# SEIKAGAKU CORPORATE REPORT 2018

SEIKAGAKU CORPORATION

# Exploring the Innovative Promise of Glycoscience

**Seikagaku has achieved sustained growth as an R&D-based pharmaceutical manufacturer specializing in glycoscience. We have used our extensive resources of technology relating to glycosaminoglycans, such as hyaluronic acid and chondroitin sulfate, which are both structural components of glycoconjugates, to create a wide range of original pharmaceuticals and medical devices.**

**We aim to achieve growth and success as a "Global Category Pharma" by contributing to the health and well-being of people all around the world through our unique drug development capabilities, and by enhancing our international competitiveness through focused R&D in our fields of specialization.**


## What is Glycoscience?

Glycoscience is a field of research into sugar chains and the complex carbohydrates, or glycoconjugates, that are formed through the binding of these sugar chains with other substances, such as proteins and lipids. Research in this field has demonstrated that sugar chains are deeply involved exchanges of information and substances among cells and are essential for various life phenomena, from the creation of life to aging.

There is also growing interest in the relevance of sugar chains to numerous diseases. Progress in the field of glycoscience is expected to lead to the development of new diagnostic methods and therapies.

**Key roles of sugar chains**

1. **Creation of life through fertilization**
   Sugar chains are involved in the fertilization process that occurs when a sperm encounters an egg.
2. **Determining blood type**
   The ABO blood type of a person is determined by the shape of sugar chains on the surface of their red blood cells.
3. **Water retention**
   Sugar chains, such as hyaluronic acid, protect cells against excessive water loss.
4. **Cell growth control**
   Sugar chains controls the activity of certain growth factors.
5. **Protecting the body against external enemies**
   When a viral or other infection invasion occurs, sugar chains activate immune cells by stimulating macrophages, which are a type of white blood cell.

**Sugar chains and diseases**

1. **Viral and bacterial infections**
   Pathogens such as the influenza virus bind to specific sugar chains on a cell's surface before penetrating the cell itself.
2. **Metastasis of cancer**
   When cells become cancerous, their sugar chains change shape and start to accelerate the proliferation and metastasis of cancer cells.
3. **Diabetes**
   Abnormal sugar chain genes are believed to be one of the causes of this disease.

# Our Strengths

## Source of Competitiveness

**Seikagaku uses its unique technology development capabilities to create and supply high-quality pharmaceuticals and medical devices. It has also built a unique business model based on specialization in R&D and manufacturing.**

### 1 Specialization in Glycoscience

Since its foundation, Seikagaku has focused its attention on the importance of glycoscience and has been working on applied research for new drug development. With our many research achievements, we are contributing to advances in medical science globally through our pioneering and specialized work in this niche field.

### 2 State-of-the-Art Technology Related to GAG*

Through its many years of glycoscience research, Seikagaku has built up a library of GAG compounds and GAG-related enzymes, as well as a wide range of technologies based on the manipulation of these substances. We use these resources to develop new drugs. In its manufacturing operations, we apply our original GAG-related technologies and expertise to various processes, such as extraction, purification and culturing.

*GAG: Glycosaminoglycans, such as hyaluronic acid and chondroitin sulfate, which are structural components known as glycoconjugates.

### 3 Unique Business Model Specialization in R&D and Manufacturing

Seikagaku does not have its own sales force. Instead, we offer our products through sales partners that have strengths in their respective product fields. This approach allows us to concentrate our management resources into R&D and manufacturing. This is evidenced by the fact that our R&D expenses account for 25% to 30% of net sales, and that one-third of our employees are involved in R&D..

《Editorial Policy》

The Seikagaku Corporate Report 2018 is an integrated report containing both financial data and information about environmental, social and governance (ESG) initiatives. Non-financial information includes the history of our growth, our value creation processes, and initiatives in various business areas.

This report was created with the aim of providing stakeholders with a fuller understanding of our business activities and the value provided by Seikagaku Corporation.

〈Target audience〉
Seikagaku stakeholders, including shareholders and investors

〈Period covered by the report〉
This report covers fiscal 2017 (April 1, 2017–March 31, 2018), but it also includes references to activities in fiscal 2018.

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# The Evolution and Growth of Seikagaku Corporation

**Early in its history, Seikagaku became aware of the potential of glycoscience. We are achieving global growth through the steady commercialization of glycoscience R&D advances spanning decades.**

## 1940s~
The world's first company to successfully produce chondroitin sulfate on a commercial scale.

## 1970s~
Pharmaceuticals using hyaluronic acid are developed.

## 1990s~
Enhances its range of pharmaceuticals using hyaluronic acid and expands its activities in overseas markets.

## 2018~
Reaches a new stage with the launch of a treatment agent for lumbar disc herniation.

Major Product Timeline

### 1950

Start of manufacture and sales of chondroitin sulfate for pharmaceutical products, following approval for pharmaceutical manufacturing in Japan

### 1987

Launch of ARTZ®, the world's first joint function improving agent with hyaluronic acid as its main active ingredient, launch of OPEGAN® as the first Japanese-made ophthalmic viscoelastic device

### 1992
Launch of ARTZ® in Sweden under the name "Artzal®," making the start of full-scale overseas marketing of ARTZ®

### 1993

Launch of ARTZ Dispo®

### 1995

Launch of OPEGAN Hi®

### 2001

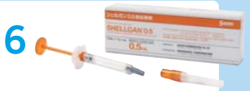
Launch of ARTZ® in the U.S. under the name "SUPARTZ®" (now SUPARTZ FX®)

### 2007

Launch of MucoUp®, a submucosal injection agent for endoscopic surgery

### 2012

Launch of Gel-One®, an intra-articular single-injection viscosupplement for the treatment of knee osteoarthritis, in the U.S.

### 2016

Launch of SHELLGAN®, an ophthalmic viscoelastic device

### 2018

Launch of HERNICORE®, a treatment for lumbar disc herniation

Business Structure Timeline

### 1947

Kosei Suisan K.K. (now Seikagaku Corporation) is established and opens the Kurihama Office (now Kurihama Plant) in Yokosuka City, Kanagawa Prefecture.

### 1949
Masakane Mizutani (a former President of Seikagaku Corporation) commences trial production with the aim of realizing the world's first production of chondroitin sulfate on a commercial scale.

### 1960
The Tokyo Research Institute (renamed the Tokyo Research Center in 1966) is opened in Shinjuku-ku, Tokyo.

### 1962
The Company changes its name to Seikagaku Corporation.

### 1968

The Tokyo Research Center (now the Central Research Laboratory) is relocated to Higashiyamato City, Tokyo.

### 1975
The Takahagi Plant is opened in Takahagi City, Ibaraki Prefecture.

### 1989
The Company's stock is registered on the Japan Securities Dealers Association market (now the JASDAQ).

### 1997

Seikagaku Corporation acquires Associates of Cape Cod, Inc. (U.S.A.)

### 1998
ISO 13485 certification is achieved.

### 2004
Seikagaku Corporation is listed on the Second Section of the Tokyo Stock Exchange.

### 2005
Seikagaku Corporation is promoted to the First Section of the Tokyo Stock Exchange.

### 2013
The CMC Research Laboratory is established in Higashiyamato City, Tokyo (on the same site as the Central Research Laboratory).

