2020.1.1～2020.12.31

With you CellSeed Vol.13

CellSeed
Regenerate the Future

CellSeed Inc.

Securities Code: 7776

CellSeed Inc.
Representative Board Director
and President/CEO
Setsuko Hashimoto

Celebrating its 20th Anniversary of CellSeed

In May 2021, CellSeed will celebrate its 20th anniversary. We would like to express our sincere gratitude to our shareholders for their continued support. Over these past 20 years, academic researchers have conducted research into which cell sheet engineering technique can be applied and have produced numerous results. At CellSeed, a clinical trial on epithelial cell sheets for esophageal regeneration was initiated, and the development of chondrocyte sheets has made steady progress.

In our regenerative medicine support business, product supply intended for the mass culturing of cells for laboratory use and enhanced collaboration in sales activities with sales partners resulted in a steady increase especially in overseas sales in the cultureware business, which generated the highest sales in our history.

In our cell sheet regenerative medicine business, an application for an additional clinical trial on epithelial cell sheets for esophageal regeneration was filed in October 2020, and the first subject was enrolled in February 2021. Tokai University started the treatment of our Advanced Medical Care B program using autologous chondrocyte sheets. CellSeed was asked to manufacture the chondrocyte sheets. Treatment using autologous chondrocyte sheets was initiated in Taiwan as well, and the sheet has been transplanted in 10 patients so far, which brought us milestone fees based on a contract with MetaTech.

Regarding the development of allogeneic chondrocyte sheets, the provision of commercially available tissues from the National Center for Child Health and Development started in 2020, and this has enabled the stable supply of chondrocyte tissues and will help accelerate R&D activities for clinical trials and marketing approval.

Medium-term Business Plan from FY2021 to FY2023

The following eight pillars will play a role in our business:

1. Epithelial sheet for esophageal regeneration: Start additional trial, aimed at submission of application for manufacturing and sales approval in FY 2025.
2. Allogeneic cartilage regeneration sheet: Expedite non-clinical study data gathering aimed at submission of clinical trial notification at the end of FY 2022.
3. Collaboration: Rebuild collaboration with MetaTech and Taiwanese JV company, aimed at acquiring further income generating opportunities.
4. Business alliance: Actively promote partnerships to globally develop cell sheet engineering originating in Japan and thereby generate increase in income.
5. Cultureware: Push up cell cultureware product sales overseas by strengthening alliance with Thermo Fisher Scientific Inc.
6. Cultureware: Expand business by developing/supplying cultureware to new markets for mass culture of cells for research needs.
7. Overseas sales: Improve and expand production system/capacity to enable us to expand overseas sales and cultureware supply to new markets, aimed at generating further increase in income.
8. Other: Promote development, OEM and consulting operations, aimed at generating further increase in income.

Future Prospects

Japan-originated cell sheet engineering has been used in regenerative medicine for patients not only in Japan but also in Taiwan and other countries.

To disseminate knowledge of the world's first Japan-originated cell sheet engineering to more researchers, the Cell Sheet Engineering Innovation Forum, which was first held in 2019, will be held in November 2021.

We will continue to strive to commercialize cell sheet regenerative medicine products so as to deliver treatment methods based on Japan-originated cell sheet engineering to patients around the globe.

We sincerely ask our shareholders for their continued support.

Around 1980

Biopharmaceuticals and genetically engineered pharmaceuticals

Biopharmaceuticals using recombinant proteins and genetically engineered pharmaceuticals using genes as pharmaceutical products

2001

CellSeed founded

Founded to conduct R&D based on cell sheet engineering

2004

RepCell® and HydroCell® launched

2007

UpCell® launched Clinical trial on epithelial cell sheets for corneal regeneration initiated in France

2010

Listing on JASDAQ

2013

Application for approval for epithelial cell sheets for corneal regeneration in Europe withdrawn

2014

Joint research agreement on chondrocyte sheets with Tokai University concluded

2016

Head office relocation to the Telecom Center Building
Clinical trial on epithelial cell sheets for esophageal regeneration initiated
Cell Processing Facility established

2017

Approval to manufacture specified cell processing products acquired
Conclusion of the contract for business alliance with MetaTech (AP) Inc.

