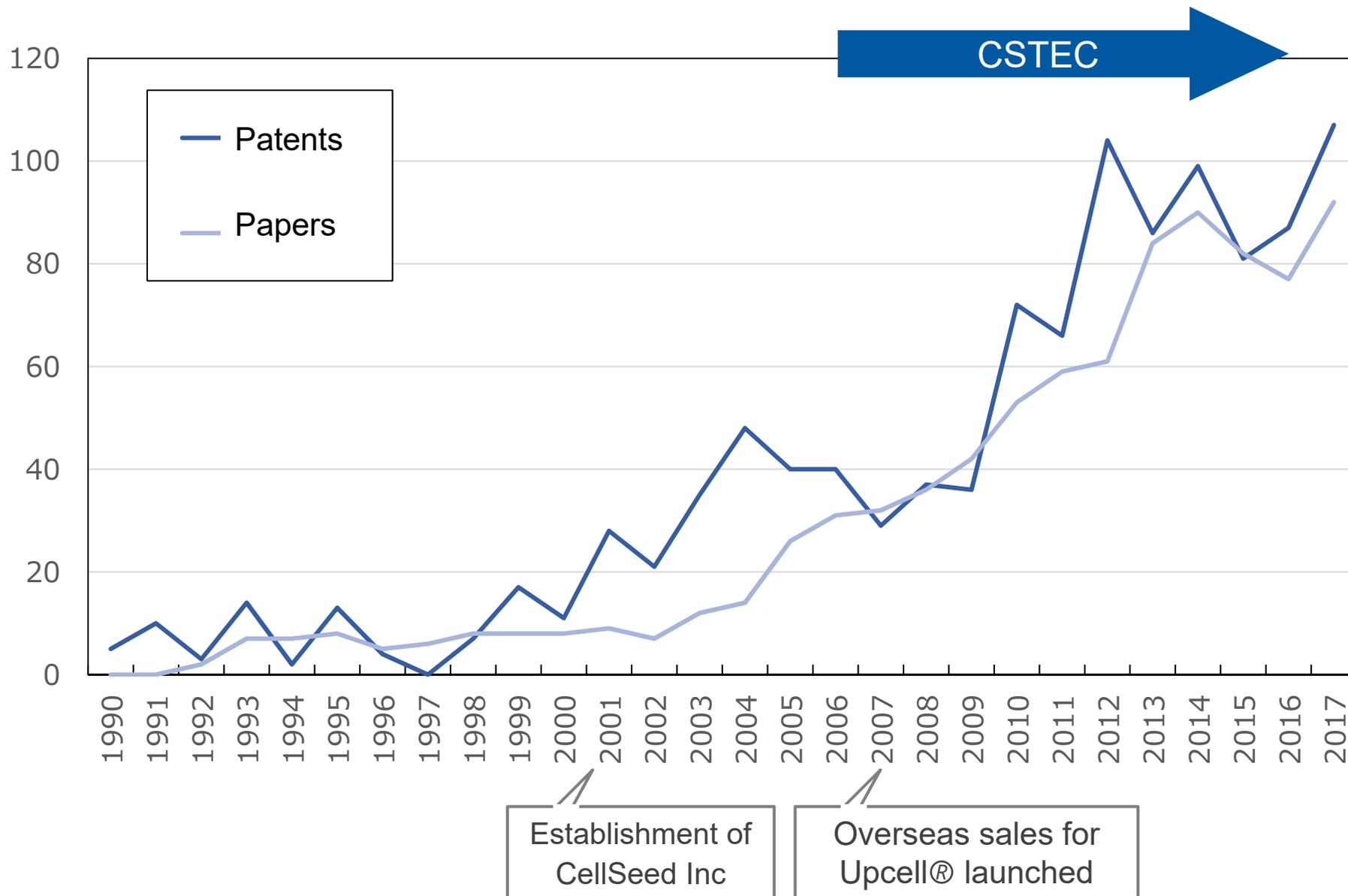
Mission

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



Expansion of Cell Sheet Engineering



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Financial Summary for the Fiscal Year Ending December 2019

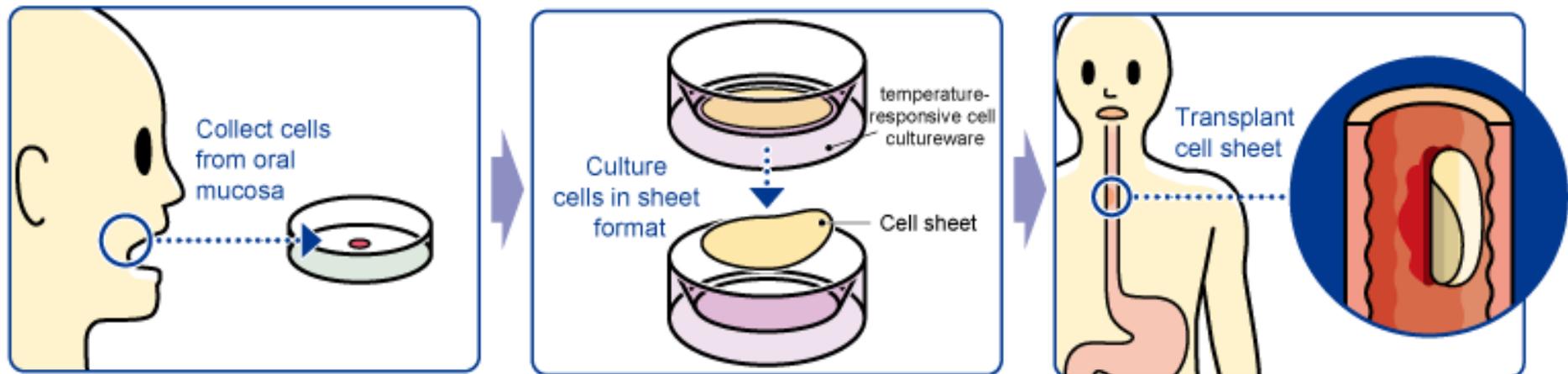
(Unit: Million yen; Presented with fractions less than one million yen rounded off)

