



# THE BIOTECHNOLOGY COMPANY™

Takara Bio Report 2019



**TAKARA BIO INC.**

# THE BIOTECHNOLOGY COMPANY™

Our corporate mission is “Contributing to the health of humankind through the development of revolutionary biotechnologies such as gene therapy.” We provide research reagents and other products and services to life science researchers around the world through our Bioindustry Business and engage in clinical development of gene therapies for target diseases such as cancer with the aim of commercialization through our Gene Therapy Business. We will contribute to society by creating new value and continuing to grow our company through these two business units.

## Corporate Philosophy

Contributing to the health of humankind through the development of revolutionary biotechnologies such as gene therapy

### Business developments

Bioindustry Business

Gene Therapy Business

**1979**

- Commenced sales of the first domestically produced restriction enzymes as reagents for genetic engineering research



**1985**

- Began DNA synthesis services

**1988**

- Acquired exclusive distribution rights in Japan for a gene amplification system using PCR technology



**1990**

- Began DNA sequence analysis services

**1993**

- Obtained worldwide, broad-ranging PCR-related patent licenses



**1995**

- Began genetic testing services

**1995**

- Developed the RetroNectin® Method for highly efficient retroviral transduction in hematopoietic stem cells



### Company history

**1925**

- **Established Takara Shuzo Co., Ltd.**

**1970**

- Developed the world's first large-scale production technology for Bunashimeiji mushrooms

**1993**

- Established Takara Biotechnology (Dalian) Co., Ltd. in China

**1995**

- Established Takara Biomedical Europe S.A. (currently Takara Bio Europe S.A.S.)
- Established Bohan Biomedical Inc. (currently Takara Korea Biomedical Inc.)

**2000**

- Established DRAGON GENOMICS CO., LTD. (merged in 2002)

**2001**

- Established Mizuho Norin Co., Ltd. (transferred in 2019)

**2002**

- **Established Takara Bio Inc.**

Took over Takara Shuzo Co.'s biotechnology business and established Takara Bio Inc. in the city of Otsu, Shiga

- Established Takara Bio Farming Center Inc. (transferred in 2019)

## Bioindustry Business

We provide high-quality research products and services and CDMO services to life science researchers around the world. We offer a wide range of services through our rapidly growing CDMO business and provide intensive support for development of advanced therapies such as gene and cell therapies as an ideal partner in regenerative medicine product development.

### Research support

Research reagents and scientific instruments

Sales

Academic and corporate

Use

- Basic research and advanced research for the life sciences
- Drug discovery and other applied research

### CDMO

Contract research and manufacturing services

Business fundamentals

- Technology and expertise cultivated through clinical development of gene therapies
- Facilities compliant with manufacturing control standards such as GMP/GCTP
- Quality control systems

### Contract services for developing regenerative medicine products

Manufacturing and development of viral vectors, cell processing, quality and safety testing, and more

### Contract gene analysis services

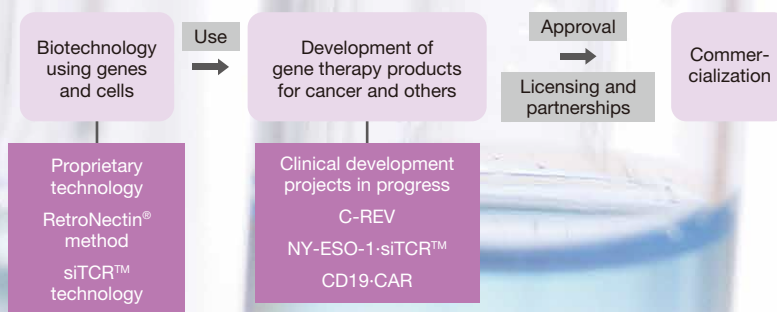
Genetic analysis such as human genome sequence analysis, etc. and research support for genetic engineering such as genome editing

\*Contract development and manufacturing organization (CDMO): Business supporting development and manufacturing of regenerative medicine products. Manufacturing of regenerative medicine products requires a large initial investment in specialized equipment and facilities, as well as advanced manufacturing technology and quality control systems. That is why it is common to outsource manufacturing starting early in development.

## Gene Therapy Business

We are working to develop gene therapies that meet unmet medical needs for target diseases such as cancer using biotechnology such as our proprietary RetroNectin® method for highly efficient gene transduction. We are steadily making process on our clinical development projects with the aim of early commercialization.

### Development and commercialization of technology for gene therapies targeted at cancer and others



#### 2000

- Launched full-scale genetic analysis services

#### 2006

- Began next-generation sequence analysis services

#### 2009

- Began iPS cell production services

#### 2010

- Acquired C-REV business

#### 2013

- Began genome editing services

#### 2014

- Completed construction of the Center for Gene and Cell Processing; Began full-scale CDMO business providing manufacturing and development support services for regenerative medicine products



#### 2015

- The Center for Gene and Cell Processing accredited as a foreign cell processor to conduct specific processed cell manufacturing

#### 2016

- Obtained CAP-LAP certification for the contract genetic analysis business

#### 2018

- Designated NY-ESO-1-siTCR™ as a product under the "SAKIGAKE Designation System"\*
- \*A system aimed at shortening the premarket review period for innovative new products

#### 2019

- Applied for marketing approval of oncolytic virus C-REV in Japan

#### 2004

- Established Takara Biomedical Technology (Beijing) Co., Ltd.
- Listed on the TSE Mothers Index

#### 2005

- Established Takara Bio USA Holdings Inc.
- Acquired U.S.-based Clontech Laboratories Inc. (currently Takara Bio USA, Inc.)

#### 2007

- Established KINOKO CENTER KIN INC. (transferred in 2019)

#### 2011

- Established DSS Takara Bio India Pvt. Ltd.

#### 2014

- Acquired Collectis AB (currently Takara Bio Europe AB)

#### 2015

- Completed construction of new research facility in Kusatsu, Shiga; Headquarters functions relocated



#### 2016

- Changed listing to the First Section of the TSE

#### 2017

- Acquired Rubicon Genomics, Inc. and WaferGen Bio-systems, Inc. (later merged into Takara Bio USA, Inc.)

#### 2018

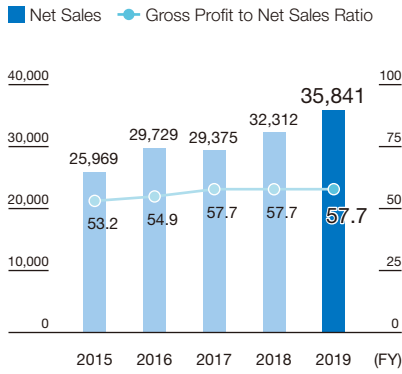
- Announced plan to expand research and manufacturing facilities for regenerative medicine products

#### 2019

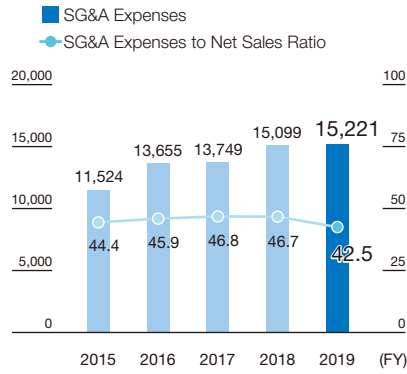
- Transferred functional food business and mushroom business

# Financial Highlights

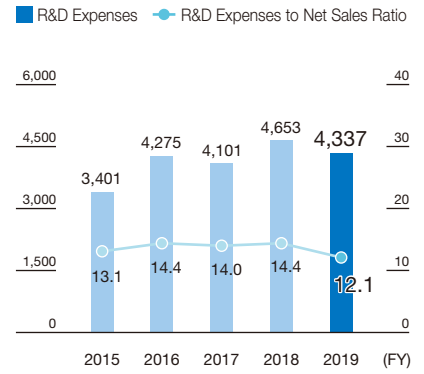
Net Sales (Million yen) /  
Gross Profit to Net Sales Ratio (%)



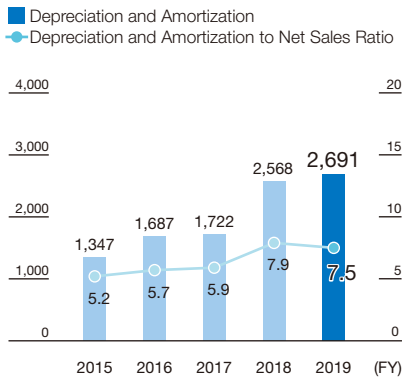
SG&A Expenses (Million yen) /SG&A  
Expenses to Net Sales Ratio (%)



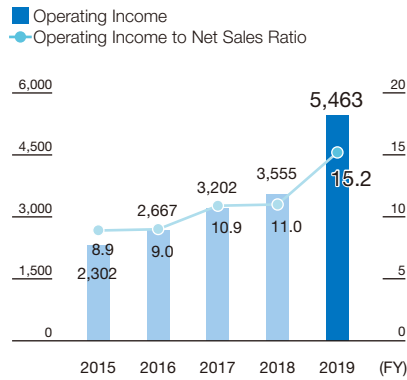
R&D Expenses (Million yen) /  
R&D Expenses to Net Sales Ratio (%)



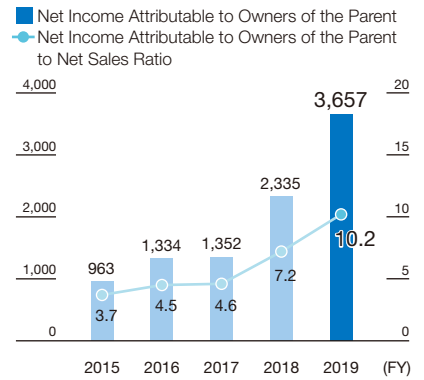
Depreciation and Amortization  
(Million yen) /Depreciation and  
Amortization to Net Sales Ratio (%)



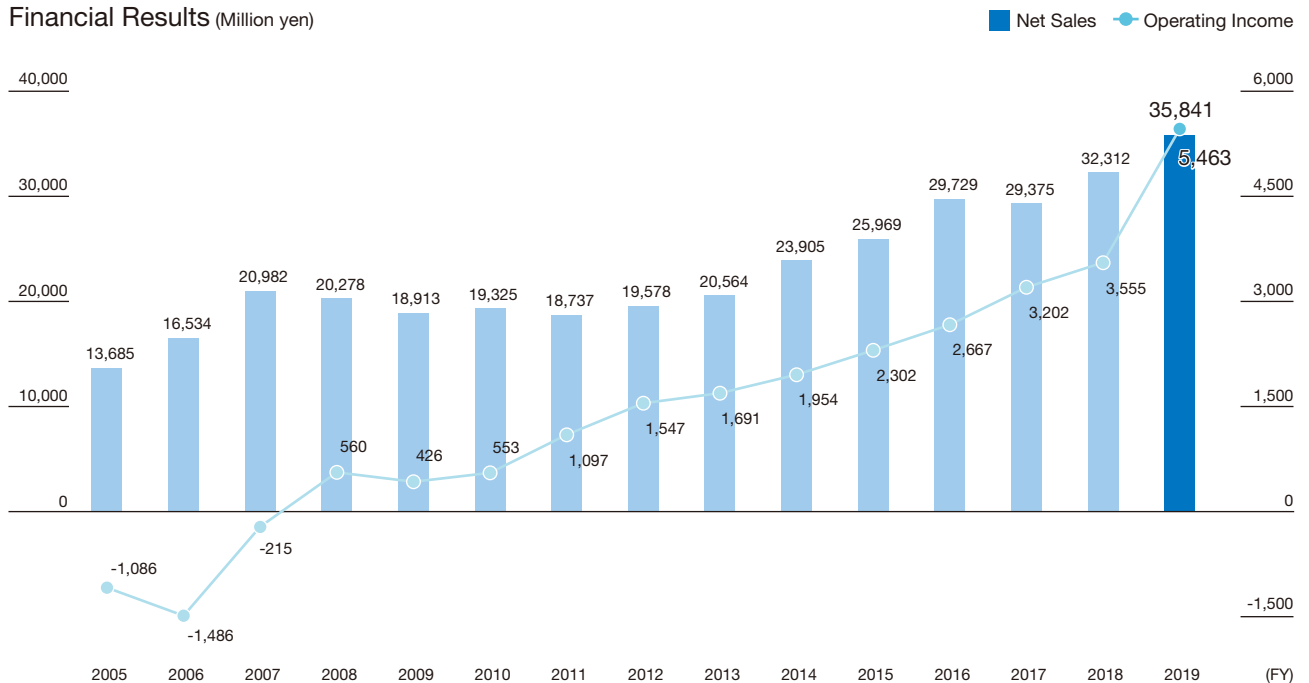
Operating Income (Million yen) /  
Operating Income to Net Sales Ratio (%)