2018

Start of regenerative medicine contract services

2020

Establishment of joint venture in Taiwan

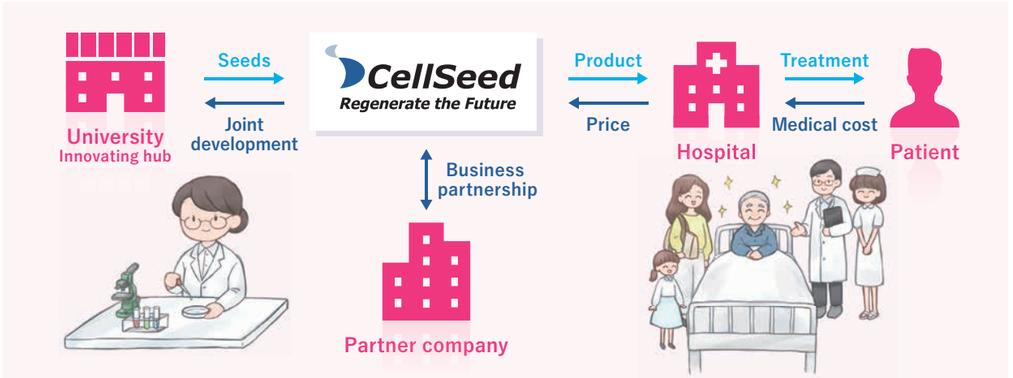
2021

20th anniversary of the foundation of CellSeed

1980 ··· 2000 2002 2004 2006 2008 2010 2012 2014 2016 2018 2020

CellSeed's Regenerative Medicine

Regenerative medicine is a new field of medicine that aims to treat and regenerate organs that are lost or damaged or for function is compromised. Using seeds created as a result of R&D conducted by university researchers, CellSeed strives to contribute to Japanese and global medicine by commercializing the regenerative medicine products developed in clinical trials that we conduct alone or with a partner company.



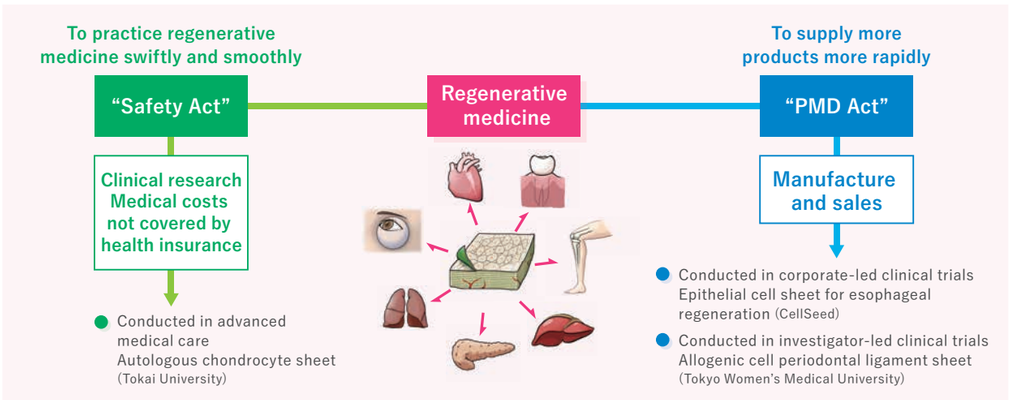
Regenerative medicine is practiced under the following two acts in Japan:

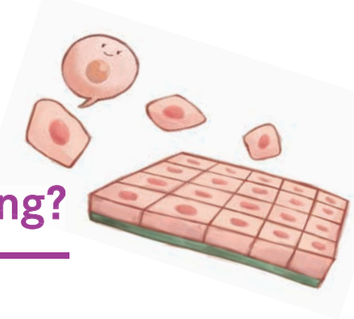
1 The Act on the Safety of Regenerative Medicine (the "Safety Act")

This act is designed to restrict regenerative medicine and dental regenerative medicine conducted under a physician's responsibility.
It applies to clinical research and advanced medical care conducted at universities. This new act allows for the contract manufacture of cells used for treatment at a facility for which approval for quality assurance systems and manufacturing ability has been granted. Our Cell Processing Facility has obtained approval to serve as a specified cell processing facility and conducts the contracted manufacture of "autologous chondrocyte sheets", which are used in the Advanced Medical Care B program implemented at Tokai University.