	Net Sales	Operating Profit	Ordinary Profit	Profit attributable to owners of parent	Profit per share—basic
Forecast (A)	300	-1,100	-1,100	-1,100	-93.6
Actual (B)	275	-780	-786	-782	-66.6
Change (Millions of Yen) (B – A)	-24	319	313	317	—
Change (%)	-8.1%	—	—	—	—
FY2018	1,026	140	140	129	¥11.35

- Regenerative medicine supporting business: Especially, the overseas sales of equipment grew considerably year on year, hitting a record high. The business of consigned manufacturing of cell sheets was launched in November 2018, using the cell processing facility, and posted sales for the first time in 2019.
- Cell sheet regenerative medicine business: The milestone sales from the exclusive business alliance contract in Taiwan stood at 158 million yen.
- Profit on sales exceeded the estimate, mainly because the expenses for outsourcing development tasks, maintaining the cell processing facility, etc. fell below the initial estimate.

Epithelial Cell Sheet for Esophageal Regeneration (CLS2702C/D)

- 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



Clinical Research and Clinical Trials of Esophageal Cell Sheet

- **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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Tokyo Women's Medical University

Basic Development Agreement



- **Clinical Trials sponsored by CellSeed**

Japan



Taiwan (MetaTech)

Europe (Sweden)

- Submitted a notification of clinical trial plan on 2016
- “SAKIGAKE Designation” in Feb. 2017
- Completed the clinical trial in Japan
- Conduct consultation with PMDA on additional trial

- MetaTech has submitted IND in Taiwan.

Cell Sheet Regenerative Medicine Business in the Fiscal Year Ended December 2019

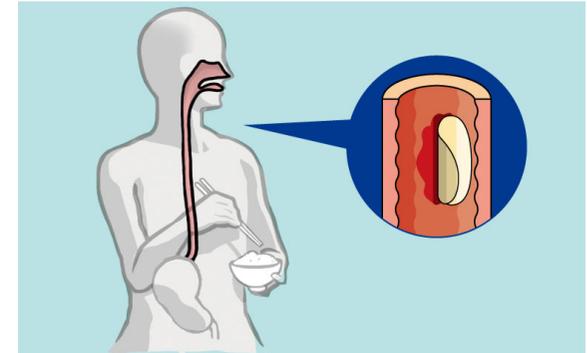
■ Epithelial Cell Sheet for Esophageal Regeneration

- Clinical trial for obtaining approval

Summer in 2016 Clinical trial commenced.

1Q in 2019 Clinical trial finished.

From 2019 Having a discussion with PMDA about additional clinical trials



- Guidelines for esophageal cancer diagnosis in 2017

Steroid became popular as a major treatment for preventing stenosis.

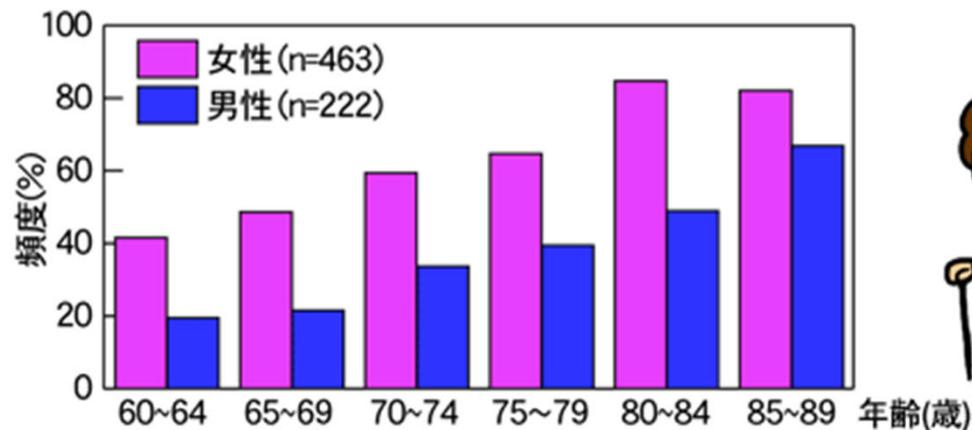


- It became necessary to apply the sheet to patients who may suffer from adverse effects of steroid administration in additional clinical trials.
- We are having a discussion with PMDA about target patients and the number of cases.