Net Income Attributable to Owners of the  
Parent (Million yen) /Net Income Attributable to  
Owners of the Parent to Net Sales Ratio (%)



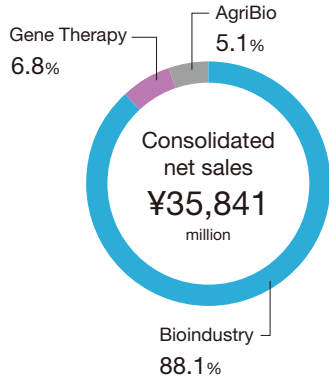
Financial Results (Million yen)



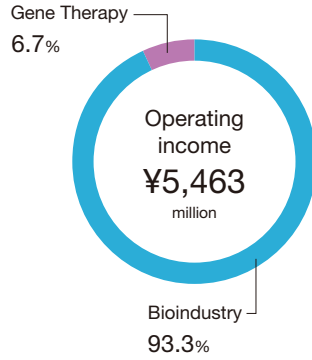
Note: FY2019 in this report refers to the fiscal year ended March 2019.

FY2019

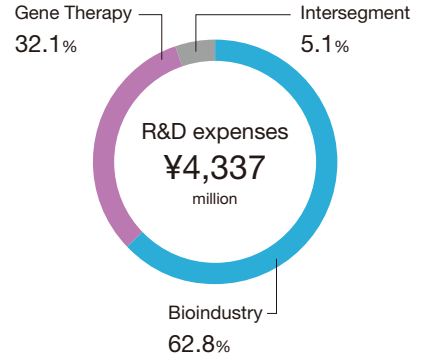
### Sales Composition



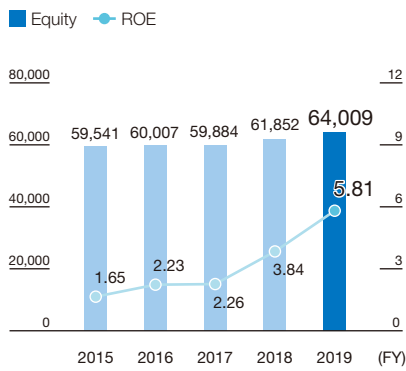
### Operating Income Composition\*



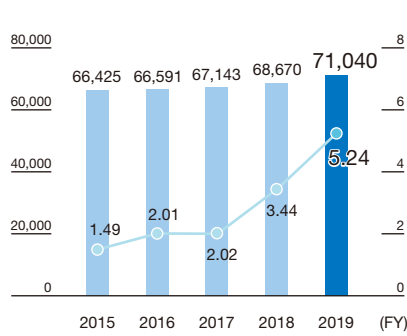
### R&D Expenses Composition



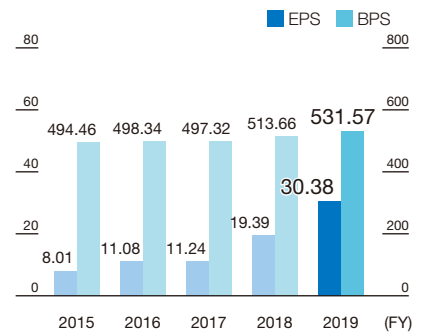
### Equity (Million yen) / ROE (%)



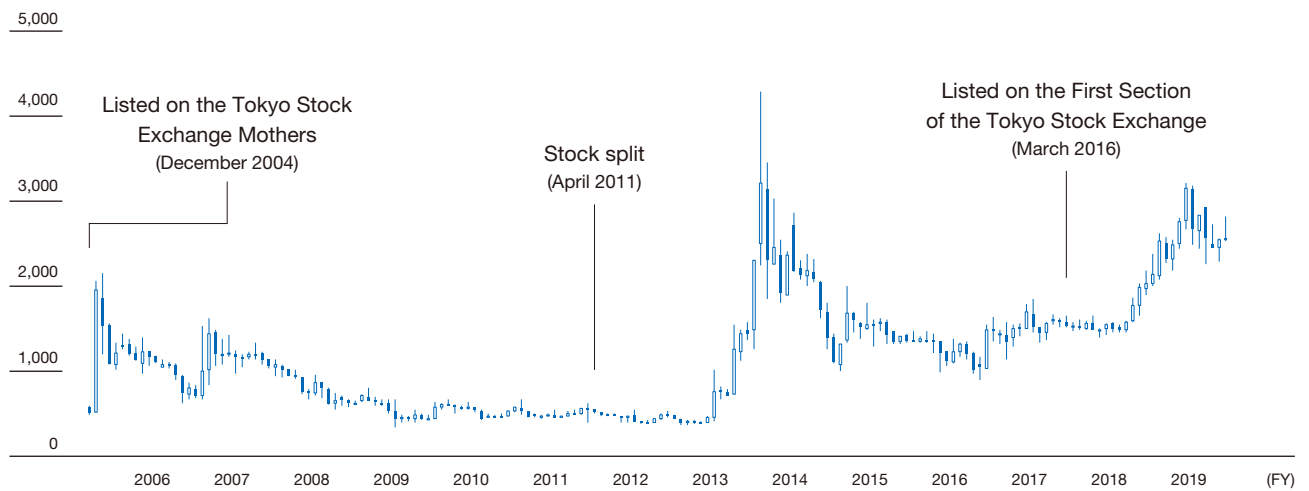
### Total Net Assets (Million yen) / ROA (%)



### EPS: net income per share / BPS: net assets per share (Yen)



### Share Values (Yen)



- Period: December 2004–March 2019
- Number of shares listed are those post stock split adjustment





TAKARA BIO INC.

Koichi Nakao

President

## Aiming for “Quantum Leap” growth as a global enterprise and regenerative medicine products company

Under our corporate philosophy of “Contributing to the health of humankind through the development of revolutionary biotechnologies such as gene therapy,” we are working to strengthen our two business segments and the business base that supports them. In addition, we have made revisions to our target figures, given our most recent progress in business and the changes to the management environment as we approach the final fiscal year of the Medium-Term Management Plan 2020 (April 2017–March 2020). In order to handle our expanding CDMO business, we have increased and expanded our research and manufacturing facilities, and we have also made advancements in commercializing gene therapies for diseases such as cancer, aiming towards even more growth.

### **FY2019 Business Performance** **(April 2018–March 2019)**

#### **Robust performance in our core business of research reagents and contract services**

In net sales for the fiscal year under review, research reagents and contract services in our core Bioindustry Business saw an increase over the previous year. In addition, with our receipt of remuneration for the fees involved in the joint development and the exclusive sales agreement for the Japanese domestic NY-ESO-1-siTCR™ gene therapy product and the CD19-CAR gene therapy product for our Gene Therapy Business, we have seen a ¥35,841 million increase in net sales (10.9% increase over the previous year). For the cost of sales, an increase in net sales has produced ¥15,155 million (11.0% increase over the previous year), and gross profit has grown to ¥20,685

million (10.9% increase over the previous year). Due to increased labor costs, etc., selling, general and administrative expenses have remained at ¥15,221 million (0.8% increase over the previous year), but operating income has increased to ¥5,463 million (53.7% increase over the previous year). Following growth in operating income, ordinary income has reached ¥5,665 million (46.7% increase over the previous year).

In addition, income before income taxes has reached ¥4,823 million (43.5% increase over the previous year), and we have increased the net income attributable to owners of the parent to ¥3,657 million (56.6% increase over the previous year).

We renewed our records for both gross sales and profits, achieving an increase in operating income and ordinary income for 10 consecutive years.

## Growth in the Bioindustry Business

We are seeing steady growth in our contract services, especially the CDMO business

We have positioned the Bioindustry Business, which offers predominantly products and services that support research and development activities in biotechnology-related fields, as our core business. We are therefore engaged in the manufacture and sales of research reagents and scientific instruments, while we also offer a range of contract services.

We are making advancements in developing new technologies and products related to reagents for research, all of which are well suited for developments in the fields of genetic engineering and cellular engineering. In addition, due to enhancement of our product lineup resulting from our acquisition of overseas manufacturers and our import and sales of merchandise from European and U.S. manufacturers, we are further expanding sales into the overall biotechnology domain. In recent years, our net sales overseas have been building steady growth.

With our contract services, we are expanding our CDMO business, which makes use of the technology and know-how we have cultivated in the field of clinical development of genetic and cell therapies. In order to accommodate rapidly expanding demand, we are proceeding with construction and expansion of research and manufacturing facilities for regenerative medicine products that will allow us to be in full operation in December 2019.

In addition, in fiscal 2019, we had a hand in subcontracting genetic testing work for cancer at Osaka University Hospital and in the development of high volume viral vector manufacturing technologies for gene therapies with the “Research and development of platform technologies for gene and cell therapy” project at the Japan Agency for Medical Research and Development (AMED), all of which is allowing us to make further expansions in our CDMO business.

## Status in the Gene Therapy Business

We are making steady progress in the clinical development of gene therapies for diseases such as cancer

With our goal of commercializing the oncolytic virus C-REV and genetically engineered T cell therapies, we are making strides in clinical development both in Japan and overseas.

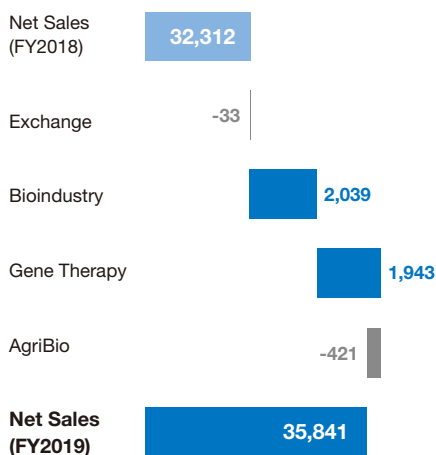
We presented the results of our phase II clinical trials of C-REV on unresectable or metastatic melanoma in Japan at primary conferences in the U.S. and Europe. In March 2019, we applied for marketing approval of C-REV in Japan. In addition, we have transitioned a phase I clinical trial on pancreatic cancer from the dose escalation stage to the expansion stage, and we are collecting data on efficacy and safety. We also have an investigator-initiated clinical trial of C-REV combined with anti-cancer agents in neoadjuvant settings in the U.S.

For our initiatives in genetically engineered T cell therapy, we are making progress with ongoing phase I/II clinical trials of NY-ESO-1-siTCR™ gene therapy (target disease: synovial sarcoma) and CD19-CAR gene therapy (target disease: adult acute lymphoblastic leukemia) in Japan.

We have entered into an exclusive license agreement with Otsuka Pharmaceutical Co., Ltd. for the development and sales of these gene therapy products, and we are going forward with developments that will allow us to obtain early approval for marketing in Japan. As of fiscal 2019, these business initiatives are in the black due to our receipt of remuneration of the fees involved in this joint development and exclusive sales agreement.