# Value Creation Process

**As a company specializing in glycoscience, Seikagaku works to find solutions to social issues, increase its corporate value, and contribute to the health and well-being of humanity, by creating novel and effective pharmaceuticals and medical devices and providing them to the world.**

## Social issues

- Unmet medical needs*
  * Situations in which healthcare needs are not met or there are healthcare needs relating to diseases for which there are no effective treatment methods.
- Super-aging society
- Rising healthcare costs
- Locomotive syndrome
  * Locomotive syndrome: Reduced mobility due to disorders affecting locomotion, such as the knee joints and hip joints—These disorders are regarded as one of the factors that can reduce healthy life expectancy.

## Assets

**Human capital**

Highly qualified personnel

**Intellectual capital**

Compound library and advanced knowledge relating to glycoscience

**Manufacturing capital**

Production and quality control systems to ensure the reliable supply of products

**Financial capital**

A stable financial base as a source of funding for drug discovery

## Sources of competitiveness

**Specialization in R&D and manufacturing**

- Lean organizational structure with no pharmaceutical marketing units
- R&D investment equivalent to 25-30% of net sales

**Glycoscience**

**State-of-the-Art Technology related to GAG**

- Advanced manufacturing basic technologies, including extraction, purification, cultivation and modification technologies
- The ability to create diverse new pharmaceuticals based on the use of GAG and related enzymes

*GAG: Glycosaminoglycans (one of the components of glycoconjugates), such as hyaluronic acid and chondroitin sulfate

## Output
Products and services

Innovative, high-quality pharmaceuticals and medical devices, etc.

**《Ethical pharmaceuticals, medical devices》**

Seikagaku contributes to healthcare in Japan and overseas by supplying ethical pharmaceuticals and medical devices based on GAG, such as hyaluronic acid and chondroitin sulfate, which are both structural components of glycoconjugates, and enzymes that act on GAG.

**<Products for the treatment of orthopedic disorders>**

- ARTZ® series: Joint function improving agent
- GEL-ONE®: Intra-articular single-injection viscosupplement
- HERNICORE®: Treatment for lumbar disc herniation

**<Ophthalmic products>**

- OPEGAN®, OPEGAN Hi®: Ophthalmic viscoelastic device
- SHELLGAN®: Ophthalmic viscoelastic device

**<Other products>**

- MucoUp®: Submucosal injection agent for endoscopic surgery
- Bulk product: Sodium hyaluronate, sodium chondroitin sulfate

**《LAL-related products》**

Seikagaku supplies endotoxin-detecting reagents and other products to pharmaceutical manufacturers, primarily for use in quality control in manufacturing processes for pharmaceuticals and medical devices.

- Endotoxin-detecting reagents
- Endotoxin-detecting equipment

P10

## Business flow

R&D P14 → Production P20 → Marketing (through sales partners) P22 → Medical institutions / Patients

Quality compliance P24

## Business risks

- Healthcare system reforms (including drug price system changes)
- Reliance on specific distributors and products
- Time and expense required for new drug development
- Procurement of animal-derived substances and restrictions on their use

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## Outcome

**Value Proposition**

Improvement of patients' quality of life (QOL)

Extension of healthy life expectancy

Minimization of treatment impacts on patients

Further development and advancement of glycoscience


## Contributing to healthcare globally as an R&D pharmaceutical company specializing in glycoscience

We, Seikagaku, aim to become an R&D Pharmaceutical Company that contributes to human well-being worldwide by supplying safe and sound pharmaceuti cal products and medical devices based on our cutting-edge glycoscience knowledge.

In the process of doing this, we always place value on creativity, fairness,dreams and passion. Since the founding of the company in 1947, Seikagaku has consistently focused on research and development that leads to the creation of unique pharmaceutical products and medical devices, such as ARTZ, the world's first joint function improvement agent using hyaluronic acid.

In recent years, research in the field of glycoscience has shown that sugar chains and glycoconjugates are deeply involved in a variety of physiological processes, which further expands glycoscience's potential role in new drug development.

We will continue to make optimal use of the glycoscience knowledge and technology accumulated by Seikagaku over many years as we take up the challenge of helping patients everywhere to enjoy healthy and fulfilling lives by supplying new drugs to meet real needs.

### CORE VALUES

## Creativity, Fairness, Dreams and Passion

**<Creed>**

We create safe and useful products for human well-being with basic research based on glycoscience.

**<Guidelines for Our Activities>**

- We create a corporate environment of mutual trust and communication using individual abilities.
- We create innovative and useful products through in-depth cooperation between industrial and academic circles.
- We assure the highest quality and safety of our products.
- We enhance interaction with society by establishing genuine trust.

Through these efforts, Seikagaku will strive to become a sound and socially responsible company that protects the natural environment and improves quality of life.

## Becoming a "Global Category Pharma"

The pharmaceutical industry is now facing various tough challenges such as soaring R&D costs, intensifying global competition and constraints on healthcare expenses. Responding flexibly to the above,

We formulated the Seikagaku Corporation Ten-Year Vision in March 2009 Under this vision, we aim to build Seikagaku into an internationally competitive "Global Category Pharma" by focusing our R&D activities on glycoscience as our core competence.

We aim to achieve sustainable growth by competing on a global basis and achieving leadership in glycoscience R&D, leading to the creation of a steady stream of new drugs and medical devices.

## Overview of the mid-term management plan

Our current three-year mid-term management plan, which was launched in April 2016, will be the final step in accomplishing the Seikagaku Corporation Ten-Year Vision.

Titled "Act for the Vision— Achieving the Ten-Year Vision and Making a Further Leap Forward" the plan pursues four high-priority initiatives: Steady progress with SI-6603, a lumbar disc herniation treatment; Powering up as a leader in the knee osteoarthritis market; Enhancement of the development pipeline; and Pursuit of an optimal production and quality management systems.

On March 23, 2018, Seikagaku reached an important milestone in its evolution as a "Global Category Pharma" by acquiring production and marketing approval in Japan for the lumbar disc herniation treatment drug "HERNICORE® 1.25 Units for Intradiscal Injection" ("HERNICORE").

In the LAL business, there was growth in overseas sales of endotoxin-detecting reagents, led by our U.S.-based subsidiary, Associates of Cape Cod,Inc. (ACC).

We will now sum up the progress on our important steps, including the above mentioned four high-priority initiatives.

## Production and marketing approval for HERNICORE in Japan

As mentioned above, we obtained approval for the production and marketing of HERNICORE in Japan and released it in August 2018 through our sales partner Kaken Pharmaceutical Co., Ltd.

HERNICORE is Japan's first treatment for lumbar disc herniation by prolapse of the posterior longitudinal ligament[1] for which sufficient improvement cannot be obtained through conservative treatment. One of the advantages of HERNICORE is that it is far less invasive to the patient than surgical procedures, which require excision or general anesthesia, because it can be administered by injection. In addition, symptoms can be expected to improve with a single dose of HERNICORE. For these reasons, we believe that HERNICORE will become the new treatment option. We are very pleased that the lengthy application process has now ended with an approval, allowing us to provide HERNICORE to patients suffering from lumbar disc herniation. We will continue to develop HERNICORE via post-launch monitoring and improvement[2] activities.