Chondrocyte Sheet

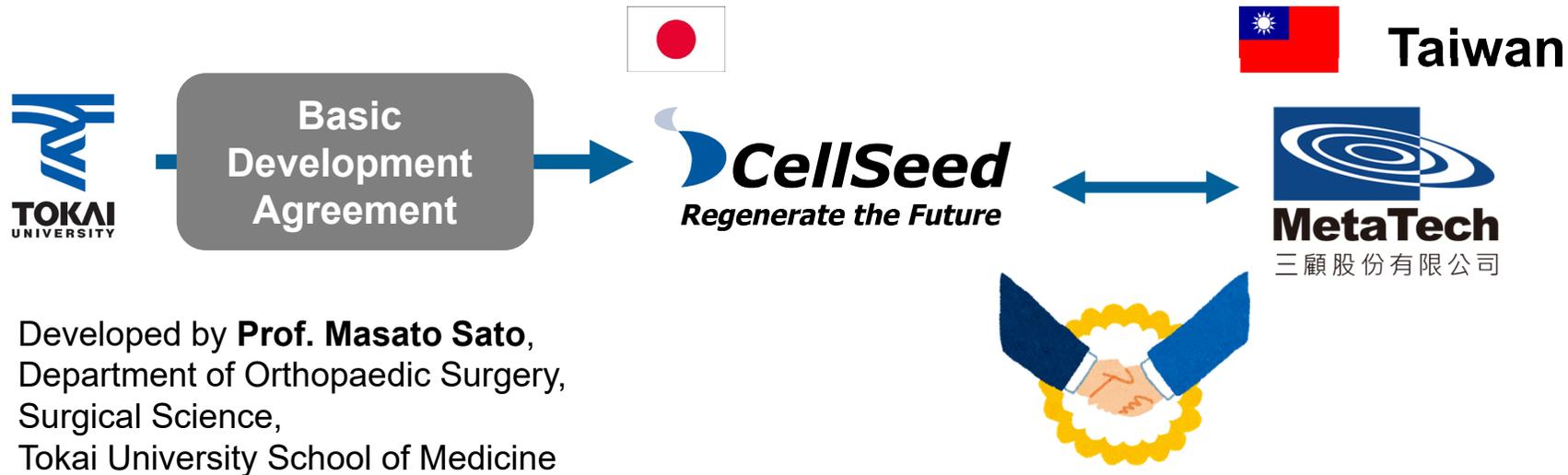
- Disease characteristics
 - Causes : ageing • obesity traumatic •
 - No treatment to regenerate lost cartilage is available
- In Japan, estimated number of potential patients 25,300,000 persons of which, 8,000,000 shows symptoms (22nd Century Medical and Research Center)

変形性ひざ関節症の男女別-年齢別割合 (61~86歳、Grade II 以上)



Go Omori, Yoshio Koga and others From epidemiological survey for osteoarthritis of the knee

Overview of Chondrocyte Sheet Project



< Autologous Cells >

- 2019/1
approved by the MHLW in the 71st
Conference on Advanced Medicine

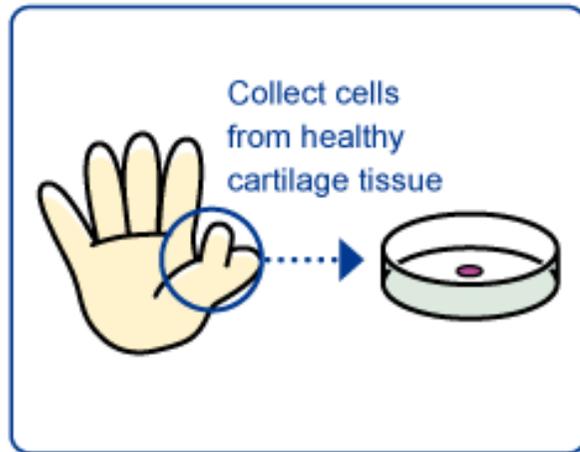
< Allogeneic Cells >

- 2019/12
completed transplants of 10 cases

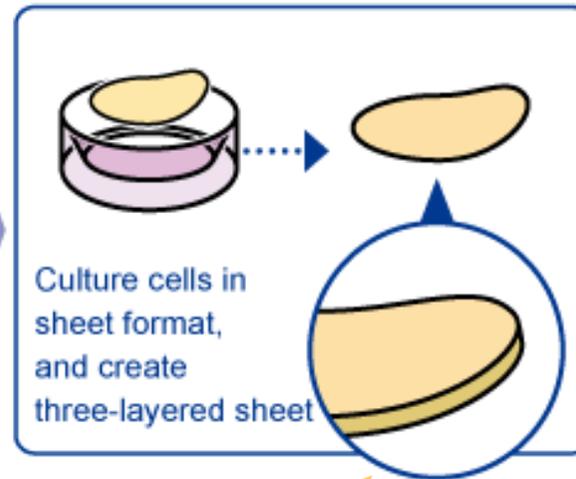
- Licensing out Autologous cell sheet to MetaTech in Taiwan
- Commercialization of Allogeneic Chondrocyte Sheet Product