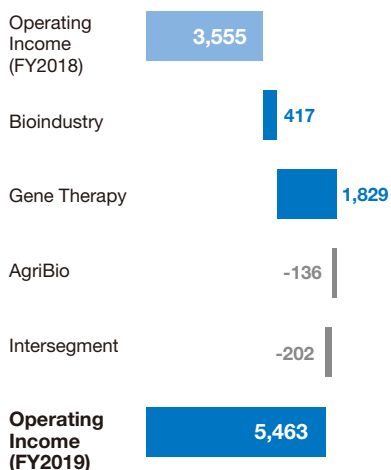
### Consolidated Net Sales

(Million yen)



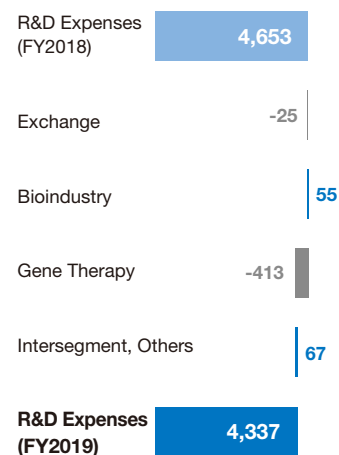
### Consolidated Operating Income

(Million yen)



### R&D Expenses

(Million yen)



## Shareholder Return

Takara Bio Group paid year-end dividends of ¥7 per share

Considering the management performance and financial condition overall, Takara Bio recognizes a basic policy aimed for profit contribution, positioning the profit distribution to shareholders as an important issue for management as well as enhancing the internal reserves to strengthen R&D activities of the two business segments: Bioindustry and Gene Therapy.

Specifically, our policy calls for a target rate of around 20% of forecasted income for the year calculated without taking into account extraordinary profit and loss stated on the consolidated financial statements. Based on this, Takara Bio decided to upwardly revise the forecasted annual dividend for fiscal 2020 from ¥6 to ¥7 (year-on-year increase of ¥2.50) due to the net income from the year beyond the forecast. We forecast a ¥8.00 per share annual dividend for fiscal 2021.

FY	2016	2017	2018	2019	2020
Dividends per Share (Yen)	1.5	1.8	4.0	4.5	7.0

## Medium-Term Management Plan

Selection and concentration of our management resources for the sustainable growth of our entire Group

Through Takara Bio's Medium-Term Management Plan 2020, we have strengthened the strategies of our Bioindustry Business, Gene Therapy Business, and AgriBio Business, along with the business base that supports these efforts. The overall policy has been to increase our presence as a global enterprise and regenerative medicine products company, with dramatic growth as our goal. However, in view of our most recent progress, we recognized that further selection and concentration of our management resources was in order, so in fiscal 2019 we decided to transfer our AgriBio Business (functional food business and mushroom business).

Net sales targets for fiscal 2020, the final fiscal year of our plan, were revised downward due to the impact of factors such as the transfer of our AgriBio Business from ¥38,500 million to ¥36,000 million. Despite that, our operating income target was raised from ¥4,000 million to ¥6,200 million.

From here on out, we will continue to make further inroads with strategies for both our Bioindustry Business and our Gene Therapy Business, and we are fully committed to achieving rapid growth.

## Medium-Term Management Plan 2020 (as of June 2019)

Overall objective	<p>To strengthen Takara Bio's three business segments, namely, the Bioindustry, Gene Therapy, and AgriBio businesses, and the business base that supports these efforts, enhance Takara Bio's standing as a global enterprise and regenerative medicine products company, and achieve prodigious growth.</p> <p>*With the aim of further selection and concentration of our management resources, we transferred our AgriBio Business in 2019.</p> <ul style="list-style-type: none"> <li>• Functional food business (January 1)</li> <li>• Mushroom business (March 1)</li> </ul>	
Quantitative targets after revision	Net Sales <b>¥36.0</b> billion	Operating Income <b>¥6.2</b> billion
Key points of revision	<p>Due to factors such as the transfer of our AgriBio Business, we revised net sales targets downward, but we revised profit targets upward</p> <p>Initial plan      FY2020 forecast</p> <p>Net sales <b>¥38.5 billion</b> → <b>¥36.0 billion</b></p> <p>Operating income <b>¥4.0 billion</b> → <b>¥6.2 billion</b></p>	



## Measures in the Bioindustry Business

We are planning for the joint acceleration of overseas business deployment and the enhancement of our Japanese domestic business

We are committed to both the acceleration of our overseas business deployment and in the enhancement of our Japanese domestic business.

Due to our maximization of synergies with the two U.S. companies we acquired in 2017 (the former WaferGen Bio-systems and the former Rubicon Genomics), we are

making further strides in expanding our business in research reagents and scientific instruments. In Japan, we are strengthening our manufacturing capability for regenerative medicine products, and we are planning for enhancements to our business, particularly our CDMO business.

In addition, we are accelerating the development of new products for research reagents, while at the same time we are pouring our efforts into the development of platform technology and developing projects for that technology so that we can create novel projects for clinical development.

### Overview of Bioindustry Business Measures

Overview of measures in each field	Research reagents	Rapid commercialization of leading-edge technologies with open innovation
	Contract services	Structural development based on GCTP/GMP <sup>*1</sup> , CAP-LAP <sup>*2</sup> , and other quality assurance and accuracy control systems, in order to expand contract services for regenerative medicine products and clinical domains
	Scientific instruments	Development of PCR-related products and systemized single-cell analysis by combinations of devices and reagents
Main R&D in Bioindustry Business		<ol style="list-style-type: none"> <li>1. Platform technology and quality control techniques for regenerative medicine products</li> <li>2. Ultra-low input nucleic acid analysis methods</li> <li>3. New technologies required for clinical sequencing</li> <li>4. Industrial uses for PCR and expansion to the clinical domain</li> <li>5. New genome editing-related technologies</li> </ol>

<sup>\*1</sup> GCTP (Good Gene, Cellular, and Tissue-based Products Manufacturing Practices) refers to the Standards for Manufacturing Control and Quality Control for Regenerative Medicine Products. GMP (Good Manufacturing Practice) refers to the Standards for Manufacturing Control and Quality Control for Pharmaceuticals.

<sup>\*2</sup> CAP (College of American Pathologists) is a U.S.-based organization whose primary functions include providing quality management system tools, accrediting laboratories, and providing education. LAP (Laboratory Accreditation Program) is an international clinical laboratory testing outcome evaluation program conducted once a year by CAP.

## Measures in the Gene Therapy Business

We are continuing developments towards commercialization, while at the same time focusing on selecting the right partnerships

In March 2019, we applied for marketing approval of the oncolytic virus C-REV for unresectable metastatic melanoma in Japan. In addition, a clinical trial for pancreatic cancer is also underway. Aside from these, we are making Japanese

domestic progress with the development of the genetically engineered T cell therapy NY-ESO-1-siTCR<sup>TM</sup>, and the CD19-CAR gene therapies.

As we move forward with these developments, we are advancing comprehensive systematic improvements in pharmaceutical affairs and manufacturing, and we aim for early commercialization of our gene therapy projects. We are also focusing our attention on selecting overseas partnerships.

### Development Status of Clinical Development Projects (as of June 2019)

Projects		Target disease	Region	Status	
Oncolytic Virus	C-REV Generic name: canerpaturev Product name: EPLICANA <sup>®</sup>	Melanoma	Japan	Under application for approval <sup>*1</sup>	
		Pancreatic cancer	Japan	Phase I trials in progress <sup>*1</sup>	
		All diseases	South Korea	Under discussion <sup>*2</sup>	
		Melanoma	U.S.	Phase II investigator initiated trials in progress	
Engineered T Cell therapy	CAR	CD19	Adult acute lymphoblastic leukemia	Japan	Phase I/II trials in progress <sup>*1</sup>
			Expanded indication	Japan	Under discussion <sup>*1</sup>
	siTCR <sup>TM</sup>	NY-ESO-1	Synovial sarcoma	Japan	Phase I/II trials in progress <sup>*1</sup>
			Expanded indication	Japan	Under discussion <sup>*1</sup>
		Solid cancer	Canada	Phase Ib investigator initiated trials in progress	

<sup>\*1</sup> In partnership with Otsuka Pharmaceuticals <sup>\*2</sup> In partnership with Dong-A ST Co., Ltd.

Japan

## Maintaining our position as the leading CDMO for regenerative medicine products

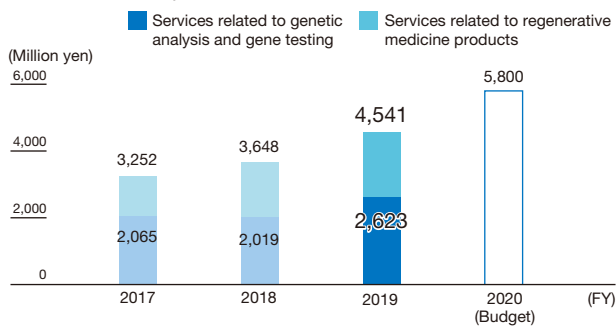
We are putting great effort into expanding our CDMO business, which offers contract manufacturing services and support as an R&D partner to organizations that develop and manufacture regenerative medicine products.

Regenerative medicine product development is accelerating in Japan and overseas, and sales of products and services such as viral vectors, cell processing services, and quality control testing are doing well as a result. To meet this growing need, we are

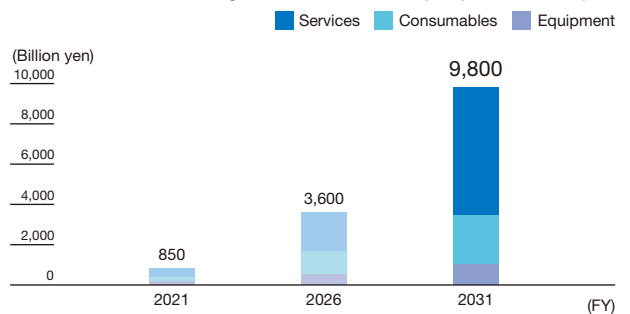
planning to increase our production capacity and efficiency through capital investment and technological improvements.

Demands for genetic analysis and testing services are also growing due to increased need for genome medicine and genetic testing. We will increase our dominance in the market through strategies such as providing added value through expanding our service offerings, increasing our analytical capabilities through capital investment, and guaranteeing data accuracy.

CDMO business performance



Market forecasts for regenerative medicine peripherals in Japan



\*From FY2017 Annual Report of the Forum for Innovative Regenerative Medicine, modified by Takara Bio

Japan

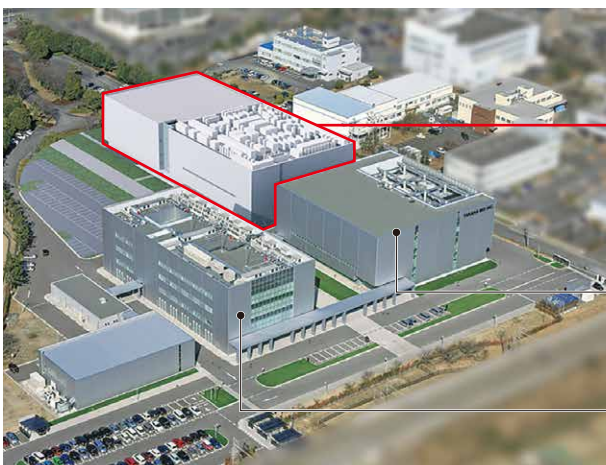
## Expanding facilities for regenerative medicine product research and manufacturing

—Work scheduled for completion in September 2019, full-scale operations to start in December—

We are building new research and manufacturing facilities for regenerative medicine products and renovating our existing facilities at our headquarters region of Kusatsu, Shiga Prefecture. The new building (about 14,500 m<sup>2</sup>) will increase our capacity to perform quality testing for regenerative medicine products and to manufacture vectors for gene

therapy. The building also includes about 4,600 m<sup>2</sup> of backup space that can be used flexibly for any of a variety of foreseeable future needs. By renovating our existing facilities, we are aiming to improve our R&D capacity and manufacturing capacity.