1 Herniation by prolapse of the posterior longitudinal ligament: a type of herniation and its structure is that it is covered by the posterior longitudinal ligament, although the hernia extends beyond the outermost layer of the annulus fibrosus.

2 Post-launch monitoring and improvement: The purpose of these activities is to enhance the ability of a drug to contribute to patient well-being through the improvement of effectiveness, safety, and administration methods, and the expansion of indication, using information gained through actual treatment.

## Future development of HERNICORE—additional study in the U.S. for SI-6603

Currently, special requirements apply to physicians and facilities that use HERNICORE, because it's the first drug to be classified as intradiscal enzyme injection therapy in Japan. Seikagaku will work with its sales partner Kaken Pharmaceutical Co.,Ltd. to achieve a gradual increase in the use of HERNICORE, while also ensuring that it is used properly and safely according to these requirements. In regards to the physician requirements, Seikagaku and Kaken will carefully examine the safety information about six months to a year after the launch upon agreement with the Pharmaceuticals and Medical Devices Agency in cooperation with the relevant societies.

Together with our overseas partner, Ferring Pharmaceuticals, we plan to introduce HERNICORE in other markets.

In the U.S, the pharmacologic effect and safety of SI-6603 have been proven through a Phase III clinical study, but unfortunately, its primary endpoint was not met.

We analyzed the results in detail and quickly made preparations for an additional Phase III clinical study, which began in February 2018. We have raised the probability of success by utilizing the knowledge gained through the previous study and we will continue to focus on obtaining approval in the U.S.

## Initiatives in the knee osteoarthritis market

We are also making good progress in gaining leadership in the knee osteoarthritis market. Demand continues to expand in the United States, which is a key overseas market. However, business conditions remain challenging because of increased competition and the imposition of stricter reimbursement conditions by some insurance companies.

Despite these challenges, we have continued to achieve steady growth in U.S. sales of Gel-One, an intra-articular single-injection viscosupplement, through strategies focusing on the unique features of this product. The U.S. market still offers growth potential, and we will proactively support the marketing activities of our sales partners with the aim of strengthening the presence of three Seikagaku products: Gel-One, the five-injection product SUPARTZ-FX, and the three-injection product VISCO-3.

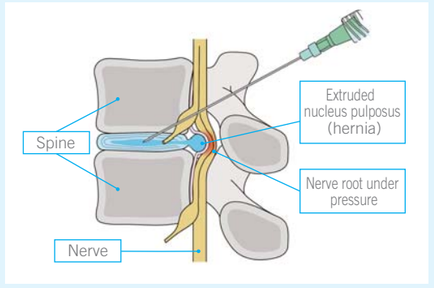
At the same time, we will actively roll out these products in new markets, while monitoring market potential, regulatory trends.

In Japan, reforms to the drug pricing system in April 2018 have caused an unprecedented decline in National Health Insurance (NHI) drug prices. This and other factors have created a challenging business environment for our joint function-improving agent ARTZ. Seikagaku will cooperate with its sales partner Kaken Pharmaceutical Co., Ltd. to implement measures,including usability improvements, in order to maintain and increase sales volumes.

Seikagaku is also making progress on the development of next-generation products. We are currently implementing clinical study in Japan and the United States for SI-613, a new osteoarthritis treatment agent. In September 2017, we established a development structure by signing an agreement with Ono Pharmaceutical Co., Ltd., providing for collaboration on the development and marketing of SI-613 in Japan. We see this as a major achievement. Under the agreement, we received an upfront payment of ¥2.0 billion from Ono Pharmaceutical, and we will also receive milestone royalties linked to progress in development and marketing.

We have positioned SI-613 as the next-generation ARTZ, and by accelerating its development we will build a solid position for Seikagaku as a leading company in the knee osteoarthritis market.

### Lumbar disc herniations and HERNICORE's mechanism of action




Administration of HERNICORE


HERNICORE® 1.25 Units for intradiscal injection

Lumbar disc herniation is the partial protrusion of the nucleus pulposus at the core of each intervertebral disc or the annulus fibrosus, the disc's outer layer. The resulting pressure on the spinal nerve root causes pain and numbness. The nucleus pulposus includes glycosaminoglycans (chondroitin sulfate and hyaluronic acid), which have long been an area of specialization for Seikagaku.

The active ingredient of HERNICORE is condoliase, an enzyme that specifically targets and degrades chondroitin sulfate and hyaluronic acid. When HERNICORE is administered directly into the nucleus pulposus of the intervertebral disc, it reduces the volume of the intervertebral disc and shrinks the herniation. This reduces pressure on the spinal nerve and can therefore be expected to improve the symptoms of a lumbar disc herniation.

## Enhancement and expansion of the development pipeline

Our third high-priority initiative is the enhancement of the development pipeline. In May 2018, we added a new development theme to the pipeline by initiating a pilot study of SI-449, a powdered adhesion barrier with cross-linked chondroitin sulfate as its main ingredient. SI-449, which has the property of absorbing moisture and swelling, is expected to prevent or mitigate post-operative adhesion formation by forming a barrier between the surgical wound site and surrounding tissues after application. The global market for adhesion barriers is estimated to be worth around ¥100 billion. We will continue to develop this product for its future introduction to the Japanese and global markets.

As this illustrates, we are making solid progress with our development themes. We will, however, further tighten our focus so that we can continue to expand and enhance our development pipeline through the discovery of innovative candidate drugs in the field of glycoscience.

## Enhancing production and quality management systems

Our fourth high-priority initiative is the pursuit of optimal production and quality management systems. We are implementing policies for both the maintaining of reliable product supplies, and also cost minimization through efficiency improvements. As part of these efforts, we have employed expert consultants to improve operational processes, especially at the Takahagi Plant. This work has already yielded measurable improvements in productivity.

Another priority is the establishment of systems to ensure reliable supplies of HERNICORE. Our production and quality management systems for existing products are based on global standards. As part of ensuring our continued ability to supply highquality products, we are further strengthening those systems in anticipation of the release of SI-6603 to the U.S. market.

## Aiming for success as a "Global Category Pharma"

The fiscal year ending March 2019 will be the final year of both the Seikagaku Corporation Ten-Year Vision and our three-year mid-term management plan. Seikagaku will continue to implement its high-priority initiatives while also working to build foundations for further growth.

We anticipate that Seikagaku will face an increasingly challenging business environment in the future, in part because of moves to curb healthcare expenditure in Japan and overseas. Our priorities in this changing environment will be to expand sales of existing products, to promote the appropriate use of HERNICORE, and accelerate the expansion of our overseas business activities, including the LAL business. We will also tighten our management of manufacturing costs with the aim of improving our income structure.

Pharmaceutical companies achieve growth by developing new drugs. Seikagaku will continue to focus on the continual creation of effective new drugs through efficient research and development activities based on clearly defined priorities.