Autologous chondrocyte sheets

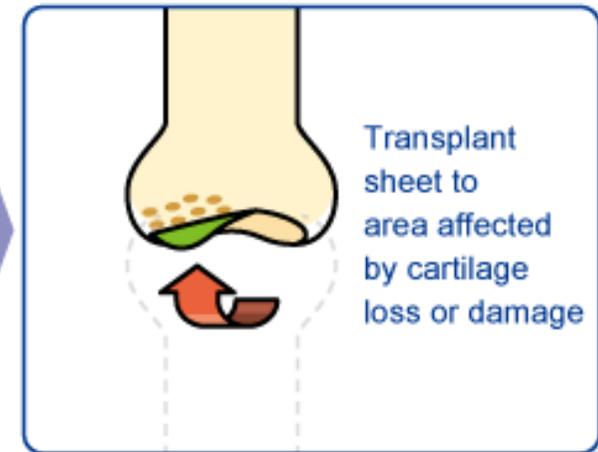
- Collect Autologous Cartilage Cells



- Manufacture Cell Sheet



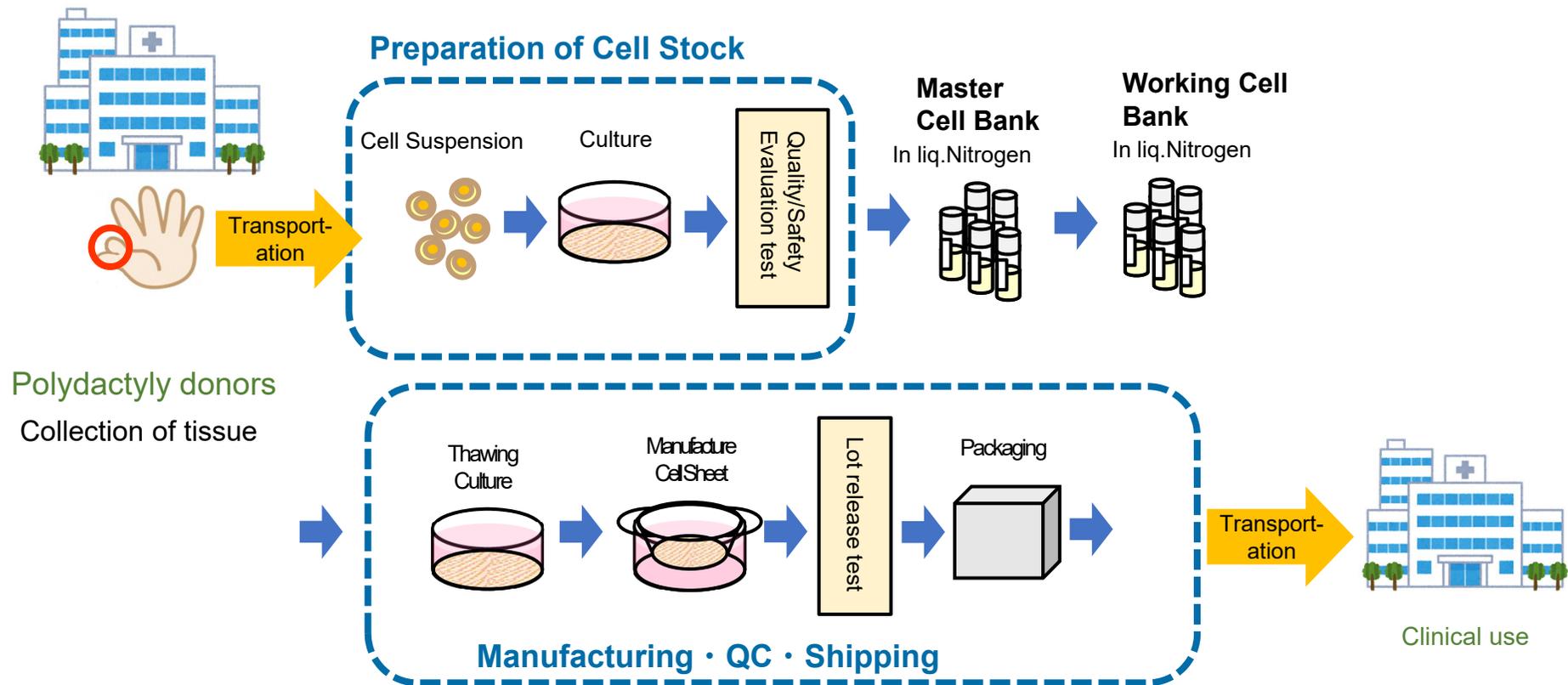
- Transplant to Patient



chondrocyte sheets

Indications : Knee Osteoarthritis

Allogeneic chondrocyte sheets



■ Clinical Research at Tokai University

- Completed in December 2019 transplants of 10 cases
- selected for the 2018 Project Focused on Developing Key Evaluation Technology: Acceleration of Developing Regenerative Medicine Technology Seeds (for 3 years, from October 2018 to March 2021.)

Cell Sheet Regenerative Medicine Business in the Fiscal Year Ended December 2019

■ Regenerated Cartilage Sheet

● Autologous Chondrocyte Sheet

➤ Jan. 2019

“The cartilage regeneration treatment with autologous cell sheets” proposed by Tokai University Hospital, with which we conduct joint research, was approved at the 71st advanced medical care meeting.

➤ Nov. 2019

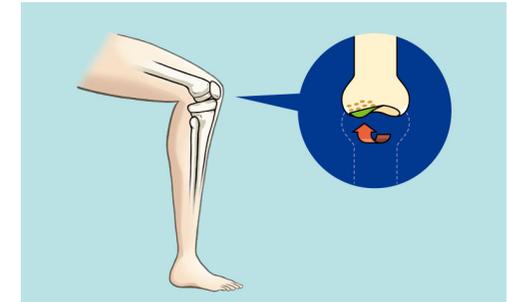
Together with Professor Sato of Tokai University, we applied for a patent regarding “manufacturing and utilization methods of cell culture sheets” in the U.S. and were granted the patent, to protect our intellectual property in Japan, the U.S., and Europe.