\*Full-scale operations launch in GCTP/GMP area planned for December 2019



CG of the completed facilities

### New building (about 14,500 m<sup>2</sup>)

- Intended to increase facility space for quality testing and increase vector manufacturing capacity
- Includes about 4,600 m<sup>2</sup> of backup space that can be used flexibly to meet CDMO service needs

### The Center for Gene and Cell Processing (about 6,700 m<sup>2</sup>)

- Continue to use quality testing area
- Expand cell processing capabilities along with cell processing room in Life Innovation Center (LIC Annex) in Kawasaki, Kanagawa Prefecture

### Third floor laboratory space at main research facility (about 1,200 m<sup>2</sup>)

- Expand genetic analysis and testing area

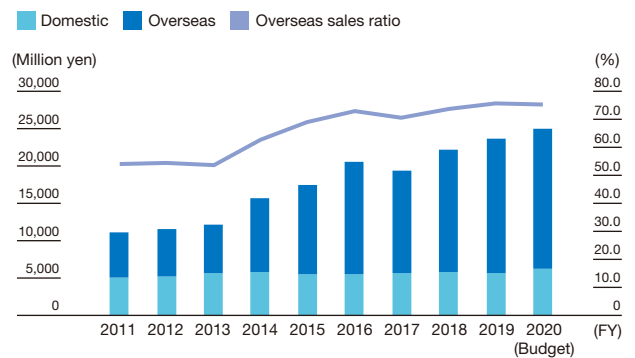
## Overseas

# Putting effort into increasing overseas sales of research reagents

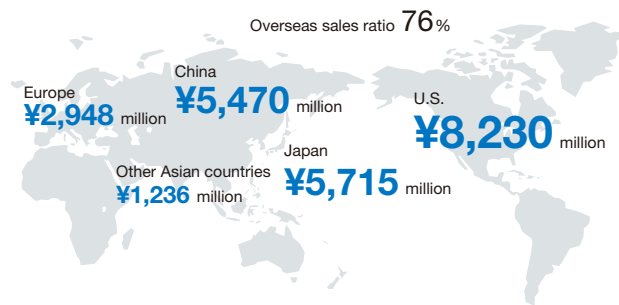
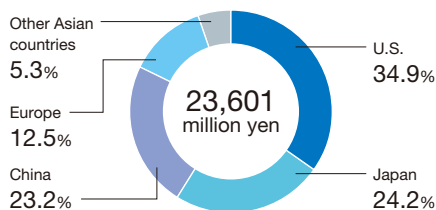
In our core Bioindustry Business, sales of research reagents primarily in foreign countries such as China and the U.S. are growing favorably, and are driving the performance of the entire company. We are working as a Group to come up with themes that target characteristics of the Japanese, American, and Chinese markets and develop new products and services within those themes.

We manufacture the majority of our research reagents at Takara Biotechnology (Dalian), our Chinese subsidiary. Moreover, we are building a system for providing Takara Bio products to life science researchers around the world through sales and marketing efforts that fit regional characteristics by having sales hubs in key regions for life sciences research.

Changes in research reagent sales and overseas sales ratio



Sales by geographic segment in FY2019



## R&D

# Accelerating development aimed at creating new gene therapy projects

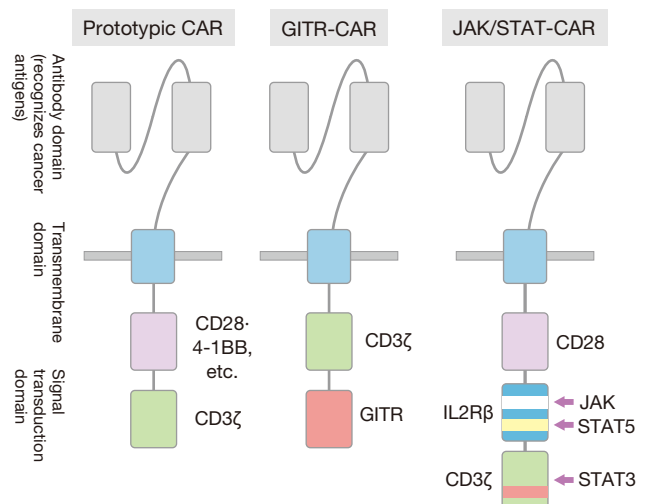
We are accelerating platform research aimed at creating new gene therapy projects. Specifically, we have narrowed our target to the field of cancer immuno-gene therapy, and are studying the potential of advanced medical technologies that can respond to diverse needs in pursuit of early commercialization.

### Research themes in the field of gene therapy

- New CAR structures: Develop intracellular signal transduction domains such as GITR and JAK/STAT
- Identify new cancer-specific antigens for T cells: Utilize neoantigen analysis
- Develop viral vectors for new gene therapies and establish large-scale manufacturing technology\*
- Develop platform technology useful in improving productivity of gene-transduced cells (including cost reduction)
- Develop platform technology related to liquid biopsy and clinical sequencing that could be applied to cancer immuno-gene therapy

### Developing CAR structures for new CAR gene therapies

Aiming to solve the issues with conventional CAR gene therapy, we are partnering with Japanese and overseas research institutions in R&D for new CAR structures.



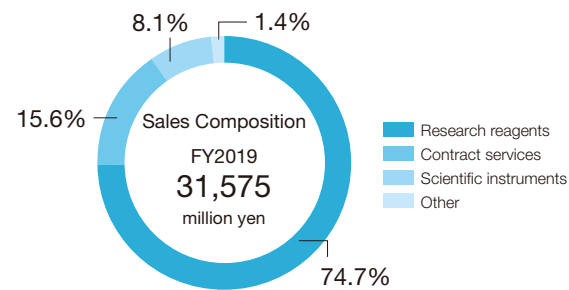
\*Began participating in AMED project for research and development of platform technologies for gene and cell therapy in April 2019

## Overview of Businesses



## Bioindustry Business

Takara Bio offers research reagents, scientific instruments, and contract services for academic and corporate life sciences research and development.



### Research Reagents and Scientific Instruments

Since launching the first domestically produced restriction enzymes in 1979, we have continued to expand our product lineup through in-house development, and gone on to acquire the U.S.-based Clontech Laboratories (now Takara Bio USA, Inc.), a company that excels in molecular biological research, and Cellartis AB (now Takara Bio Europe AB), a company that manufactures reagents for research on stem cells such as iPS and ES cells. These acquisitions gave us ownership of the three brand names Takara®, Clontech®, and Cellartis®.

In 2017, we acquired WaferGen Bio-systems, which owns a single-cell analysis system (device), and Rubicon Genomics, which owns ultra-low input DNA analysis technology. These acquisitions allowed us to maximize the utility of these companies' proprietary technology so we could newly expand our business in the field of ultra-low input nucleic acid analysis.

## Clontech Takara cellartis

### Contract Services

In our contract development and manufacturing organization (CDMO) business, we leverage our genetic and cellular engineering technology gained through research reagent development, as well as our expertise in gene therapy clinical development to support development and manufacturing of regenerative medicine products.

Our CDMO services provide a seamless package of regenerative medicine development support services and genetic testing support services such as genetic analysis for genome sequence and regenerative medicine products.

#### Clontech®

Has a lineup of products optimized for advanced research in fields such as molecular and cell biology.

- (Main products)
- Analytical reagents for next-generation sequencers
  - Single-cell analysis systems
  - Gene expression research reagents and fluorescent proteins
  - Genome-editing research reagents

#### Takara®

Offers a wide range of products for genetic engineering and all other kinds of biotechnology research applications. Provides contract services that leverage expertise in the development of regenerative medicine products, in addition to genetic analysis and testing services.

- (Main products and services)
- Genetic research reagents
  - Genetic testing kits
  - Genome analysis services
  - Development and manufacturing support for regenerative medicine products

#### Cellartis®

Offers iPS cell products and other products used in stem cell research, as well as contract services in the field.

- (Main products)
- iPS cell research reagents
  - Products for stem cell culturing and induction of differentiation
  - Contract services for iPS cell production and induction of differentiation

#### 1. Contract Service for Developing Regenerative Medicine Products

Our contract services include not only development and manufacturing of viral vectors and gene-transduced cells for regenerative medicine products, which are the key to gene therapy, but also related services such as quality and safety testing and cell banking. We have already expanded into the Life Innovation Center Annex in Kawasaki, Kanagawa Prefecture, with the Center for Gene and Cell Processing, which is compliant with the GMP/GCTP quality control standard, as our core facility.



We are working to further expand the research and manufacturing facilities at our headquarters.

## 2. Contract Services for Supporting Genetic Testing

In addition to genetic testing support services such as human genome sequence analysis, comprehensive analysis of cancer-related genes, and intestinal flora analysis, we offer support services for advanced genetic engineering research using state-of-the-art technologies and equipment for next-generation sequencing and genome editing. We are also supporting Osaka University Hospital in their efforts to analyze genetic mutations in cancer patients to provide advanced cancer genomic medicine.



Main Research Building

Center for Gene and Cell Processing

### Genetic testing

- Genetic testing for regenerative medicine products
- Whole human genome sequence analysis
- Comprehensive cancer gene analysis
- Gene expression analysis

### Regenerative medicine products

- Cell processing
- iPS cell production
- Vector production
- Cell banking

## Future Initiatives

### 1) Maximize business synergy through acquisition of two U.S. companies

Integrate technologies obtained through acquisition of WaferGen Bio-systems and Rubicon Genomics with our proprietary technologies, offer a wider range of products and services in the field of ultra-low input nucleic acid analysis, and accelerate global expansion.

### 2) Expand CDMO business

Further expand our CDMO business through R&D and expansion and renovation of manufacturing facilities for regenerative medicine products to maintain our position as a leading CDMO business.

### 3) Intensify development of platform technologies

Proactively pursue development of new research reagent products and CDMO services while strengthening efforts to generate next-generation gene therapy pipelines.

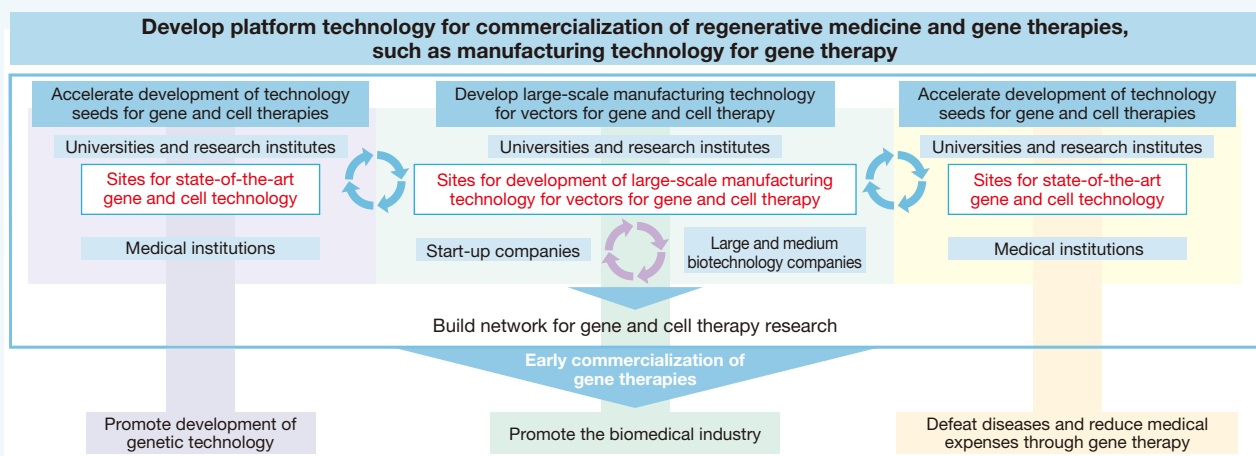
## TOPICS

### Joined AMED project for development of manufacturing technologies for gene therapies

We joined a project for research and development of platform technologies for gene and cell therapy launched by the Japan Agency for Medical Research and Development (AMED) in fiscal 2019 through our membership in the Manufacturing Technology Association of Biologics, and are working to develop technology for large-scale production of viral vectors for gene therapy for the project. In recent years, development and advanced large-scale manufacturing techniques for viral vectors has been a major challenge to the commercialization of cell and gene therapies. We are bringing the technology and expertise we have cultivated over

the years to this project so as to develop useful domestic technology and products as part of a nationwide effort to support Japanese industry.