We are determined to overcome the challenges in our business environment and ensure our future success as a "Global Category Pharma." We are deeply aware of our social mission and responsibilities as a pharmaceutical manufacturer, and we are committed to management transparency backed by high ethical standards. We will continue to enhance our corporate governance and work toward sustainable improvement in our corporate value.

We look forward to the continuing guidance and support of our stakeholders.

*President & CEO*
*Ken Mizutani*

# BUSINESS ACTIVITIES AND PRODUCTS

**Seikagaku has two business segments, each with original and unique products: the Pharmaceuticals business, and the LAL business for endotoxin-detecting reagents.**

## Pharmaceuticals Business

The Pharmaceuticals business is Seikagaku's core business segment. Seikagaku manufactures pharmaceuticals and medical devices with glycoconjugates, specifically, glycosaminoglycans (GAG) such as hyaluronic acid, as their main ingredient, as well as enzymes that act on GAG. As a pioneer and leading company in glycoscience, Seikagaku provides high-quality products globally with its unique technologies and knowledge that has been developed for many decades.


## LAL Business

Seikagaku manufactures and sells endotoxin-detecting reagents in Japan and overseas. They are primarily used to test for endotoxins in pharmaceuticals and medical devices.

### What is the LAL business?

The main products of the LAL business are endotoxin-detecting reagents made from limulus amebocyte lysate (LAL), which is extracted from the blood cells of horseshoe crabs.

### What are endotoxins?

Endotoxins are one of the major components of the outer membrane of gram-negative bacteria. Serious side effects can be triggered by endotoxin contamination of injectable pharmaceuticals, biological products, and medical devices, even with extremely minute quantities, due to their strong pyrogenetic activity.

## Joint Function Improving Agents

### ARTZ®, ARTZ Dispo®, SUPARTZ FX®*1, VISCO-3™

ARTZ, a vial, containing hyaluronic acid as its main active pharmaceutical ingredient, became the world's first joint function improving agent. ARTZ Dispo is a prefilled syringe product*2 that saves the step of aspirating the drug solution into a syringe. These products have been approved and are supplied not only in Japan but also in overseas markets, including the U.S., Asia, and Europe.

*1 SUPARTZ FX is sold in the U.S. under its brand name *2 A kit with injectable syringe that have the solution been filled.

ARTZ Dispo®


SUPARTZ FX®

### Gel-One®

Gel-One is an intra-articular single-injection viscosupplement developed for the U.S. market for the treatment of knee osteoarthritis. It contains only 3 mL of cross-linked hyaluronate hydrogel, which is Seikagaku's original technology, and provides long-lasting benefits with a single dose. The sales in the U.S. are growing steadily.

Gel-One®

## Treatment for Lumbar Disc Herniation

### HERNICORE®

HERNICORE, which contains enzyme named "condoliase" as its active pharmaceutical ingredient, is Japan's first product for the treatment of lumbar disc herniation with direct intradiscal injection. It can be administered without general anesthesia, and the administration can be less invasive for the patient compared to surgical technique because of the local injection.

HERNICORE®

## Ophthalmic Viscoelastic Devices (OVD)

### OPEGAN®, OPEGAN Hi®, SHELLGAN®

OPEGAN series of products allows the creation of appropriate intraocular space in cataract surgery. The product range includes seven types of different volumes and viscoelastic properties to meet specific treatment needs.

OPEGAN® series

## Submucosal Injection Agent for Endoscopic Surgery

### MucoUp®

MucoUp is an endoscopic surgical aid that utilizes the excellent viscoelastic properties of hyaluronic acid. By injecting MucoUp into the submucosa beneath the lesion during the endoscopic resection of tumors in the gastrointestinal tract such as esophagus, stomach and large intestine, it creates a durable tissue uplift and provides improved procedural maneuverability and efficiency for ESD/EMR*.

* Endoscopic Submucosal Dissection/Endoscopic Mucosal Resection


MucoUp®

## Bulk Products

### Sodium hyaluronate and Sodium chondroitin sulfate

Seikagaku manufactures high-purity and high-quality sodium hyaluronate and sodium chondroitin sulfate with its unique extraction and purification technologies. The bulk products are primarily used as raw materials for pharmaceuticals and cosmetics products.

Bulk products

## Endotoxin-detecting Reagents

### ENDOSPECY®, TOXICOLOR®, Pyrochrome®, etc.

The Endotoxin-detecting reagents that Seikagaku produces with its own technologies are mainly used in quality control of injectable pharmaceuticals, biological products, and medical devices, manufacturing processes, and water quality control of dialysate used in artificial dialysis.

Endotoxin-detecting reagents

## Endotoxin-detecting Devices

### Endotoxin-detecting Systems

Seikagaku provides a wide range of endotoxin-detecting solutions to meet customers' needs, such as fully automatic and simultaneous multi-analyte measurement.

Automatic endotoxin-detecting systems

# REVIEW OF OPERATIONS (April 1, 2017 - March 31, 2018)

## Overall net sales and income

In the fiscal year ended March 31, 2018 (fiscal 2017), net sales were ¥30,175 million, up 2.0% year on year. The result is attributable to higher sales volumes of pharmaceuticals to the U.S. and strong overseas sales in the LAL business, despite a decrease in sales of domestic pharmaceuticals.

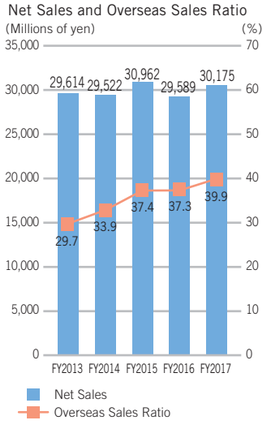
With regard to earnings, operating income rose 10.9% year on year to ¥1,421 million, reflecting the sales increase as well as a decrease in the cost of sales ratio, which resulted in part from production efficiency improvement, despite an increase in selling, general and administrative expenses. These were mainly R&D expenses accompanying progress on development themes such as SI-613, an osteoarthritis treatment. Total R&D expenses in fiscal 2017 increased 7.3% year on year to ¥8,408 million, or 27.9% of net sales.

Ordinary income rose 115.1% year on year to ¥5,327 million, and net income attributable to owners of parent rose 119.4% year on year to ¥3,922 million, reflecting a substantial increase in royalty income, among other factors.

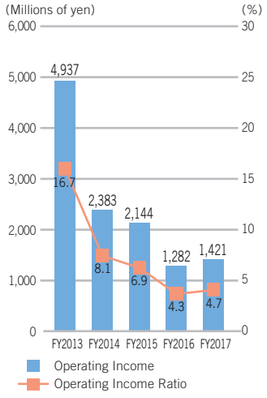
(Millions of yen)

| | FY2016 | FY2017 | Year on Year |
|---|---|---|---|
| Net Sales | 29,589 | 30,175 | +2.0% |
| Operating Income | 1,282 | 1,421 | +10.9% |
| Ordinary Income | 2,477 | 5,327 | +115.1% |
| Net Income | 1,787 | 3,922 | +119.4% |
| R&D Expenses | 7,834 | 8,408 | +7.3% |

Net Sales and Overseas Sales Ratio




Operating Income and Operating Income Ratio

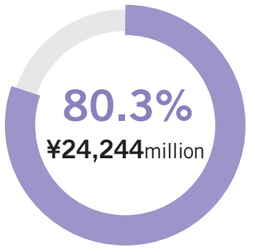



## Net sales by segment

### Pharmaceuticals business

The Pharmaceuticals business is the core business of our company, which manufactures and sells pharmaceuticals and medical devices based on glycoconjugates such as hyaluronic acid. In the Pharmaceuticals segment, net sales increased 0.4% year on year to ¥24,244 million, accounting for 80.3% of total sales.