● Allogeneic cells

➤ Dec. 2019

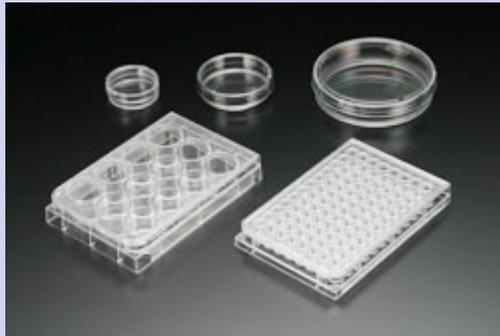
In Tokai University, allogeneic cartilage cell sheets were transplanted into 10 patients in clinical research.

➤ Since the system for supplying human tissue for commercial use had not been established, it took time to obtain human tissue and the commencement of clinical trials was delayed.

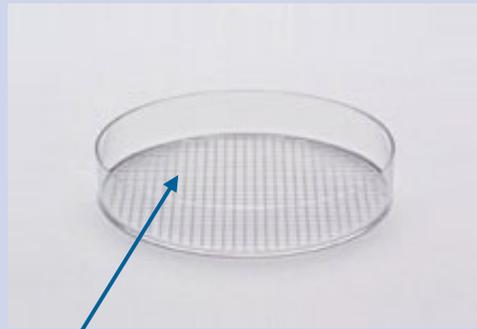


CellSeed Temperature Sensitive Cell Cultureware Lineup

UpCell®
Cell Sheet Recovery
(Temperature Sensitive)



RepCell™
Cell Recovery
(Temperature Sensitive)



3 x 3 mm Grid Wall

HydroCell™
Ultra-Low Adhesion Cell
Cultureware



Acquisition of ISO 9001: 2015 Certification

We offer consistent quality and services in the design of and manufacturing control of cell cultureware. To further improve client satisfaction, we have constructed a quality management system and acquired certification under the international standard, ISO9001: 2015. Aiming to boost client satisfaction, we will comply with this standard and with all relevant laws and regulations as we carry out continuous improvement of quality management.

- Date of registration : January 6, 2020
- Period of validity : January 6, 2023
- Scope of registration : Design and manufacturing control of cell cultureware
Sales of special cell monitoring devices
and measuring instruments



Regenerative Medicine Supporting Business

1. Regenerative Cell Sheet Product Manufacture Method Development, Consigned Manufacture

- Consigned manufacture
- Manufacture method development
- Quality testing
<Characteristics>
 - Cell sheet manufacturing using UpCell®
 - Certified facility for specific cell processing (FA3160008)
 - Japanese Society for Regenerative Medicine Certified Clinical Culturing Specialist, including large number of staff with bountiful experience and knowledge of culturing technologies



2. Facility Management, Application Submission Support

- Support for certification application, notification for specific cell processing
- Document creation for procedural manual, standard handbook, others consulting
- Cell processing center facilities, support management structure, maintenance provision
- Application document creation, others



3. Cell Culturing Technician Training

- Cell sheet culturing training
- Cell sheet peeling training, others



Regenerative Medicine Supporting Business in the Fiscal Year Ended December 2019

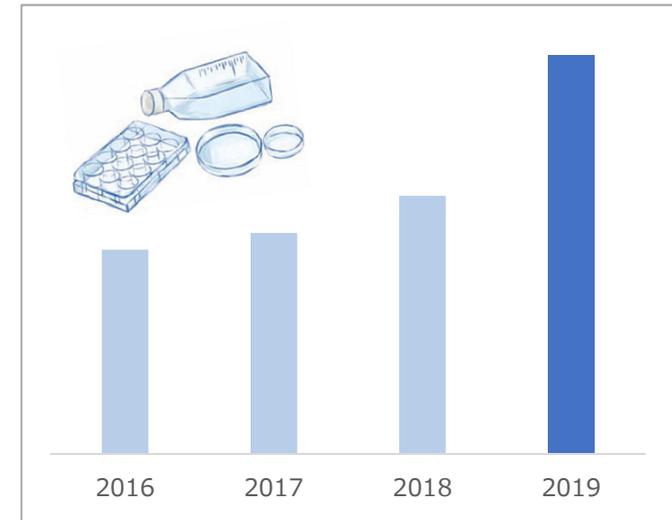
■ Sales of Equipment

- We collected information on sales of equipment from major distributors and conducted marketing activities in cooperation with distributors for sales promotion.
- We participated in many exhibitions, to promote sales actively.
- Especially, overseas sales increased considerably.



Sales hit a record high.

Variation in sales of equipment



■ Contract Development and Manufacturing Service

- Received the first order for the cell sheet for doctor-led clinical trials of periodontal ligament cell sheets from Tokyo Women's Medical University.
- Conducted cell sheet culture training for academia.



Close collaboration with academia

■ 1st Cell Sheet Engineering Innovation Forum July 19, 2019

200 people attended

◆ Keynote speech : Prof. Teruo Okano

◆ Presentations of clinical applications

- Dr. Takanori Iwata : periodontal ligament
- Dr. Goshi Shiota : liver diseases
- Dr. Shuichi Sekine : construction of 3D organ
- Dr. Masato Sato : osteoarthritis

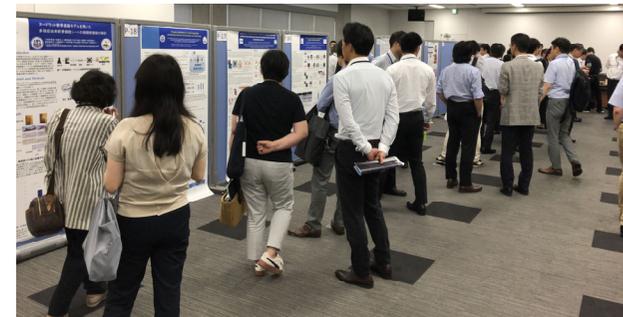
◆ Poster awards for young researchers

• **Best Performance Award**

- Dr. Tetsuya Imamura (Shinshu Univ.)