We are also lending space (about 1,000 m<sup>2</sup> of floor space) in our Kusatsu facility to the Manufacturing Technology Association of Biologics to serve as the technology development hub for the project. As we start operations at our new research and manufacturing facility for regenerative medicine products in December of this year, we are aiming to further contribute to this gene therapy project and expand and develop our CDMO business.



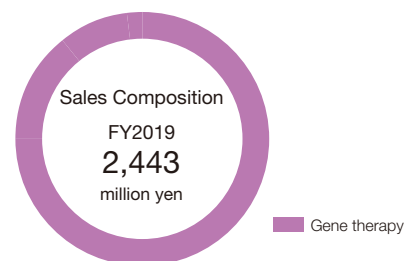
Source: Japan Agency for Medical Research and Development (AMED)





## Gene Therapy Business

Takara Bio is engaged in clinical development of gene therapies for cancer, etc., including the oncolytic virus canerpaturev (C-REV) and engineered T cell therapy.



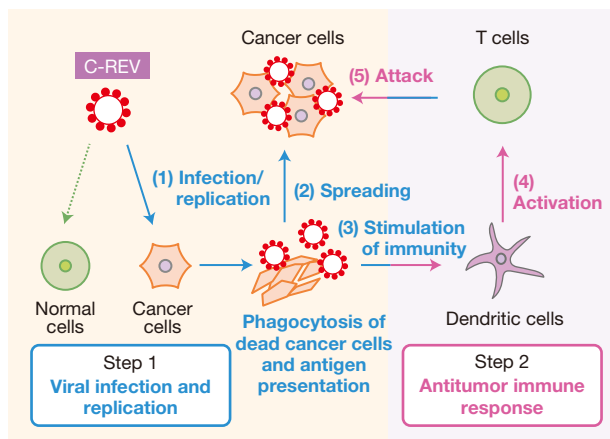
### Gene Therapy

#### Oncolytic Virus

##### Canerpaturev (C-REV)

Canerpaturev (C-REV) is an attenuated strain of the herpes simplex virus type 1 (HSV-1) that exhibits antitumor activity upon local injection into a tumor due to tumor lysis. Treatment with C-REV also strengthens general immunity against cancer cells, and shows promise for producing an antitumor effect even in tumors not directly injected with C-REV. This type of virus is called an oncolytic virus. These viruses selectively

#### Action mechanism of C-REV



- (1) Virus destroys cancer cells by infecting them and replicating inside of them (does not replicate inside normal cells)
- (2) Virus spreads further and destroys other cancer cells by repeated infection and replication
- (3) Dead cancer cells stimulate an immune response
- (4) Stimulation activates T cells
- (5) T cells attack and destroy cancer cells

replicate within and destroy tumor tissue without excessively damaging normal tissue, and are being developed as new treatment agents for cancers.

At Takara Bio, we are conducting clinical trials of C-REV both in Japan and overseas for the indications of melanoma and pancreatic cancer. For melanoma, we completed a phase II trial of C-REV in combination with an immune checkpoint inhibitor, and submitted an application for marketing approval as a regenerative medicine product in Japan. For pancreatic cancer, we are currently conducting a phase I trial of C-REV in combination with anticancer drugs used for standard treatments.

#### Engineered T Cell Therapy

##### 1. siTCR™ Gene Therapy

T cell receptor (TCR) gene therapies involve collecting immune cells called T cells from a cancer patient, transducing TCR genes that have the ability to recognize cancer cells into those T cells, expanding the cells, and administering the cells back into the patient. These transduced T cells gain the ability to specifically recognize and attack cancer cells, and are thus utilized in cancer therapy. At Takara Bio, we are also developing siTCR™ gene therapies that use our proprietary siTCR™ vector technology, which we believe will improve treatment efficacy.

We are currently conducting phase I/II clinical trials of NY-ESO-1-siTCR™ gene therapy for synovial sarcoma in Japan.

## 2. CAR Gene Therapy

Chimeric antigen receptors (CARs) are made by artificially combining T cell surface antibodies that recognize cancer cells with cytotoxic components derived from T cell receptors. CAR gene therapies involve infusion of T cells transduced with CAR genes into the patient, allowing these genetically engineered T cells to specifically recognize and attack cancer cells.

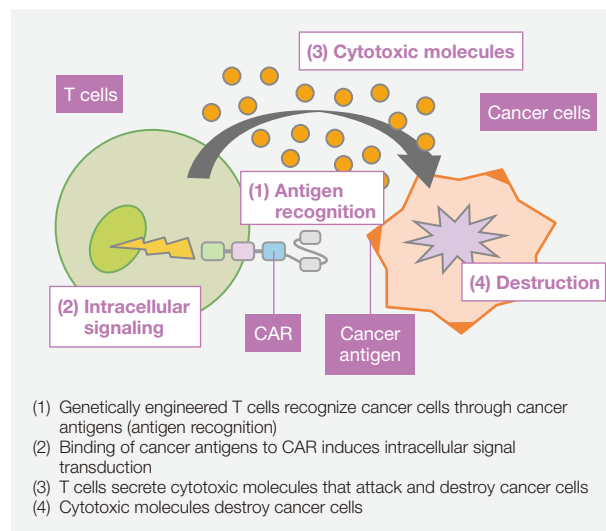
We are currently conducting phase I/II clinical trials of CD19-CAR gene therapy for adult acute lymphoblastic leukemia in Japan.

### Proprietary Technology Advancing Gene Therapy

Genetically engineered T cell therapies such as TCR and CAR therapies involve a process of collecting T cells from a patient's body and transducing them with therapeutic genes that increase the ability of the cells to attack cancer. In this process, it is important to enhance transduction efficiency and utilize expansion culture for efficient cell expansion.

Our proprietary RetroNectin® technology is widely used in this process, and we out-license it to many companies and research institutes developing gene therapy products.

### Action mechanism of CAR gene therapy



## Future Initiatives

### 1) Domestic joint projects

Progress joint development of three projects (C-REV, NY-ESO-1-siTCR™, and CD19-CAR) with domestic partner Otsuka Pharmaceutical Co., Ltd. in pursuit of early production and marketing approval.

### 2) New partnerships for international development

Signed licensing agreement with Dong-A ST Co., Ltd. for exclusive development and marketing of C-REV in South Korea in August 2018. Will put effort into forming international partnerships in other regions and for other projects as well.

## TOPICS

### Presented preliminary results for domestic phase I clinical trial of oncolytic virus C-REV for unresectable advanced pancreatic cancer

In January 2019, Takara Bio presented preliminary results of a domestic phase I clinical trial of our oncolytic virus C-REV at the 2019 Gastrointestinal Cancers Symposium of the American Society of Clinical Oncology (ASCO-GI).

This phase I trial in Japanese patients with unresectable advanced pancreatic cancer was conducted to determine the recommended dose of C-REV in combination with gemcitabine and nab-paclitaxel. At the time of preliminary result reporting, no dose-limiting toxicities\* of C-REV were observed, and there was only one possibly C-REV-related adverse event of grade 3 or higher. The best overall response rate and disease control rate at 16 weeks among the six efficacy-evaluable patients were 67% and 100% respectively. On the basis of these results, the presentation concluded that

combination of C-REV with standard first-line chemotherapy was highly safe and yielded an excellent antitumor effect.

An expansion cohort study (30 patients) of multiple treatment patterns is currently underway. An additional study of 40 patients is planned after completion of the expansion cohort study.

\*Toxicities that increase when the dose of a drug is increased. Signifies the maximum tolerable toxicity (side effect) of patients.

### Phase I clinical trial of C-REV for pancreatic cancer (dose-titration stage)

Best overall response (N = 6)	16 weeks later
Response rate (CR + PR)	4 (67%)
Disease control rate (CR + PR + SD)	6 (100%)
Complete response (CR)	0 (0%)
Partial response (PR)	4 (67%)
Stable disease (SD)	2 (33%)

We deliver “Good Science” through our TaKaRa®, Clontech®, and Cellartis® product lines.

Junichi Mineno

Director  
President of Bioindustry Business Unit



The bioindustry business of Takara Shuzo, which was the predecessor to our current Bioindustry Business, got its start in 1979 when they became the first to domestically manufacture and sell restriction enzymes, a type of research reagent used in genetic recombination experiments. This was just at the time that genetic recombinant technology was developed in the U.S., and once that technology began to spread, the number of researchers in the field increased in Japan as well. However, research reagents for genetic recombination experiments were often imported from the U.S. or were DIY efforts made by the researchers themselves, which made it a difficult environment for Japanese researchers to conduct their research in those years.

Our company's mission at the time was to “deliver domestically produced products of superior quality to research laboratories at a reasonable price in a timely manner.” In other words, we wanted to build a system for not only providing quality products but also providing seamless service from product delivery to academic support. The method of packaging enzyme products in a Styrofoam container with a layer of dry ice on the bottom and the product on top of the central insert that is commonly seen today is a delivery method devised in that era, and the company also wrote detailed instructions and references needed for research in the product catalog as another effort to support genetic recombination experiments.

Forty years have passed since then. Over those years, a series of new technologies such as PCR, genome projects, DNA microarrays, RNA interference, viral vectors, stem cells, and genome editing were developed, and research topics began shifting as well. We responded to these shifts in the landscape by increasing our product offerings through additional product development internally and in collaboration with external organizations, as well as through acquisitions. We currently offer over 7,000 products under our three brand names TaKaRa®, Clontech®, and Cellartis®. In our CDMO business, we offer development and manufacturing support services to

organizations that develop or manufacture gene therapies or other regenerative medicine products. We recently began operating this business at full scale, and are increasing our contract services.

Alongside these efforts to develop products and service offerings, we are also putting effort into building a global sales network and customer support system. Our overseas sales now exceed domestic sales, and in the area of research reagents, the ratio of overseas to domestic sales grew from 26% in fiscal 2006 to 76% in fiscal 2019.

When we first went into business, our stated goal was to “put effort into not only product development but also product quality, price, delivery, and support in order to support life science research in Japan.” Since then, our customer base has become more diverse, and has come to include not only academic customers such as universities but also private companies, and an increasing number of overseas customers as well. That is why we decided to update our Bioindustry Business slogans to these: **“Best-in-class products” “Expert support” “Superior value” ... “That's GOOD Science!”** We will keep these in mind as we continue to support research activities.



“That's Good Science!” is the brand slogan of the Takara Bio Group.