Pharmaceuticals Business Sales Composition




### Domestic pharmaceuticals (¥16,125 million, down 0.9% year on year)

Deliveries to medical institutions and the Company's sales of ARTZ, a joint function improving agent, declined, partly as a result of the impact of restrained purchasing by medical institutions in connection with National Health Insurance (NHI) drug price reductions implemented in April 2018.

Deliveries to medical institutions and market share of the OPEGAN series, ophthalmic viscoelastic devices, rose sharply as a result of vigorous sales promotion activities for SHELLGAN, and the Company's sales increased as well.

The Company's sales of MucoUp, a submucosal injection agent for endoscopic surgery, were at the prior-year level.

### Overseas pharmaceuticals (¥7,113 million, up 5.0% year on year)

U.S. sales of Gel-One, an intra-articular single-injection viscosupplement for the treatment of knee osteoarthritis, increased as a volume increase compensated for the impact of a decline in local selling unit prices accompanying price adjustments for some major customers.

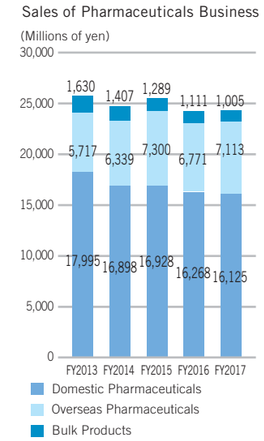
The Company's sales increased due to the local sales increase coupled with the impact of yen depreciation. U.S. sales of SUPARTZ FX, an intra-articular 5-injection viscosupplement for the treatment of knee osteoarthritis, fell, reflecting a preference in the U.S. market for products that require a low number of injections, such as single-injection and 3-injection products. The Company's sales increased due to a sales partner inventory buildup.

The impact of a Chinese government price-curbing policy is running its course, and sales of ARTZ in China (P.R.C.) returned to growth. The Company's sales decreased, following a concentration of shipments in fiscal 2016 accompanying a local inventory buildup.

### Bulk products (¥1,005 million, down 9.6% year on year)

Sales decreased due to fierce competition in the market for hyaluronic acid.

Sales of Pharmaceuticals Business




### LAL business

We manufacture and sell endotoxin endotoxin-detecting reagents used for quality control testing for endotoxin in pharmaceuticals and medical device in Japan and overseas. Sales of LAL business for the fiscal year under review were ¥5,931 million, up 9.1% from the previous fiscal year.

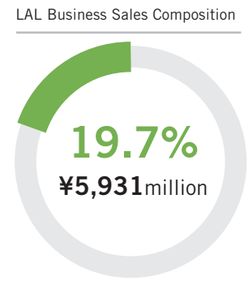
### LAL business (¥5,931 million, up 9.1% year on year)

Sales of the LAL business rose 9.1% year on year to ¥5,931 million as a result of strong overseas sales of endotoxin-detecting reagents and other products, mainly at the U.S. subsidiary, despite a decrease in sales to dialysis facilities in Japan.

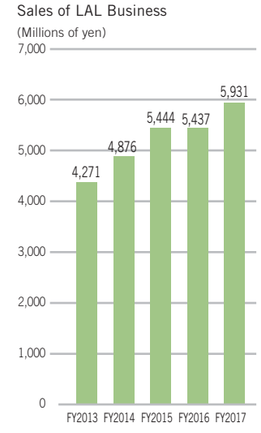
(Millions of yen)

| Sales by Segments | FY2016 | FY2017 | Year on Year |
|---|---|---|---|
| Pharmaceuticals Business | 24,152 | 24,244 | +0.4% |
| Domestic Pharmaceuticals | 16,268 | 16,125 | -0.9% |
| Overseas Pharmaceuticals | 6,771 | 7,113 | +5.0% |
| Bulk Products | 1,111 | 1,005 | -9.6% |
| LAL Business | 5,437 | 5,931 | +9.1% |
| **Total** | 29,589 | 30,175 | +2.0% |
| (Overseas Sales) | 11,029 | 12,051 | +9.3% |

LAL Business Sales Composition




Sales of LAL Business



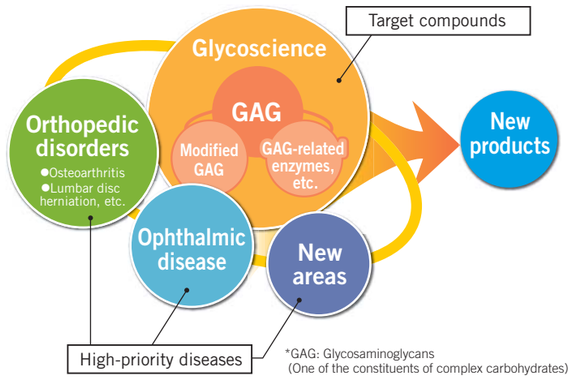
# RESEARCH AND DEVELOPMENT

**Seikagaku engages in research and development of innovative drugs that contribute to health and fulfill the lives of people around the world.**

## R&D policy

In order to rapidly and continuously create new products, Seikagaku engages in efficient R&D activities by focusing on target compounds and prioritizing target diseases. The focus of our drug discovery is glycosaminoglycans (GAG), which are the structural components known as glycoconjugates.

In research spanning nearly 70 years, we have accumulated a wealth of experience and expertise related to GAG drug discovery research and GAG production and formulation technologies. Today, we apply hyaluronic acid or unmodified GAG in pharmaceuticals and also engage in research and development of modified GAG produced using a cross-linking technology as well as enzymes and other substances that act on GAG. Given the properties of GAG, we focus mainly on orthopedic disorders and ophthalmic diseases as high-priority areas for now.




## Seikagaku and glycoscience

Seikagaku's Management Creed states: "Under the principle of respect for learning, we contribute to human well-being by creating and supplying the world with safe and useful pharmaceutical products based on glycoscience." In keeping with this creed, we have made glycoscience the core foundation of our business and explicitly adopted a stance of respect for learning. Seikagaku's origin is closely bound up with this creed.

In 1950, Seikagaku became the first company in the world to successfully produce chondroitin sulfate, which is a sort of GAG, on a commercial scale. This breakthrough laid the foundation for our current business, which is centered on glycoscience. The manufacture of chondroitin sulfate marked the starting point for expansion of our business to bulk products, as well as reagents and diagnostics, and this has led to the strengthening of our ties to glycoscience-related academia and research institutes.