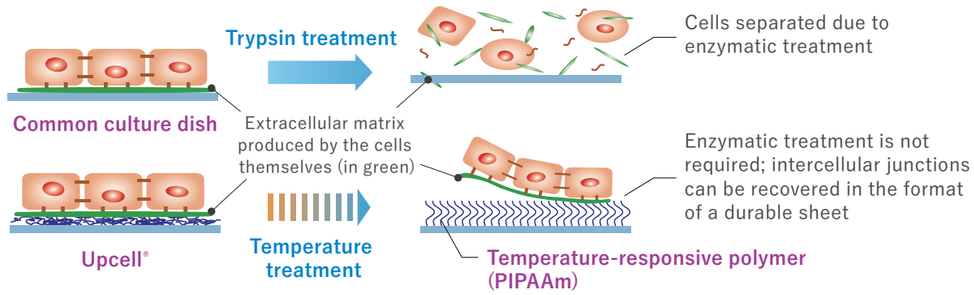
2 The Act on Pharmaceuticals and Medical Devices (the "PMD Act")

In case a corporate entity applies for approval for a product, the product's manufacture, sales, and approval will be implemented according to the Act on Pharmaceuticals and Medical Devices. The development of "epithelial cell sheets for esophageal regeneration," which CellSeed intends to commercialize, is conducted under this act.

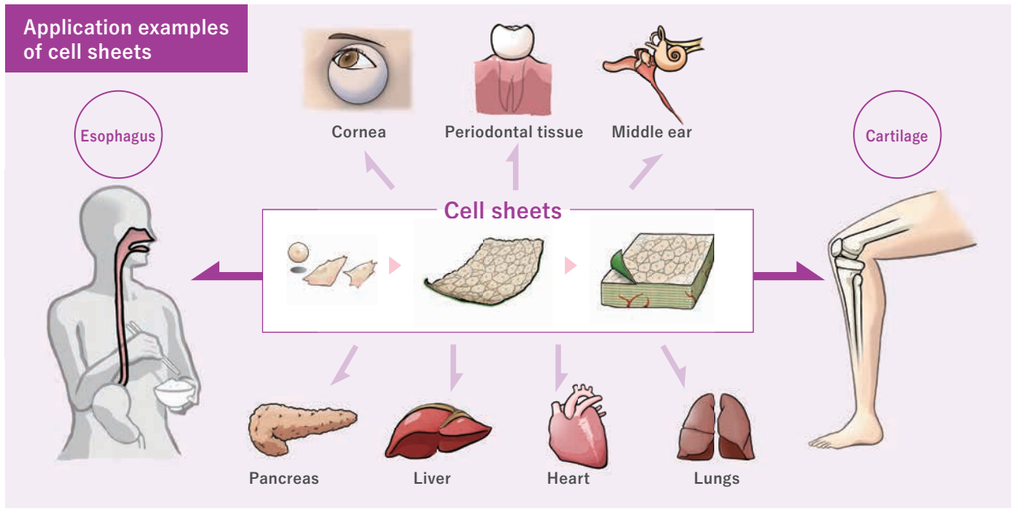




What Is Cell Sheet Engineering?

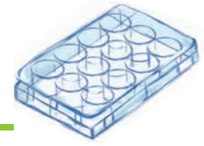


Cell sheet engineering is a technology that recovers cells in sheet format using temperate-responsive cell cultureware developed by CellSeed. Unlike existing technology, enzymatic treatment is not required; culture cells can be recovered simply by changing the culture temperature. Because recovered cells are not affected by enzymatic treatment, proteins between two cells can be recovered intact in sheet format. Adhesive proteins that the cell forms between the cell and cultureware surface during the culturing process remain intact; therefore, the recovered cell sheet can be immediately absorbed into bodily tissue, and this allows a layer of cell sheets to be adhered together. Additionally, because these cell sheets are not affected by enzymatic treatment, the original function of cells is retained, which is one of the key benefits.
Cell sheets developed via this technology will likely make it possible to treat diseases that cannot be treated by conventional medicine.



CellSeed currently promotes the development of epithelial cell sheets for esophageal regeneration and chondrocyte regenerative sheets as our pipeline for early commercialization.

From the Birth of CellSeed's Cell Cultureware to Today



In 1989, Professor Teruo Okano, an emeritus professor at Tokyo Women's Medical University, engaged in the development of artificial blood vessels and developed temperature-responsive cell cultureware with temperature-responsive polymers fixed to the surface by taking advantage of the characteristics of the polymers.
Using temperature-responsive cell cultureware, cells can be detached simply by lowering the temperature to 20°C; cells can be recovered intact in the format of one sheet.
Now that temperature-responsive cell cultureware is available worldwide, many researchers actively conduct R&D activities on treatment using such cell sheets.
Currently, applications for such sheets are in widespread use, ranging from regenerative medicine to the mass culture of cells for laboratory use and other new purposes. We will make further efforts to improve and expand the production system to address increased product supply and overseas sales. To provide consistent quality and services, as well as to achieve higher customer satisfaction, we established a quality management system and obtained IS09001:2015—an international standard.