## We are getting closer to bringing gene therapies to patients.

Masanobu Kimura

Director  
President of Gene Therapy Business Unit

In 2014, the former Pharmaceutical Affairs Law was extensively revised and became the Pharmaceutical and Medical Device Act. The Pharmaceutical and Medical Device Act added a new product category called “regenerative medicine products” alongside the previous categories of “pharmaceutical products” and “medical devices.” Regenerative medicine products are characterized by use of biological components such as genes or cells as a product. The addition of regenerative medicine products as a new category under the law enabled faster and more appropriate review of applications in a manner suited to the characteristics of those products, which allowed new treatment methods to reach patients more quickly. The gene therapies we are developing, as well as therapies using iPS cells, which have become a popular topic lately, fall under this category of “regenerative medicine products.”

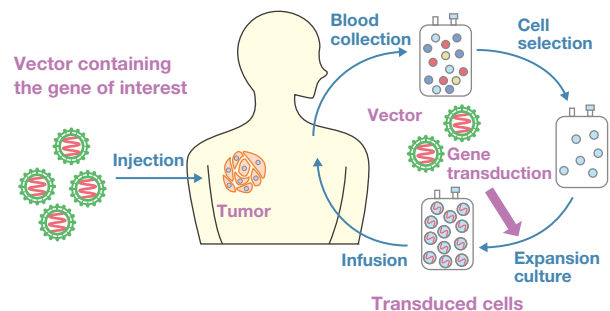
Gene therapy involves harnessing the power of genes that regulate biological responses in order to treat disease. This is done by two specific methods: *in vivo* and *ex vivo* gene therapy. In the former, a gene with therapeutic potential is inserted into an attenuated virus known as a “vector,” and is brought into cells by direct injection into (inoculation of) the body or lesion. In the latter, immune cells or stem cells removed from the body are transduced with a therapeutic gene, and those transduced cells are re-infused into the body as a treatment. The therapeutic genes used in these treatments include genes that issue orders to seek out and destroy cancer cells and genes that induce immunity. In gene therapy for genetic diseases, a healthy gene is used as the therapeutic gene to replace a gene with a congenital defect or mutation causing loss of function.

Rapid technological innovations have improved the safety and effectiveness of gene therapy in recent years, and the regulatory environment has become more accommodating as well. These developments have led to new product approvals

in developed countries over the past few years, and an ever-accelerating pace of development. The therapy that has gained the most attention recently is CD19-CAR gene therapy. It can achieve a remission rate of about 80% for some types of blood cancers, and this extremely good treatment outcome has generated great interest. Gene therapy is also very effective for congenital genetic diseases that previously had no effective treatments, and is producing remarkable results.

At Takara Bio, we have worked on research reagents that use genes and cells for many long years, and have built up a large number of platform technologies. We have therefore been involved in the development of gene therapy products from early on. We are currently engaged in clinical development of three gene therapy products: the oncolytic virus C-REV, NY-ESO-1-siTCR™, and CD19-CAR. All of these therapies are for rare diseases (melanoma, pancreatic cancer, synovial sarcoma, adult acute lymphoblastic leukemia, etc.) with unmet treatment needs.

We are working quickly to commercialize these gene therapy products through daily development efforts in order to bring new therapies to patients as soon as possible.



*In vivo* gene therapy (left) and *ex vivo* gene therapy (right)



## Environment

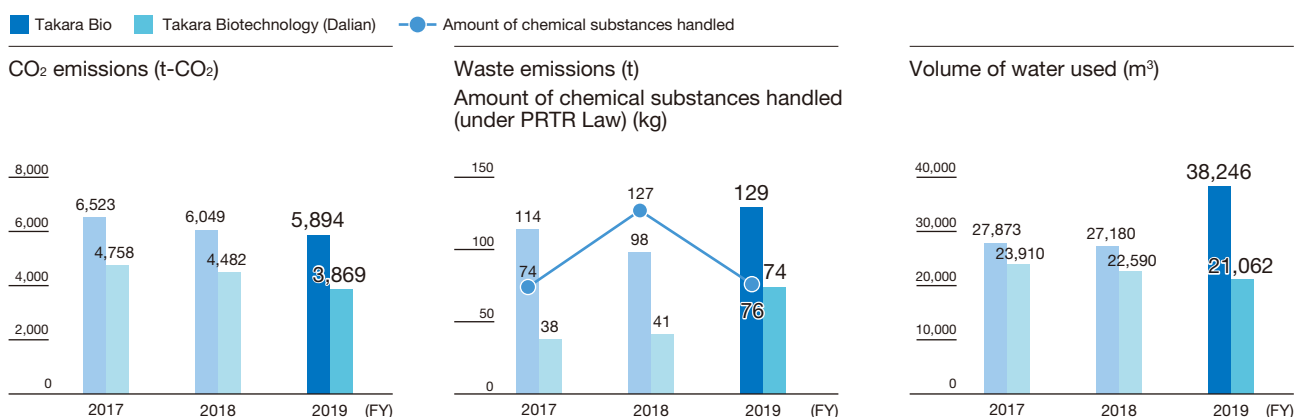
### Fundamental Views on Environmental Activities

We consider the preservation of the global environment and the harmonious conduct of our business activities to be an important topic in the way we manage the company, and to that end we strive to observe the applicable environmental laws, ordinances, and regulations as we proactively take part in natural conservation activities and work to conserve resources and energy. We are working to reduce the environmental burden generated by all of our processes, ranging from research and development of merchandise and the procurement of raw materials to production, distribution, sales, and consumption.

### Environmental Preservation Strategies

We have adopted structural designs at our headquarters and our primary facilities for manufacturing and research that incorporate innovative technologies with enhanced environmental performance. In particular, we have put in place

initiatives to prevent risks from biohazards at our research and manufacturing facilities, and we are aggressively and actively tackling the issues surrounding sustainability, starting with social and environmental problems.



- Lists environmental burden data items for our primary production bases Takara Bio and Takara Biotechnology (Dalian).
- Waste emissions: Lists the amount of chemical substances (based on the PRTR Law) that Takara Bio handles, in addition to waste emissions. In fiscal 2019 our waste emissions increased due to the impact of plant renovation closures and repair work. The waste emissions for Takara Biotechnology (Dalian) include hazardous chemical substances. The increase in emissions in fiscal 2019 is due to partial changes in the waste handling category for emissions.
- Volume of water used: The increase for Takara Bio in fiscal 2019 is due to business expansion.

### Fundamental Views on Contribution to Society

We are making advancements in the development of gene therapies driven by our proprietary technologies, aimed at patients of rare diseases and serious diseases such as cancer for which treatment methods are yet insufficient. In addition, we make day-to-day efforts to contribute to society by providing researchers worldwide with the research reagents and kits that are essential to leading-edge life sciences research.

### Support for Research in the Life Sciences and the Social Implementation of Gene Therapies

We are developing a wide array of products in the life sciences field, ranging from those for basic research to those with industrial applications. In addition to the nearly 7,000 research reagents we produce, we are supporting the growth of research in the life sciences by providing universities and businesses around the world with contract services to support the development and manufacturing of regenerative medicine products.

We are also putting the biotechnologies we have cultivated over many long years to work to make progress in the clinical development of advanced medical technologies for gene therapy and other treatments aimed at conditions such as cancer. In order to contribute to the betterment of people's health, we are working towards the social implementation of gene therapies intended to resolve unmet medical needs.

### Quality Control

Japan's Takara Bio and other major Group subsidiaries across the world have obtained ISO certification, and we continue to strive towards improving the quality of our products and services. In March 2019, our main factory that manufactures research reagents, Takara Biotechnology (Dalian), obtained ISO 13485 certification, an international standard for quality management systems for medical devices and diagnostic manufacturing.

The Center for Gene and Cell Processing and its LIC Annex (Kawasaki, Kanagawa Prefecture) are constructing quality control systems based on GCTP/GMP, and have acquired approval to conduct specific processed cell manufacturing. The office also newly obtained certification for the manufacturing of regenerative medicine products in March 2019, and for the marketing of those products in May of the same year.



In addition, our CDM Center, which offers genetic analysis services and carries out genetic testing support work, has been registered as a CAP/LAP (a certification system for genetic testing laboratories) certified clinical testing laboratory.

#### ISO Certification Status

Certified organization	Applicable standard
Takara Bio, Inc.	JIS Q 9001:2015 (ISO9001:2015)
Takara Bio USA, Inc.	ISO13485:2016
Takara Bio Europe S.A.S	ISO9001:2015
Takara Biotechnology (Dalian) Co., Ltd.	ISO9001:2015 ISO13485:2016
DSS Takara Bio India Private Limited	ISO9001:2015

### Implementation of Animal Testing with Consideration of Animal Welfare

We have formulated internal Guidelines on Animal Testing and the Regulations for Implementation of Animal Testing in line with laws, ordinances, and guidelines established by relevant organizations, and make efforts to engage in strict and fair animal testing. Our animal testing facilities have been recognized for their performance of proper animal testing with scientific perspective, under voluntary control efforts and with consideration of animal welfare. The facilities have been accredited by the Japan Health Sciences Foundation's Center for Accreditation of Laboratory Animal Care and Use.

### Cultivation of Human Resources

We have put in place systems and training programs for our personnel as we strive to achieve a corporate climate that can best reflect the skills possessed by and challenges faced by our employees in our management and business practices. With our system of stratified training that is carried out according to an employee's position or job-related role, we enable executives, middle management, newly-appointed managers, and mid-level and new employees to acquire the skills needed for their position, to learn about their roles, and to formulate career plans. In addition, we offer a diverse array of objective-based training designed to nurture a can-do attitude in all of the employees in the Takara Group, including our field trip program to the Takara Holdings Corporate History Museum, education and training on compliance, and our study seminar to improve IT skills.

#### Examples of objective-based training programs in FY2020

Intended participants	Objectives and details
Young tech-oriented employees and those who need the training for their jobs	Intellectual property follow-up training
Employees involved in manufacturing and quality control	Education and training needed for manufacturing control and quality control
All employees	Education and training on compliance
All employees	Study seminar to improve IT skills
All employees	Field trips to the Takara Holdings Corporate History Museum
All employees	Safety confirmation and evacuation drills

### Promotion of Diversity

The existence of diverse viewpoints and senses of values that reflect different experiences, technical skills, and attributes regardless of gender or nationality among employees is the strength that allows a company to continuously grow. At Takara Bio, we are working towards creating a workplace environment that allows our employees to be continuously active, and which fosters a work-life balance. We support the balance between work and child rearing, and since fiscal 2014, 100% of mothers who have taken leave to raise children after giving birth have returned to their jobs with us. In addition, we are promoting the proactive use of shorter work day systems, time off for nursing babies and infants, time off for pregnancy and baby/infant health screenings, and flextime systems. In fiscal 2006, we were awarded the Shiga Labor Bureau Director's Prize, which commended us as a Family-friendly Enterprise.

#### Targets based on the Act on Promotion of Women's Participation and Advancement in the Workplace

By March 31, 2022, we will appoint at least 10 women to managerial positions, or have at least 25% of managerial positions occupied by women.  
(compared to the number of managerial employees as of the end of March 2016)

### Our Initiatives for Labor Environments

We are working hard to put workplace environments and labor environments in place that will allow our employees to work comfortably. We are also supporting the health of all of our employees via regular health checkups and mental health care, as well as offering health consultations in coordination with occupational physicians. In addition, we have established a help line that enables internal reporting of inappropriate conduct, so that our employees are not placed at a disadvantage and so violations of laws and ordinances and unfair practices are prevented before they can happen.

#### Employee information (Takara Bio Group) As of March 31, 2019

Items	Breakdown	FY2017	FY2018	FY2019	
Number of employees by region	Japan*	468	502	480	
	Overseas	U.S.	151	198	207
		China	577	590	588
		Europe	71	76	71
		Other	77	82	89

\*Including our subsidiaries (Mizuho Norin Co., Ltd./Takara Bio Farming Center Inc., KINOKO CENTER KIN INC.)