Through this close relationship with academia, we acquired the idea of applying hyaluronic acid in pharmaceuticals. R&D activities spanning many years culminated in 1987 with the successful development and launch of ARTZ, the world's first joint function improving agent whose main ingredient is hyaluronic acid. The development of HERNICORE, a treatment for lumbar disc herniation that contains condoliase, an enzyme that degrades GAG, also originated from collaboration with academia.

Seikagaku will continue to make glycoscience the central focus of R&D activities and, on the basis of research results in the field of glycoscience achieved in collaboration with universities and research institutes, strive to create pharmaceuticals and medical devices and deliver them to patients around the world.

## The difficulty of applying glycoconjugates to pharmaceuticals

GAG are formed when amino sugars (sugars that include nitrogen atoms) and uronic acids (a class of sugar acids) or galactose are linked together to form chain-like structures (sugar chains). GAG exist in living organisms as structural components of glycoconjugates. Sugar chains are known in the life sciences as the third biological chains, along with nucleic acids and proteins. They have complex chemical structures and pose characteristic difficulties in research in areas such as structural analysis, automatic synthesis, and large-scale synthesis.

Some years ago, an industry-government-academia research project focused on glycoscience was formed and its activities advanced the structural analysis and synthesizing technologies of GAG. In addition, the genes of sugar-chain synthesizing enzymes and degrading enzymes have been comprehensively identified, and our understanding of the functions of sugar chains in living organisms is advancing. This progress in glycoscience technologies is closely linked with Seikagaku's drug discovery research.

## Direction of R&D and future drug discovery approach

Seikagaku possesses a GAG compound library, GAG-related enzymes, and wide-ranging technologies for manipulating these substances. We actively utilize these assets, accumulated in the course of research spanning many years, in drug discovery activities. We have also developed a global network of collaborating glycoscience researchers and engage in multiple joint research projects with universities and research institutes.

Specifically, we have given orthopedic disorders and ophthalmic diseases high-priority for research and development. Recently, we have also begun development of adhesion barriers used in surgery as a new R&D area. At the same time, we are considering ways of enhancing the product value (expansion of indications, additional formulations, and improvements in dosage and administration) of products already on the market and themes currently in the development stage.

Until now, Seikagaku has followed a drug discovery approach of increasing the bioactivity of GAG, mainly through GAG modification and processing, and we are currently applying GAG to drug delivery systems (DDSs). Furthermore, going forward, we will also adopt an approach focused on the biological functions of sugar chains to open up new possibilities in drug discovery.

In our DDS, we are researching technologies that utilize the characteristics of modified GAG to freely control drug dose and the location and timing of release. We will pursue drug discovery and development capable of responding to a wide range of unmet medical needs by combining Seikagaku's DDS technologies with drugs and technologies that other companies possessed, not only low-molecular compounds, but also proteins and middle molecules such as peptides and nucleic acids.

**Topics**

### TATENO Forum

Each year the Central Research Laboratory holds the TATENO Forum, an internal forum for presentations relating to new ideas and technology creation. The forum showcases oral and poster presentations of research results for about fifty entries. In addition to researchers, many employees from the head office and manufacturing plants participate in the forum, strengthening exchanges and interaction through active discussion and information sharing.

By providing a forum for actively presenting new ideas and further refining them through open discussion, the Central Research Laboratory contributes to enhancement of Seikagaku's R&D and technological capabilities and aims to generate candidate substances for future development.

* The forum name was taken from the location of the Central Research Laboratory (Tateno, Higashiyamato City, Tokyo).

# RESEARCH AND DEVELOPMENT

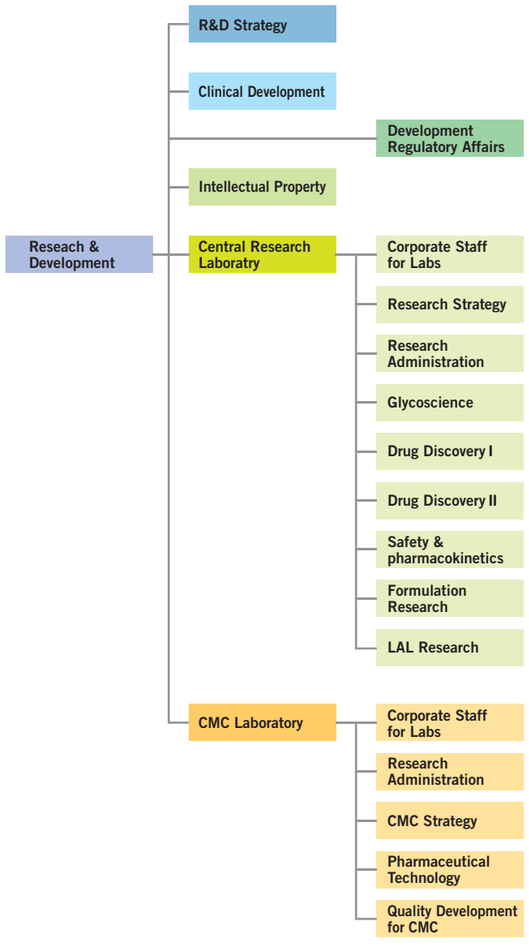
## Research and development organization

To ensure close coordination of the drug development process from its upstream to downstream, Seikagaku has put in place an organizational structure in which the departments involved in R&D are consolidated under the control of the Research & Development Division. This integrated organization covers every R&D activity from clinical development to new drug application (NDA) and intellectual property strategy. In this structure, the Central Research Laboratory is in charge of exploring candidate substances and evaluating efficacy, safety, and pharmacokinetics, and the CMC* Laboratory is responsible for production of investigational drugs, design of manufacturing processes, and consideration of commercial production.

* CMC is an abbreviation for Chemistry, Manufacturing and Controls, which refers to the physicochemical properties and standards of active pharmaceutical ingredients (API) and formulations, their manufacturing processes, and quality control.

### Research & Development Division Structure

(As of January 1, 2019)




## Central Research Laboratory

The Central Research Laboratory, Seikagaku's drug discovery research center, cultivates the creativity of researchers in a fulfilling research environment, equipped with advanced facilities, and places importance on fostering a self-help culture. At the Central Research Laboratory, we accumulate proprietary glycoscience-related knowledge, technologies, and expertise. We also collaborate with academic research institutes and companies in Japan and overseas and actively engage in basic research to promote the search for new ideas and development of new technologies. Through these efforts, we work to, create original pharmaceuticals and medical devices on the basis of specialized technologies and creative ideas.

**<Overview of Research Units>**

- Glycoscience: Exploration of GAG (glycosaminoglycan) and related compounds as pharmaceutical candidate substances
- Drug Discovery: Synthesis of new candidate substances, efficacy evaluation, and research on the mechanisms of action
- Safety & Pharmacokinetics: Evaluation of pharmacokinetics and toxicity profiles of candidate substances in vivo
- Formulation Research: Exploratory formulation research by basic physicochemical examination

## CMC Laboratory

The CMC Laboratory produces investigational drugs, designs manufacturing processes, engages in quality development, and examines commercial production of products under development created by the Central Research Laboratory.