Supplying cultureware to companies developing cells for laboratory use to tackle COVID-19

Our client, MiCAN Technologies Inc., specializes in the development of a variety of cells for laboratory use for the treatment of infectious diseases, such as COVID-19, and immune disorders, and they have adopted our "HydroCell®" cell cultureware in their development process.
Their project, known as "Cell development for the evaluation of ADE in vaccine development for COVID-19," has been selected as a "Project for developing technology to tackle viral infectious diseases, etc.," via an open request issued by the Japan Agency for Medical Research and Development (AMED).

▲HydroCell® developed by CellSeed

Main Cell Cultureware Sold by CellSeed

1 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.

2 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.

3 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.

4 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.

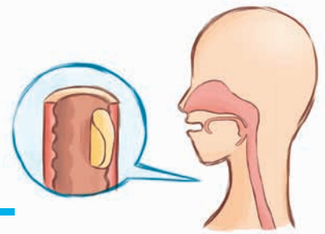
5 ThermoPlate®|||

This is a transparent heating element made from hardened glass via special processing that enables microscopic observation by placing the culture dish on the product while keeping the entire dish at a uniform temperature.

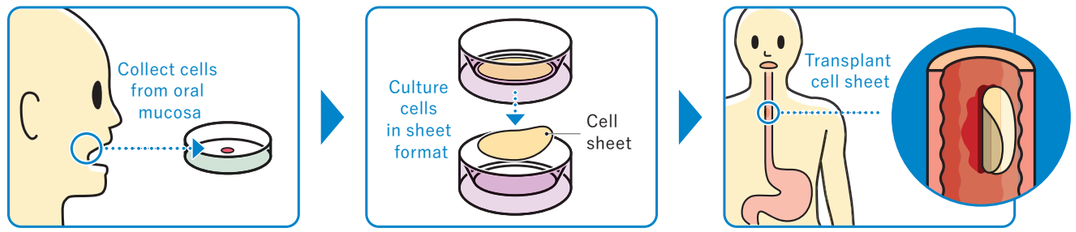
● Other various products are also available.

Cell culture equipment

Epithelial Cell Sheet for Esophageal Regeneration



In Japan, 90% of patients with esophageal cancer are given a diagnosis of squamous cell carcinoma, and their five-year survival rate is under 50% in both men and women—41% in men and 46% in women. While more endoscopic submucosal dissection (ESD) is performed as a treatment method, this causes the adverse effect of postoperative esophageal stenosis.

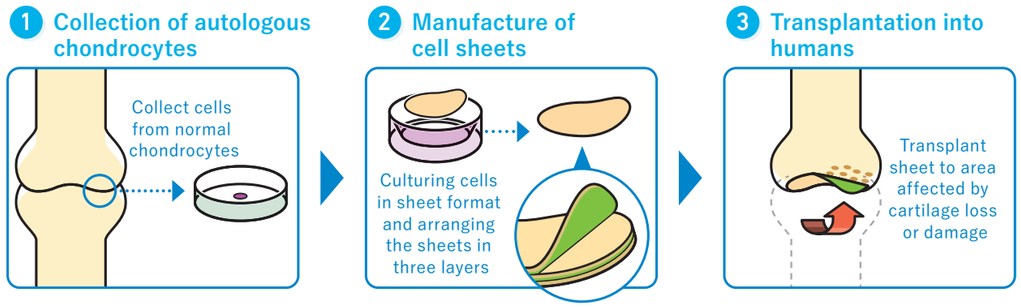


To solve problems in early stage esophageal cancer treatment, Tokyo Women's Medical University developed treatment using cell sheets. The treatment involves the attachment of a cell sheet created from tissues (oral mucosa tissues) that are collected from the patient's mouth to the cancer-resected area. Promoted healing of the resected area is used has an effect to reduce the frequency of esophageal stenosis, and this will help improve the patient's postoperative quality of life (QOL).