• **outstanding performance award**

- Dr. Takumi Takahashi (Tokai Univ.)
- Dr. Tetsutaro Kikuchi (Tokyo Women's Medical Univ.)



Production of Application Notes

■ Dr. Tetsuya Imamura of Shinshu University

At the first cell sheet engineering innovation forum, he received the most excellent poster award.

He engages in regenerative medicine research with the tissue engineering method using mesenchymal stem cells in the department of urology.

Dr. Tetsuya IMAMURA

Assistant Professor

Shinshu University

Department of Urology, School of Medicine

● Research Field

Regenerated Medicine, Lowr Urinary Tract Medicine



Application Note | UpCell®

温度応答性細胞培養器材 UpCell® を利用した細胞シート工学によって Tissue Engineering の未来を開拓する

＝骨髄由来細胞シートを利用した下部尿路症状の新規治療の開発＝

信州大学 医学部 泌尿科学教室
医学博士
助教 今村 哲也

下部尿路症状に対する標準治療は、薬物療法であるが、薬物に対して抵抗性を示す下部尿路症状は、治療に難渋し患者の生活の質を著しく低下させる。したがって、新規治療開発は患者の生活の質の向上の為に最も急務な研究課題である。（※膀胱の炎症・尿道の機能的低下が生じる膀胱トロッピング）
現在、間葉系幹細胞を用いて、Tissue Engineering 手法を駆使して下部尿路の再生医療研究を進めており、その一つが、UpCell® を利用した細胞シート工学の応用【骨髄由来細胞シートのパッチ移植】である。

● 温度応答性細胞培養器材 UpCell® を利用した細胞シートとの出会い

UpCell® を利用した細胞シートを用いた膀胱再生医療研究に着手した背景には、骨髄由来細胞を直接注入移植する形での考慮がある。尿道構築を促すための薬剤や、膀胱癌抑制による傷害を有する膀胱の膀胱癌腫モデルに、細胞を直接注入移植する方法を試みて、一部平滑筋の再生など、一定の効果を観察した。しかし、移植細胞の増殖、もしくは生存率が低く、また、細胞活性の低下や移植による炎症と組織での構築の遅延の懸念を有する懸念があった。このことから、直接移植方法よりも、効果的な移植細胞のアリバイシステム

そこで、UpCell® を利用して作成した細胞シートを膀胱の外傷からパッチ移植する方法を考えた。特に、温度応答性材料を用いた温度応答性細胞培養器材 UpCell® は、37℃から 20～25℃に温度を下げるだけで容易に付着した細胞シートの細胞外マトリックスを壊すに反応できる為、細胞活性の高い、良質な細胞シートが利用可能で、最適な培養器材として選択した。

● UpCell® を利用した細胞シートによる膀胱再生

UpCell® を用いて作成した骨髄由来間葉系幹細胞シートを膀胱癌腫新化した膀胱癌腫に、パッチ移植すると機能的な膀胱が再生し、その再生態勢は、細胞シートを形成している骨髄由来幹細胞のバックリン効果であることを明らかにした。(1)

本稿では、UpCell® を用いた骨髄由来幹細胞シートの前製方法及び膀胱へのパッチ移植の方法について紹介する。

参考文献
1. Imamura, Ogawa, Minagawa, Yokoyama, Nakazawa, Nishizawa, and Ishizuka. Engineered bone marrow-derived cell sheets restore structure and function of radiation-injured rat urinary bladder. *Tissue Engineering Part A* 21: 1600-1610, 2015 DOI: 10.1089/ten.tea.2014.0292

2nd Cell Sheet Engineering Innovation Forum

- Date : October 15, 2020
- Venue : Miraikan
- Capacity : 200 people
- Theme : “Cell Sheet” or research using “temperature-responsive cell cultureware”
- Presentations of clinical applications
 - Dr. Tatsuya Shimizu (Tokyo Women’s Medical Univ.)
 - Dr. Yuji Miyahara (Tokyo Medical and Dental Univ.)
 - Dr. Ryoichi Sakiyama (Osaka Institute of Technology)

第2回細胞シート工学イノベーションフォーラム
The 2nd Cell Sheet Engineering Innovation Forum

～細胞シートの未来を語ろう!～

2020年10月15日(木)
13:30～(受付12時) 懇親会18:00～

science bar INCUBATOR
出張出張

会場: 日本科学未来館 7階
定員: 200名(事前登録制、先着順)
参加費・懇親会費: アカデミア: 無料
企業の方: 3,000円

※ 会場は事前確認となります。
※ 日本科学未来館の常設展の入場は別途料金が必要です。

講演者
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東京女子医科大学 先端生命医科学研究所 所長、教授
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東京医科歯科大学 生体材料工学研究所 所長、教授
崎山 亮一
大阪工業大学 工学部生命工学科 准教授