By engaging in development from the R&D stage in collaboration with the Production Division, the CMC Laboratory aims to ensure the stable supply of high-quality pharmaceuticals and medical devices that comply with regulations in Japan, the United States, and Europe and to increase the speed of new drug development under a system integrated from research to production.

**<Overview of Research Units>**

- Pharmaceutical Technology: Design of active pharmaceutical ingredients, pharmaceutical formulations, packaging, and manufacturing processes for candidate substances and consideration of commercial production
- Quality Development for CMC: Research of physicochemical properties, development of testing methods for quality evaluation, and quality assurance of investigational drugs

Central Research Laboratory / CMC Laboratory

## Ethical considerations concerning research using human biological materials

Progress in biological science has been accelerating in recent years, together with accompanying innovation of medical technologies. In particular, experiments and research using human biological materials, including genetic information, are yielding new knowledge that is expected to lead to the development of novel, highly beneficial pharmaceuticals.

In keeping with the intent of the Japanese government's guidelines on handling of human materials,* Seikagaku has established the Code of Ethics for Research Using Human Specimens to make it possible to conduct comprehensive reviews, including evaluation of ethical and scientific validity, when experiments and research using human materials are conducted. To carry out the intent of the Code of Ethics, we have established the Ethical Review Committee for Research Using Human Specimens and publish a list of committee members and minutes of committee meetings through the Japan Agency for Medical Research and Development's Ethical Review Committee Reporting System.

* Ethical Guidelines for Human Genome and Genetic Sequencing Research and Ethical Guidelines for Medical and Health Research Involving Human Subjects

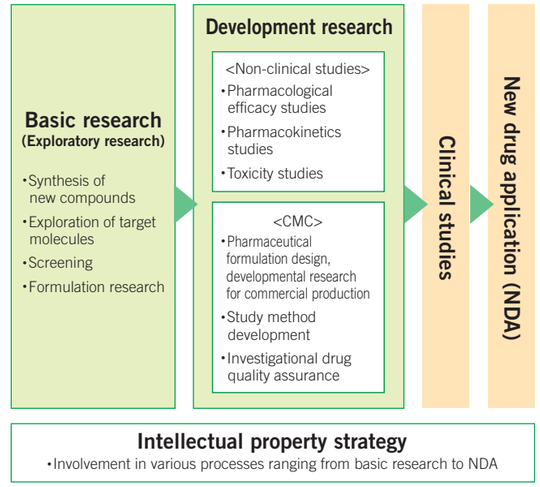
## Ethical considerations in non-clinical studies

In the development of pharmaceuticals and medical devices, research activities using laboratory animals are indispensable to confirm the efficacy and safety of candidate substances, and deeply contribute to the progress and advancement of medical science.

Seikagaku strives to rigorously address ethical considerations in animal experiments and has formulated internal regulations that comply with the Act on Welfare and Management of Animals and Basic Guidelines for Animal Experimentation at Institutes under the Jurisdiction of the Ministry of Health, Labour and Welfare. Also, an ethics committee established within Seikagaku evaluates whether all animal experiments, including outsourced experiments, are planned and conducted in accordance with the 3Rs Principle.* These initiatives at Seikagaku have been evaluated as conformant with the 3Rs Principle by the Japan Health Sciences Foundation's Center for Accreditation of Laboratory Animal Care and Use, a third-party organization

* 3Rs Principle: Methods that avoid or replace the use of animals (Replacement), methods that minimize the number of animals used per experiment (Reduction), and methods that minimize animal suffering (Refinement)

### Processes of New Drug Research




## Topics SI-449 advances to the clinical study stage

SI-449 is an adhesion barrier original to Seikagaku whose main ingredient is cross-linked chondroitin sulfate developed using a glycosaminoglycan cross-linking technology. A number of issues have been encountered in laboratory basic research and non-clinical studies for SI-449, and numerous employees have invested their experience and enthusiasm to resolve them one by one. As a result, we successfully advanced SI-449 to the clinical study stage in May 2018.

SI-449 is a powdered formulation that has unique physical properties, and little reference information is available for guidance in conducting studies. From the initial development stage until the present, development has been a continuous process of trial and error. The experience and knowledge gained by the developers in the involved departments through this development process will be an important asset in future development.

SI-449 has at last reached the starting point of medical device development. The project team members will unite to proceed with development to enable delivery of a product that will bring smiles to the faces of patients.

SI-449 Project manager and Research, CMC, and Clinical project leaders

# RESEARCH AND DEVELOPMENT

## The clinical study process and paths of new drug development

To create new drugs, it is necessary to conduct various studies to evaluate efficacy and safety. Clinical studies are conducted to confirm whether drug candidates are actually beneficial to humans, following completion of research processes such as basic research and non-clinical studies. Clinical studies are ordinarily divided into three phases and conducted at medical institutions such as hospitals in conformance with rigorous standards after the consent of subjects (healthy persons or patients) has been obtained.

Phase I clinical study, the initial phase, is ordinarily conducted for the main purpose of examining the pharmacokinetics (absorption, distribution, metabolism, and excretion) and safety (adverse events and side effects) of investigational drugs in a small number of healthy subjects. Phase II clinical study examines efficacy, safety, and pharmacokinetics and confirms optimal dosage and usage in a small number of patients. Phase III clinical study, the final phase, objectively verifies efficacy and safety in comparison to existing approved drugs or placebos in large numbers of patients.

Ordinarily, more than ten years is required from discovery of a candidate substance until its approval as a new drug. Within the long, difficult new drug development process, clinical development is considered to hold the key to whether an NDA can be filed.

## Clinical development structure

Seikagaku conducts various clinical studies in Japan and the U.S. in cooperation and collaboration with medical experts, medical institutions, and external contract research organizations (CROs) and site management organizations (SMOs). The Clinical Development Department is responsible for the creating the integrated development plan (protocols); monitoring of clinical studies; planning and execution of enrollment acceleration; and data management and analysis of study results. It also communicates with the regulatory authorities in various countries and develops dossiers necessary at the time of NDA filing.

In developing protocols, the Clinical Development Department closely communicates with medical monitors and regulatory authorities, identifies requirements for NDA approval and finalizes the study design. In monitoring of clinical studies, the Department works through medical institutions to ensure the quality of studies by confirming whether they are being conducted in conformance with Good Clinical Practice (GCP) and regulatory requirements by ascertaining the condition of subjects and reviewing study data.