CellSeed initiated a clinical trial in April 2016 and completed it in March 2019. While safety was confirmed, further data on efficacy was requested by the Pharmaceuticals and Medical Devices Agency (PMDA). Thus, we applied for additional clinical trials in October 2020. In an additional clinical trial targeting patients having a high risk in steroid administration due to changes in the treatment method to prevent esophageal stenosis, the first subject for the additional clinical trial was enrolled in February 2021.

Chondrocyte Sheet

Knee osteoarthritis is a slowly progressive, intractable degeneration of articular cartilage for which no definitive care has been established. As it is predicted that more patients will contract this disease due to our aging society, CellSeed currently conducts joint research with Professor Sato from Tokai University for the regeneration of knee cartilage (hyaline cartilage).

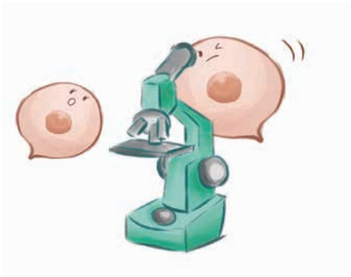


Autologous chondrocyte sheets

Professor Sato initiated a clinical trial in 2011 and completed eight cases in 2014.
At the 71st Advanced Medical Conference held by Japan's Ministry of Health, Labour and Welfare in January 2019, "cartilage regenerative treatment using autologous cell sheets" for which Tokai University Hospital made an application was approved as an Advanced Medical Care B program.
In July 2020, surgery was started for the first patient of the Advanced Medical Care B program.
Additionally, we concluded an out-licensing agreement with MetaTech, a Taiwanese company with which we concluded a contract for a business alliance in 2017.
Taiwan incorporated the same advanced medical care system as Japan, due to a revision of relevant acts in September 2018.
With this as a background, E-Da Hospital in Kaohsiung City, Taiwan, made an application for a treatment plan using autologous chondrocyte sheets and began treatment in 2020. So far, transplant surgeries have been performed on more than 10 patients.

Allogeneic chondrocyte sheets

Allogeneic chondrocyte sheets are a product currently under development and are used for the allogeneic transplant of missing areas of cartilage by collecting chondrocytes from waste tissues of the patient with polydactyly and culturing them in sheet format.
Because establishing a cell bank allows for the transplant of allogeneic chondrocyte sheets without collecting chondrocytes from the patient, it is expected to be a treatment method that is less invasive and more cost effective.
In the commercialization of this product, the world's first transplant surgery using an allogeneic chondrocyte sheet was performed in 2017 as part of clinical research conducted by Tokai University, and a total of 10 patients received a transplant during the three years until 2019.
Regarding the procurement of chondrocytes, the provision of commercially available tissues from the National Center for Child Health and Development started in 2020, and this enabled the stable procurement of chondrocyte tissues and will help accelerate R&D activities for clinical trials and marketing approval.



Regenerative Medicine Contract Services

Our Cell Processing Facility, located on the sixth floor of our Telecom Center, offers contract services such as cell sheet manufacture, site operation, and the preparation of applications. Our experienced staff provide safe and high-quality products and services via a manufacturing and control system compliant with “Good Gene, Cell and Tissue Practice (GCTP) Guidelines” pursuant to the “Act on the Safety of Regenerative Medicine.”
In addition to the contracted manufacturing of cell sheets, we also provide clients with assistance in responding to the PMDA step-by-step, from product development to manufacturing and sales, along with creating applications for approval, acquiring manufacturing and marketing approval, and providing technicians with training.

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.

List of Directors and Financial Information

Management Team of CellSeed

Representative Board Director and President/CEO
Setsuko Hashimoto

Board Director and CFO
Jun Onodera

External Board Director
Kenji Oeda

External Board Director
Audit and Supervisory Committee Member
Toshio Yamaguchi

External Board Director
Audit and Supervisory Committee Member
Noriko Taji

External Board Director
Audit and Supervisory Committee Member
Mariko Hirose

Transitioning to a company with an audit and supervisory committee

Along with making the existing corporate structure more streamlined and efficient, and to strengthen the supervisory function of the board and improve corporate governance by including audit committee members in charge of audits of the director’s execution in the board, CellSeed transitioned to a company with an audit and supervisory committee as resolved at the shareholders’ meeting on March 26, 2021.