#### Employee information (Takara Bio)

Items	Breakdown	FY2017	FY2018	FY2019
Number of employees	Male	271	286	287
	Female	163	185	193
Number of newly-graduated employees	Male	4	12	14
	Female	14	13	24
Diversity	Disabled person employment rate	2.0%	2.2%	2.2%
	Proportion of women in managerial positions	19.6%	20.5%	20.5%



Fundamental Views on Corporate Governance

We will pursue sustainable growth and enhancement of our corporate value in the medium- to long-term by fulfilling our social responsibility as a corporation, and by meeting the expectations of our various stakeholders, including our shareholders.

Our Corporate Governance

Guided by its corporate philosophy of “Contributing to the health of humankind through the development of revolutionary biotechnologies such as gene therapy,” Takara Bio leverages biotechnology, its fundamental technology, to engage in two businesses. The Bioindustry Business is a stable revenue base providing research reagents, scientific instruments, and various contract services to universities and companies around the world. The Gene Therapy Business is engaged in the clinical development and commercialization of gene therapies that target diseases such as cancer, and it will enable us to create new value, realize sustainable growth, and in turn contribute to society.

Takara Bio believes it is necessary to retain earnings in order to proactively implement R&D in each field. Takara Bio is presently at the stage where it is making prior investments in R&D. The current three-year Takara Bio’s Medium-Term Management Plan FY2020, which will be in its final fiscal year in 2020, is a policy which aims to strengthen Takara Bio’s two core business segments and the business base which supports these efforts, in order to enhance Takara Bio’s standing as a global enterprise and regenerative medicine products company. The management plan also aims to achieve prodigious growth and therefore Takara Bio considers operating income to be the most important factor in determining the current state of business.

On the other hand, Takara Bio has placed appropriate shareholder return with awareness of capital efficiency as an important issue for management, and is implementing a basic policy of redistributing profits while taking full consideration of business results and financial conditions.

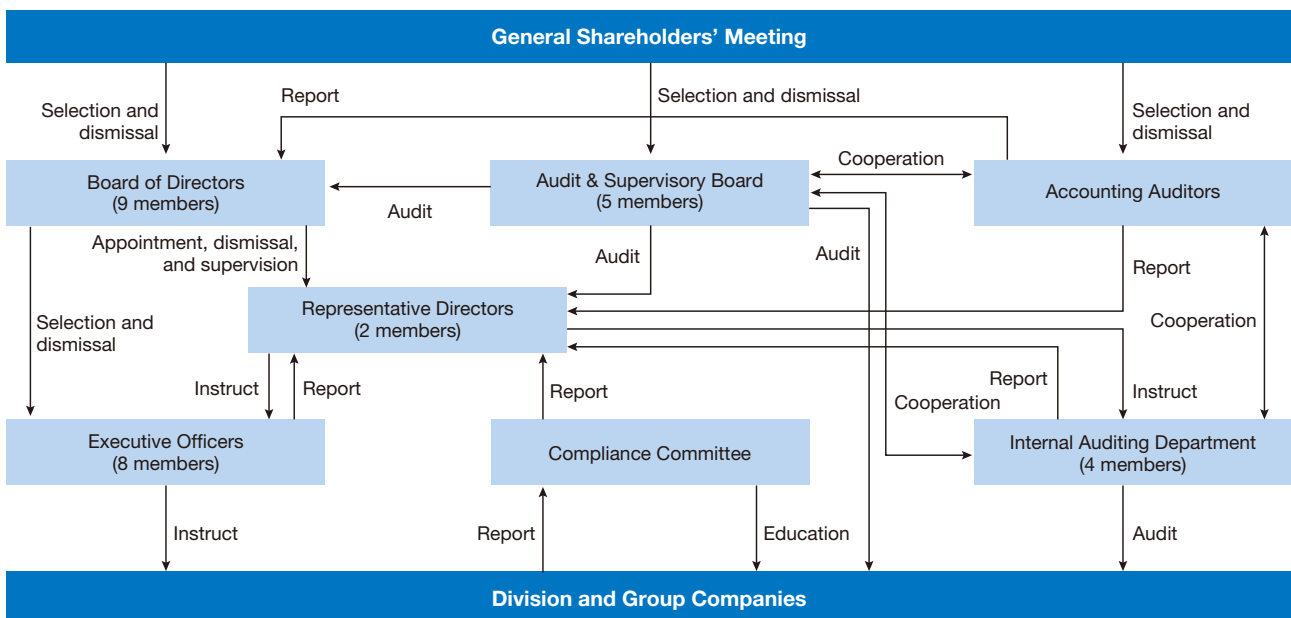
In this way and based on its corporate philosophy, in order to achieve sustainable growth and enhance corporate value over the medium- to long-term, Takara Bio recognizes that it should endeavor to cooperate with various stakeholders, including shareholders, employees, customers, creditors, and local communities in an appropriate manner and while recognizing that a corporate governance structure which promotes honesty and fairness throughout all its corporate activities at all times is essential, Takara Bio is working towards establishing specific policies one by one.

Corporate Governance Structure

Director and Board of Directors

The Board of Directors of Takara Bio is composed of nine individuals, of whom three are external directors.\* The current three-member system of external directors came about via our 17th annual meeting of stockholders in June 2019 in order to pursue sustained growth and medium- to long-term improvement of corporate value. In addition, in order to rapidly respond to the management environment and to clarify the management responsibilities of a director, the term of office of a director has been set to one year.

Diagram of Corporate Governance Structure



## Audit & Supervisory

The Audit & Supervisory Board of Takara Bio is composed of five individuals, of whom three are external auditors.\* The auditors and Audit & Supervisory Board of Takara Bio are to make appropriate decisions from an independent and objective standpoint regarding their role and the performance of their duties. In addition, the auditors must attend meetings of the Board of Directors and various important management meetings as well as conduct appropriate financial and operational audits via an exchange of opinions, etc., between management and the internal auditing department, etc., and they must also make a variety of proposals to management when they are determined to be needed.

\*The Tokyo Stock Exchange has been notified that the three external directors and three external auditors are independent executives.

## About Our Parent Company (Takara Holdings)

As of June 27, 2019, Takara Holdings Inc. (1st section of the Tokyo Stock Exchange) is the parent company of Takara Bio, possessing 60.92% of the voting rights. The following section describes the relationship between the two companies.

### (1) The position of Takara Bio. in Takara Holdings Inc.

Takara Bio was established as a 100% subsidiary of Takara Holdings Inc. spun off during the extraordinary general meeting of stockholders of Takara Shuzo Co., Ltd (the current Takara Holdings Inc.) on February 15, 2002, in order to maximize the business value it was engaged in: the alcoholic beverages and foods business and the bio business. Since then, via allocation of new stocks to a third party and public stock offering Takara Holdings now owns 60.92% of Takara Bio's voting shares. The Takara Holdings Group is made up of the holding company Takara Holdings, 60 subsidiaries, and two affiliated companies. Among those, Takara Bio is positioned as a subsidiary specializing in biotechnology, and promotes its bio business along with nine other subsidiaries.

### (2) About corporate management of the Takara Holdings Inc.

The Takara Holdings Group has established and put into operation Group Company Management Rules based on its consolidated business management objectives, but those objectives are intended to maintain the individuality and autonomy of each of the Group companies, while maximizing corporate value for the Group as a whole. Takara Bio has also applied the same rules and is reporting the matters resolved at meetings of the Board of Directors, but these resolutions do not need prior approval, and we are operating our business independently. While there are other meeting structures in place in addition to this one, all are intended for business reporting, and none have infringed on Takara Bio's autonomy or independence.

## Compliance

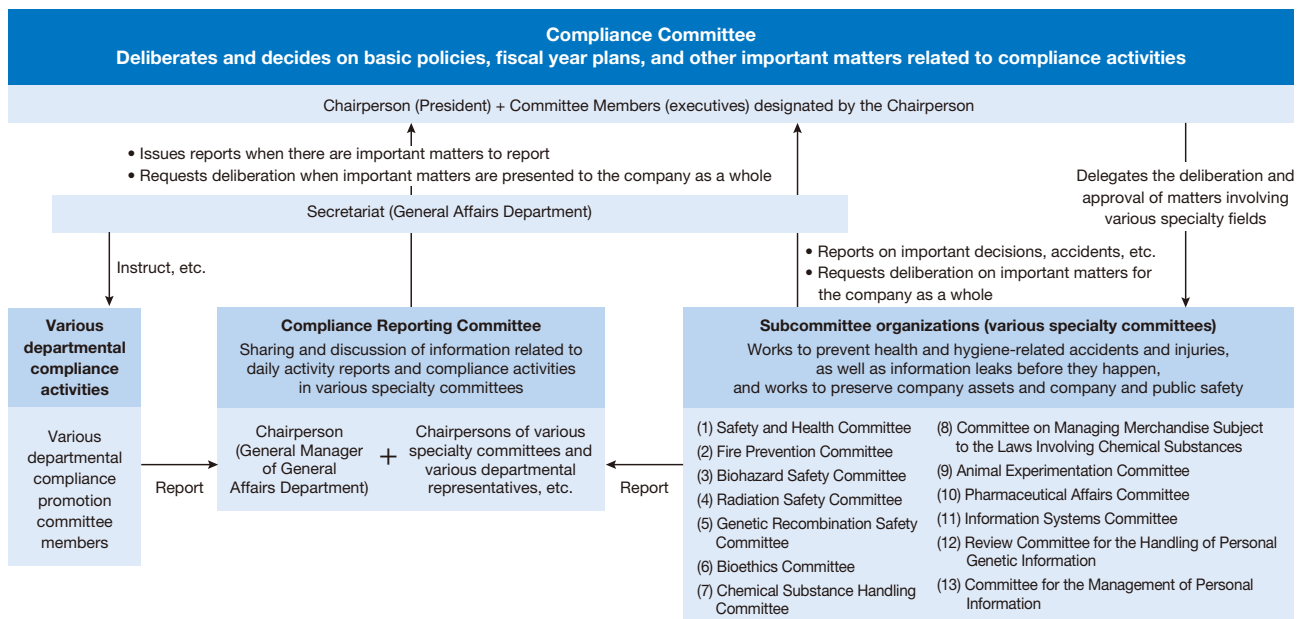
The Takara Group, which includes Takara Bio, has established its own Guiding Principles for Compliance Conduct. Each of the Group companies suitably abides by the law and social ethics and undertakes risk management, enabling the Takara Group as a whole to fulfill its corporate social responsibility and to improve its corporate value.

In addition, Takara Bio has established its own Compliance Committee, with the President as the Chairperson in order to enhance the system for promoting compliance for the Group as a whole.

## Risk Management

Our Group carries out regular workplace inspections in normal times in order to understand and strategize for risks, and the results of those inspections are discussed at the Compliance Committee. We are also proactive in risk management, such as our introduction of strategies for business continuity planning (BCP) that takes into account events such as large-scale disasters and systems that allow for executive and employee safety confirmation.