※ 講演者については変更される可能性があります。

CellSeed
Regenerate the Future

ポスター演題募集

テーマ 「細胞シート」、「温度応答性細胞培養器材」及び周辺技術に関する研究

最優秀賞 30万円×1名
優秀賞 5万円×4名
奨励賞 1万円×数名

※ 賞金は賞状と併せて、最優秀賞候補の方には特別賞金(1万円)を行っていただきます。

旅費支援
関東圏外の方: 交通費全額+宿泊費一律1万円
関東圏内の方: 交通費のみ一律2千円

※ 旅費支援はポスター発表に採択された方が対象となります。

Other activities FY12/2019

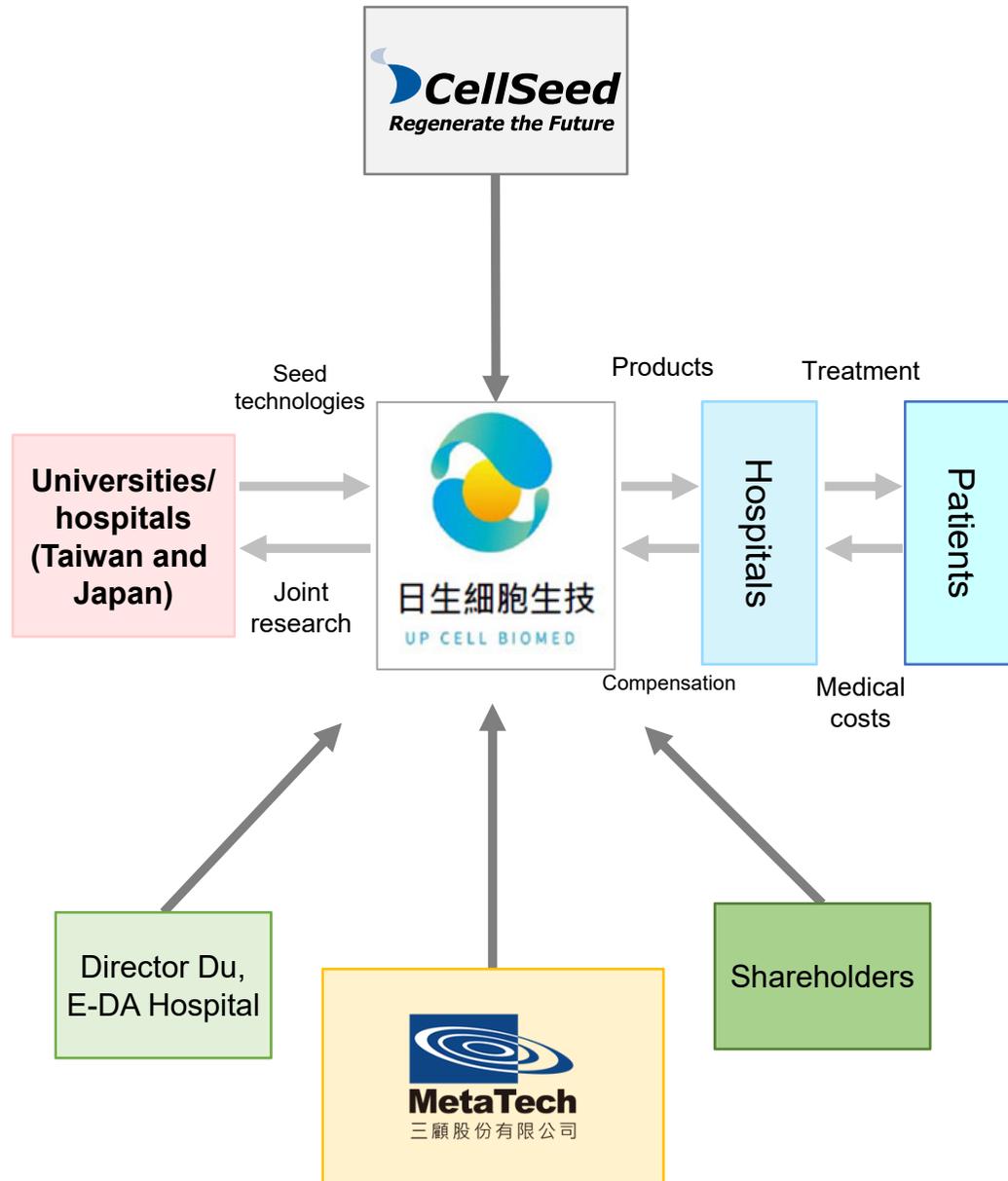
- Nov. 2019: Our company and MetaTech in Taiwan took the initiative in joint investment.
- Dec. 2019: Held a press conference in cooperation with MetaTech at Healthcare EXPO TAIWAN.
- Jan. 2020: Established a joint venture.



Establishing Up Cell Biomedical Co.

Name	Up Cell Biomedical Co.
Address	14F.-2, No. 75, Sec. 1, Xintai 5th Rd., Xizhi Dist., New Taipei City 221, Taiwan (R.O.C.)
Representative	President Andrew H.-J. Wang
Business operations	establish utilize the seeds technology provided by Japanese or Taiwanese universities and research institutions in order to develop regenerative medicine products and therapies using cell sheet engineering
Capital	NT\$130,000,000 (at establishment; approx. 500,000,000 yen)

Overview of Up Cell Biomedical Inc.