Financial Information

Consolidated Income Statement

FY2020 (January 1–December 31, 2020)

Sales	199
Selling expenses	857
Operating income	- 719
Yearly profit attributable to owners of parent company	- 783

Consolidated Financials

End of FY2020 (Current as of December 31, 2020)

Total assets	1,806
Cash and securities	1,460
Liabilities	280
Net assets	1,526

(Unit: million yen; Note: Fractions smaller than 1 million are rounded off)

Highlights

In our regenerative medicine support business, our product supply intended for the mass culturing of cells for laboratory use and our enhanced collaboration and promotion of sales activities with sales partners resulted in a steady increase in overseas sales in our cultureware business, generating the highest sales in our history.
In our cell sheet regenerative medicine business, an application for additional clinical trials on epithelial cell sheets for esophageal regeneration was filed in October 2020, and the first subject was enrolled in February 2021. We also started treatment via the Advanced Medical Care B program using autologous chondrocyte sheets. This type of treatment was initiated in Taiwan as well, and these sheets have been transplanted in 10 patients so far, which brought us milestone fees based on a contract with MetaTech.
Regarding the development of allogeneic chondrocyte sheets, the provision of commercially available tissues from the National Center for Child Health and Development started in December 2020, and this has enabled the stable procurement of chondrocyte tissues and has significantly accelerated commercialization.

Corporate Overview

As of March 26, 2021

Company name	CellSeed Inc.
Main businesses	Cell sheet regenerative medicine business Regenerative medicine support business
Head office	Telecom Center Building, East Tower 15F Aomi 2-5-10, Koto-ku, Tokyo 135-0064 Japan
Date established	May 2001
Fiscal year end	December
Listed market	JASDAQ Growth (7776), Tokyo Stock Exchange
Subsidiary	CellSeed Sweden AB
Affiliated company	Up Cell Biomedical Co.

The 2nd Cell Sheet Engineering Innovation Forum

The 1st Cell Sheet Engineering Innovation Forum, which was held in summer 2019, welcomed many participants, including those from academia. The 2nd Cell Sheet Engineering Innovation Forum will be held in November 2021 and will help further disseminate knowledge to researchers regarding the world's first Japan-originated cell sheet engineering technique. For more details, please check our corporate website.

Stock Information

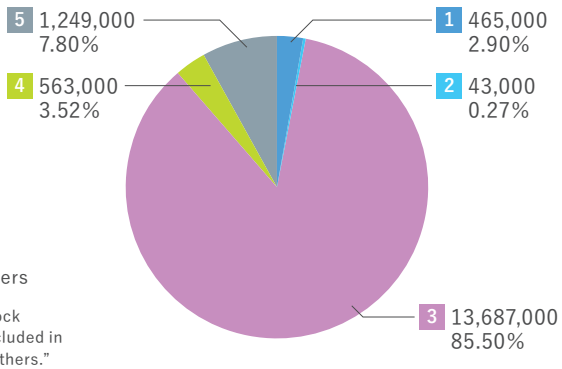
As of December 31, 2020

Total no. of issuable shares ·····35,537,600
Total no. of issued shares·····16,008,319
No. of shareholders ·····13,982
No. of shares constituting one unit·····100

Stock Distribution by Owner

1 Foreign corporations, etc.
2 Financial institutions
3 Individuals and others
4 Other corporations
5 Financial instrument brokers

Note: Treasury stock (154 shares) is included in "Individuals and others."



Notes for Shareholders

Fiscal year end ····· December 31
General Shareholders' Meeting ···· March
Dividend declaration date ····· December 31 (Interim dividends declared June 30)
Shareholder registry administrator ····· IR Japan, Inc.
Special account management institution
100-6026
Securities Administration Division, IR Japan, Inc.
Kasumigaseki Bldg. 26F
Kasumigaseki 3-2-5, Chiyoda-ku, Tokyo
Tel: 0120-975-960 (toll-free)

Public notice posted online URL:https://www.cellseed.com

(However, if posting online is not possible due to unavoidable circumstances, public notice will be issued in the Nihon Keizai Shimbun.)

Notes:
1. Along with the electronic conversion of stock certificates, we comply in principle with petitions for changes of address, purchase requests, and other types of procedures pertaining to the shareholder made through account management institutions (stock brokerage firms, etc.), where shareholders have established accounts. Please contact the stock brokerage or other institution where the account has been established. Please note that these changes cannot be handled by the shareholder registry administrator (IR Japan, Inc.).
2. With regard to procedures related to shares recorded in special accounts, please contact the special account management institution (IR Japan, Inc.).