## Our Organizational Systems for Compliance Activities



## Board of Directors



### Hisashi Ohmiya

Chairman, Director

Apr. 1968 Joins Takara Shuzo Co., Ltd. (currently Takara Holdings Inc.)  
 May 1974 Director, Takara Shuzo Co., Ltd.  
 Jun. 1982 Managing Director, Takara Shuzo Co., Ltd.  
 Jun. 1988 Senior Managing Director, Takara Shuzo Co., Ltd.  
 Jun. 1991 Vice President, Takara Shuzo Co., Ltd.  
 Jun. 1993 President, Takara Shuzo Co., Ltd.  
 Apr. 2002 Chairman (incumbent)  
 President, Takara Shuzo Co., Ltd.  
 Jun. 2012 Chairman, Takara Holdings Inc. (incumbent)  
 Chairman, Takara Shuzo Co., Ltd. (incumbent)



### Koichi Nakao

President, Chairman & President of Subsidiaries, Representative Director

Apr. 1985 Joins Takara Shuzo Co., Ltd. (currently Takara Holdings Inc.)  
 Apr. 2002 Director  
 Jun. 2003 Managing Director & Executive Officer  
 Jun. 2004 Senior Managing Director & Executive Officer  
 Apr. 2006 Senior Managing Director & Executive Officer, COO  
 Jun. 2007 Vice President & Executive Officer, COO  
 Jun. 2008 Vice President, COO  
 May 2009 President (incumbent)  
 President, Takara Bio USA Holdings Inc. (incumbent)  
 Jun. 2009 Director, Takara Holdings Inc. (incumbent)  
 Jun. 2015 Chairman & President of Subsidiaries, Representative Director (incumbent)



### Shuichiro Matsuzaki

Executive Vice President

Apr. 1980 Joins Takara Shuzo Co., Ltd. (currently Takara Holdings Inc.)  
 Jun. 2005 Director, Takara Holdings Inc.  
 Jun. 2007 Director, Takara Shuzo Co., Ltd.  
 Jun. 2008 Managing Director, Takara Shuzo Co., Ltd.  
 Jun. 2010 Senior Managing Director, Takara Shuzo Co., Ltd.  
 Jun. 2014 Senior Managing Director  
 Jun. 2015 Senior Managing Director & Senior Corporate Executive Officer  
 Jun. 2017 Executive Vice President & Senior Executive Vice President (incumbent)  
 Jun. 2019 Executive Vice President (incumbent)



### Junichi Mineno

Director & Senior Corporate Officer

Apr. 1984 Joins Takara Shuzo Co., Ltd. (currently Takara Holdings Inc.)  
 Apr. 2011 Executive Officer  
 Jun. 2012 Senior Executive Officer  
 Jun. 2014 Managing Director  
 Jun. 2015 Managing Director & Senior Executive Officer  
 Jun. 2019 Director (incumbent) & Senior Executive Officer (incumbent)



### Masanobu Kimura

Director & Senior Executive Officer

May 2013 Joins Takara Bio Co., Ltd.  
 Jun. 2016 Executive Officer  
 Jun. 2017 Director (incumbent) & Senior Executive Officer (incumbent)



### Tsuyoshi Miyamura

Director & Senior Executive Officer

Apr. 1988 Joins Takara Shuzo Co., Ltd. (currently Takara Holdings Inc.)  
 Jun. 2009 Executive Officer  
 Jun. 2014 Senior Executive Officer (incumbent)  
 Jun. 2018 Director (incumbent)



### Jawaharlal Bhatt

Director (External Director)

Apr. 1985 Director, Cooper Laser Sonics, Inc.  
 Jun. 1990 President & CEO, Bio Nova Tek International, Inc.  
 May 2000 President & CEO, Jay Bhatt, Inc.  
 Jun. 2010 Director (incumbent)



### Nobuko Kawashima

Director (External Director)

Apr. 1986 Joins The Long-Term Credit Bank of Japan  
 Sep. 1987 Joins Dentsu Communication Institute Inc.  
 Sep. 1991 Research fellow at the Centre for Cultural Policy Studies of the University of Warwick  
 Apr. 1999 Full-time lecturer with the Faculty of Economics at Doshisha University  
 Apr. 2004 Professor with the Faculty of Economics at Doshisha University (incumbent)  
 Jun. 2016 Director (incumbent)



### Kazuko Kimura

Director (External Director)

Apr. 1976 Joins the Ministry of Health and Welfare (current Ministry of Health, Labour and Welfare)  
 Jul. 1997 Seconded to the pharmaceutical department of the World Health Organization  
 Jul. 1999 Seconded to the Organization for Pharmaceutical Safety and Research  
 Apr. 2000 Professor of International Medical Research Laboratory, Institute of Medical, Pharmaceutical and Health sciences, Kanazawa University  
 Jun. 2013 Director (External Director), Affresa Holdings Corporation  
 Sep. Representative Director, Medicines Security Workshop  
 Apr. 2017 Professor Emeritus at Kanazawa University (incumbent)  
 Oct. Specially Appointed Professor with the Graduate School of Medical Sciences at Kanazawa University (incumbent)  
 Jun. 2019 Director (incumbent)

## Audit & Supervisory Board Members

### Akihiko Kita

Standing Audit & Supervisory Board Member

Apr. 1984 Joins Takara Shuzo Co., Ltd.  
 Apr. 2014 Executive Officer  
 Jun. 2016 Standing Audit & Supervisory Board Member (incumbent)

### Masahide Tamaki

Standing Audit & Supervisory Board Member

Apr. 1983 Joins Takara Shuzo Co., Ltd.  
 Apr. 2007 Executive Officer  
 Jun. 2016 Senior Executive Officer  
 Jun. 2019 Standing Audit & Supervisory Board Member (incumbent)

### Kunihiko Kamata

External Audit & Supervisory Board Member

Apr. 1992 Registered as an attorney at law (Osaka Bar Association)  
 Mar. 1993 Registered as a patent attorney  
 Apr. 2007 Part-time lecturer at Meijo University (incumbent)  
 Jan. 2011 Daiichi Law Office, P.C. (incumbent)  
 Jun. 2016 Audit & Supervisory Board Member (incumbent)

### Yasuo Himejiwa

External Audit & Supervisory Board Member

Aug. 1983 Joins the accounting firm of Peat Marwick Mitchell & Co. (currently KPMG)  
 Aug. 1990 Registered as a Certified Public Accountant of Japan  
 Aug. 1994 European Director at KPMG Project Japan  
 Jan. 1996 Century Audit Corporation (currently Ernst & Young ShinNihon LLC)  
 Feb. 2001 Senior partner at Ernst & Young ShinNihon LLC  
 Sep. 2003 Partner at KPMG AZSA LLC  
 Jul. 2009 Director, AZSA LLC Osaka GJP (Global Japanese Practice)

May 2015 National Employee Association Chairman, KPMG AZSA LLC  
 Jun. 2016 Director, Himejiwa Accounting Office (incumbent)  
 Audit & Supervisory Board Member (incumbent)  
 Jun. 2017 Outside Director (Member of Audit & Supervisory Committee), Sharp Corporation (incumbent)

### Masaaki Makikawa

External Audit & Supervisory Board Member

Apr. 1996 Professor with the Faculty of Science and Engineering, Ritsumeikan University  
 Apr. 2003 Head of the Liaison Office, Biwako-Kusatsu Campus, Ritsumeikan University  
 Apr. 2011 Visiting Professor with the Graduate School of Medicine, Osaka University (incumbent)  
 Apr. 2012 Dean of the Research Division, Ritsumeikan University  
 Apr. 2017 Specially Appointed Professor with the Faculty of Science and Engineering, Ritsumeikan University (incumbent)  
 Jun. 2017 Audit & Supervisory Board Member (incumbent)

## Executive Officers

### Yoh Hamaoka

Senior Executive Officer

### Masaharu Watabe

Senior Executive Officer

### Kazuki Yamamoto

Senior Executive Officer

### Mutsumi Sano

Senior Executive Officer

### Katsuhiko Kusakabe

Executive Officer

### Akira Kodera

Executive Officer

### Noritaka Nishiwaki

Executive Officer

### Masanari Kitagawa

Executive Officer

## Corporate Data

Trade Name	Takara Bio Inc.	Lines of Business	Production and sales of research reagents, scientific instruments and others, related contract services, and commercialization of gene therapy
Head Office	7-4-38 Nojihigashi, Kusatsu, Shiga 525-0058, Japan Telephone: +81-77-565-6920 PR and IR Department: +81-77-565-6970	Number of Employees of Takara Bio Group	1,435 (consolidated)
Established	April 1, 2002	URL	www.takara-bio.com
Issued Capital	¥14,965,828,496		

### Main Offices

Headquarters	7-4-38 Nojihigashi, Kusatsu, Shiga 525-0058, Japan	Eastern Japan Sales	2-15-10 Nihonbashi, Chuo-ku, Tokyo 103-8232, Japan
Kusatsu Office	7-2-62 Nojihigashi, Kusatsu, Shiga 525-0058, Japan		

Consolidated Subsidiaries	Location	Issued Capital and Subscription	Line of Business
Takara Biotechnology (Dalian) Co., Ltd.	Dalian, People's Republic of China	¥2,350 million	Development, production and sales of research reagents, and related contract services
Takara Korea Biomedical Inc.	Seoul, Korea	<del>₩</del> 3,860 million	Sales of research reagents and scientific instruments
Takara Biomedical Technology (Beijing) Co., Ltd.	Beijing, People's Republic of China	¥1,330 million	Sales of research reagents and scientific instruments
DSS Takara Bio India Pvt. Ltd.	New Delhi, India	₹110 million	Production and sales of research reagents
Takara Bio USA Holdings Inc.	Mountain View, U.S.A.	\$70,857 thousand	Subsidiary management
Takara Bio USA, Inc.	Mountain View, U.S.A.	\$83 thousand	Development and sales of research reagents and scientific instruments
Takara Bio Europe S.A.S.	Saint-Germain-en-Laye, France	€891 thousand	Sales of research reagents and scientific instruments
Takara Bio Europe AB	Gothenburg, Sweden	kr2,222 thousand	Production and sales of research reagents, and related contract services

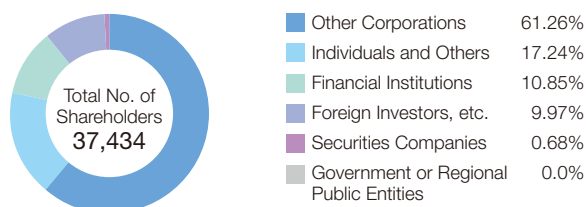
## Investor Information

Common Shares	
Authorized	400,000,000 shares
Issued	120,415,600 shares
Total Number of Shareholders	37,434
Stock Listing	First Section of Tokyo Stock Exchange (securities code number: 4974)
Fiscal Year	From April 1 to March 31 of the following year
Annual Meeting of Shareholders	Every June
Record Date	Dividends March 31 Interim dividends September 30 Other record dates will be posted in advance if necessary
Share Unit Number	100 shares

### Major Shareholders

Name	Number of Shares Held	Percentage of Issued Shares
Takara Holdings, Inc.	73,350,000	60.91%
Japan Trustee Services Bank, Ltd. (trust account)	4,307,200	3.58%
The Master Trust Bank of Japan, Ltd. (trust account)	2,605,100	2.16%
STATE STREET LONDON CARE OF STATE STREET BANK AND TRUST, BOSTON SSBTC A/C UK LONDON BRANCH CLIENTS-UNITED KINGDOM	1,176,300	0.98%
Japan Trustee Services Bank, T5	1,026,300	0.85%
Trust & Custody Services Bank, Ltd. (Securities Investment Trust Account)	722,400	0.60%
JP MORGAN CHASE BANK 385151	719,244	0.60%
Japan Trustee Services Bank, T1	682,100	0.57%
Japan Trustee Services Bank, T2	638,200	0.53%
BBH/SUMITOMO MITSUI TRUST (UK) LIMITED FOR SMT TRUSTEES (IRELAND) LIMITED FOR TOKIO MARINE JAPANESE EQUITY FOCUS CLT AC	611,400	0.51%

### Distribution of Shareholders





# TAKARA BIO INC.

7-4-38 Nojihigashi, Kusatsu, Shiga 525-0058, Japan  
Telephone: +81-77-565-6920  
URL: <http://www.takara-bio.com/>

## Inquiries

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