■ Board Members

- President / Andrew H.-J. Wang
- Vice President / Ho Hung-Neng
- Director / Setsuko Hashimoto

■ Advisor

- Yang, Zhi-Hui

■ Scientific Advisory Board

- Chen Yaochang
- Huang Yen-Hua
- Masayo Takahashi

Promoting Global Business Alliances

■ Scheduled Participation in Exhibitions in 2020 (Outside Japan)

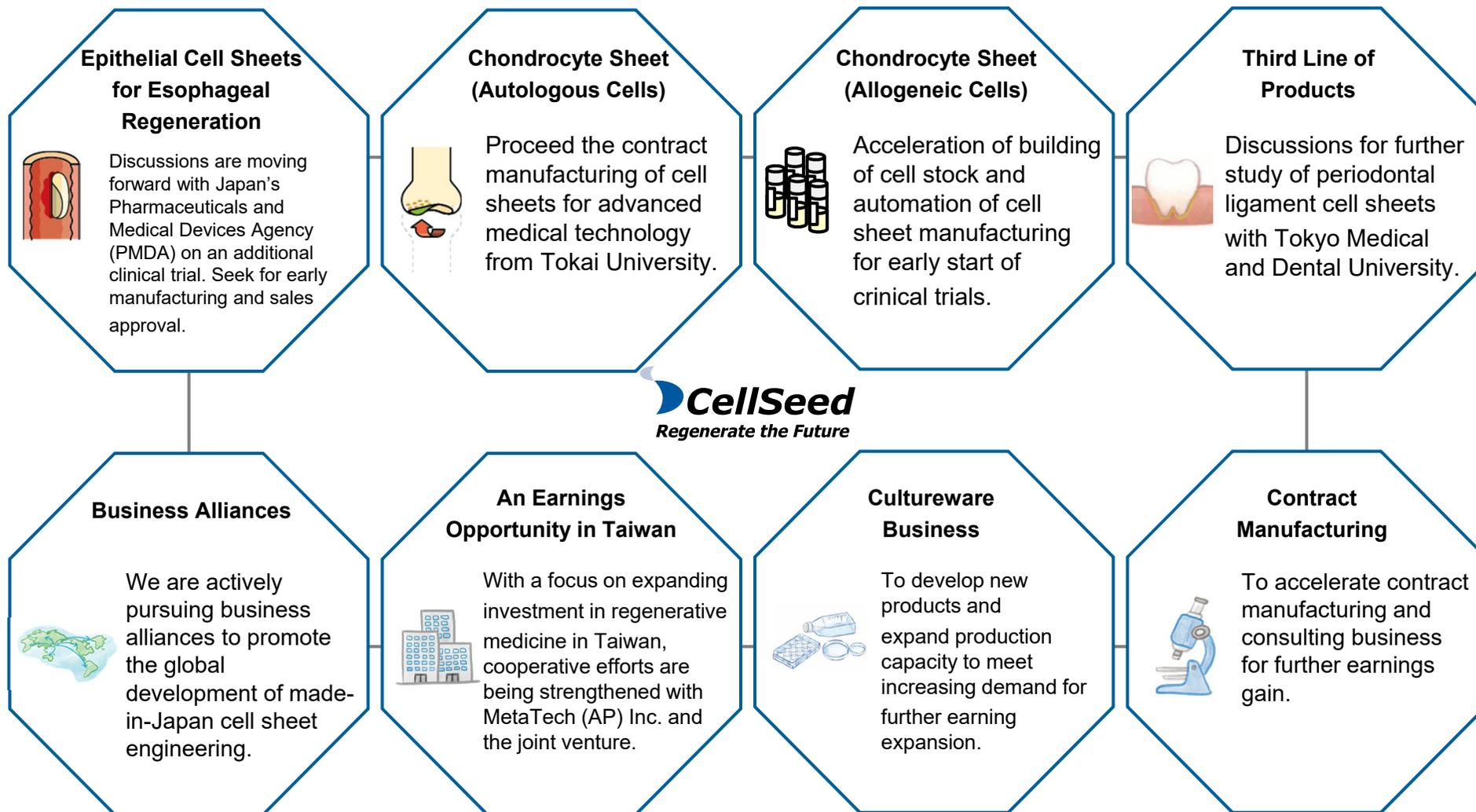
- May / China BIO (Suzhou)
- December / BioUS (San Diego)
- June / Bio Asia Taiwan (Taipei)
- July / BIO Partnering APAC 2020 (Shanghai)
- September / BIOEU Fall (Germany)
- October / Healthcare EXPO TAIWAN (Taipei)



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Mid-term Business Plan Fiscal Year 2020 to Fiscal Year 2022



Mid-term Business Plan (2020 – 2022) Financial Targets

(Unit: Million yen; Presented with fractions less than one million yen rounded off)

	Net Sales	Operating Profit	Ordinary Profit	Profit attributable to owners of parent
FY2020 (Estimate)	310	-1,020	-1,020	-1,020
FY2021 (Target)	360	-1,030	-1,030	-1,030
FY2022 (Target)	1,400	10	10	8

*sales composition (Millions of yen)

Regenerative Medical Products Business

FY2020 : 230 FY2021 : 320 FY2022 : 390

Regenerative Medicine Supporting Business

FY2020 : 80 FY2021 : 40 FY2022 : 1,010



This presentation is made by CellSeed Inc. solely for the disclosure of the financial statements, and not published for the purpose of soliciting sales or purchases of securities in Japan and any other regions.