### The Drug Research and Development Process

| Discovery and origination of new compounds that become drug candidates | New compound efficacy and safety research | Confirmation of efficacy and safety in humans | Filing of new drug application with the Ministry of Health, Labour and Welfare (MHLW) and expert review | MHLW approval and listing in the National Health Insurance drug price list | Post-marketing check of safety and directions for use |
|---|---|---|---|---|---|
| 1 Basic research 2-3 years | 2 Non-clinical studies 3-5 years | 3 Clinical studies 3-7 years | 4 New drug application and review Approx. 1 year | 5 Approval and launch | 6 Post-marketing surveillance and clinical studies (Phase IV) |

| Phase I | Phase II | Phase III |
|---|---|---|
| Confirmation of safety, such as side effects, in a small number of healthy persons | Confirmation of effective, safe dosage and administration method in a small number of patients | Confirmation of efficacy and safety in comparison to existing medications in a large number of patients |

Reference: "JPMA Guide," Japan Pharmaceutical Manufacturers Association

### Development Pipeline

(As of November 7, 2018)

<Pharmaceuticals>

| Development code, substance name | | Indication | Developed in | Phase I | Phase II | Phase III | NDA |
|---|---|---|---|---|---|---|---|
| SI-6603 | Condoliase | Lumbar disc herniation | USA | | | | |
| SI-613 | Hyaluronic Acid-Diclofenac Conjugates | Osteoarthritis | Japan | | | | |
| | | Knee osteoarthritis | USA | | | | |
| SI-613-ETP | Hyaluronic Acid-Diclofenac Conjugates | Enthesopathy | Japan | | | Late-stage Phase II | |
| SI-614 | Modified Hyaluronate | Dry eye | USA | | | Phase II/III | |

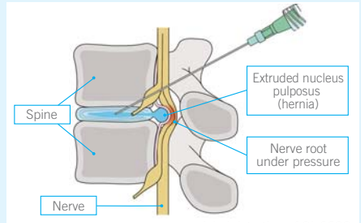
<Medical Devices>

| Development code, substance name | | Description | Developed in | Pilot study | Pivotal study | NDA |
|---|---|---|---|---|---|---|
| SI-449 | Cross-linked Chondroitin Sulfate | Adhesion barrier | Japan | | | |

### SI-6603 (treatment for lumbar disc herniation)

SI-6603, which contains condoliase as its active pharmaceutical ingredient, is a treatment directly injected into the intervertebral disc. A single injection of SI-6603 is expected to reduce nerve root impingement resulting in improvement of the symptoms of lumbar disc herniation by reducing intervertebral disc pressure. Treatment with SI-6603 is less invasive to the patient than surgical removal of the herniation.

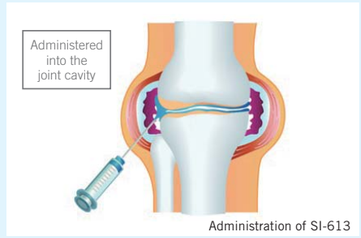
SI-6603 was launched in Japan in August 2018 as HERNICORE 1.25 units for intradiscal injection. In the U.S., although the expected pharmacological effect was demonstrated in a Phase III clinical study, the study did not meet its primary endpoint of improvement in pain. In response to this result, we initiated a Phase III clinical study (an additional study) in the U.S. in February 2018. Together with Switzerland-based Ferring Pharmaceuticals, the sales partner for the U.S. and other overseas markets, we will consider expansion to countries where it is possible to obtain approval using study data from Japan.



Administration of SI-6603

### SI-613 (treatment for osteoarthritis and enthesopathy)

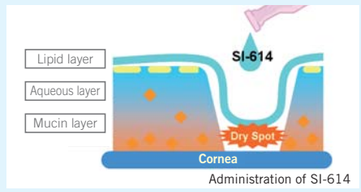
SI-613 is a formulation in which hyaluronic acid and a diclofenac (anti-inflammatory drug) are chemically bound using Seikagaku's own proprietary technology that is expected to provide prompt and sustained relief of the pain associated with osteoarthritis and enthesopathy. In Japan, we are conducting a Phase III clinical study initiated in February 2017 for the treatment of osteoarthritis and a late-stage Phase II study initiated in September 2017 for the treatment of enthesopathy (SI-613-ETP). We concluded an agreement concerning a co-development and marketing collaboration for SI-613 in Japan with Ono Pharmaceutical Co., Ltd. in September 2017. In the U.S., we are conducting a Phase II study for the treatment of knee osteoarthritis initiated in June 2017.



Administration of SI-613

### SI-614 (treatment for dry eye)

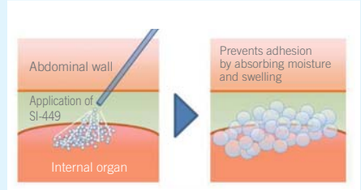
SI-614 is a modified hyaluronate that is produced using Seikagaku's proprietary technology. Ocular instillation of SI-614 is expected to protect the ocular surface and promote corneal wound healing. Many factors are involved in dry eye, and SI-614 is thought to have the potential of providing a therapeutic option based on a new mechanism unavailable from existing drugs with anti-inflammatory mechanisms in the U.S. Phase II/III clinical study was completed in January 2015, and Seikagaku is currently proceeding with selection of a development and sales partner.



Administration of SI-614

### SI-449 (adhesion barrier)

SI-449 is a medical device whose main ingredient is cross-linked chondroitin sulfate developed using Seikagaku's proprietary glycosaminoglycan cross-linking technology. SI-449 is expected to prevent or mitigate post-operative adhesion formation by absorbing moisture and swelling to form a barrier between the surgical wound site and surrounding tissues. Since it is a powdered formulation, it adheres well to uneven tissue surfaces and is thought to offer excellent utility in laparoscopic surgery, an increasingly common surgical procedure. Seikagaku initiated a pilot study in May 2018 and will proceed with development with a view to global development.



Use of SI-449

# PRODUCTION

**Seikagaku steadily manufactures high-quality products at its two pharmaceutical manufacturing plants in Japan and endotoxin-detecting reagent manufacturing plant in the U.S.**

## Production structure compliant with global standards

Companies that manufacture pharmaceuticals and medical devices must comply with the current regional regulations and engage in stable, continuous manufacturing. In order to deliver high-quality products to patients, Seikagaku complies with Good Manufacturing Practice (GMP) in Japan, the U.S., and Europe and strives for ever more rigorous manufacturing processes. We are also working to improve production efficiency through periodic checking and improvement of manufacturing processes using computerized systems for manufacturing and quality control. We will continue to pursue continuous improvement and focus on the manufacture and supply of high-quality products that comply with global standards.

## Ensuring a stable supply of products

Providing a stable supply of products is an important mission of a pharmaceutical company. Seikagaku prepares against major disasters and other risks by diversifying raw materials suppliers and maintaining appropriate inventory levels. At the Takahagi Plant, which is responsible for manufacturing the finished products, we have introduced a quake-absorbing structure that reduces shaking for the main production buildings when an earthquake occurs. Through these measures, we have put in place a system capable of stable, reliable product production even in an emergency.

Furthermore, to cope with product supply risk from distribution network disruption following a disaster, we maintain a certain level of product inventory and have product warehouses in two separate locations: within the Takahagi Plant in Takahagi City, Ibaraki Prefecture in the Kanto region and in Hirakata City, Osaka in the Kansai region.

## Environmental impact reduction initiatives

Seikagaku is keenly aware of the importance of protecting the global environment. We observe environment-related laws and regulations and voluntarily engage in environmentally friendly business activities. At our plants, in the treatment of water used in pharmaceutical production, we have introduced electro-deionization facilities that use no hydrochloric acid or caustic soda and, in wastewater treatment, we have adopted a system that uses ozone treatment and the activated sludge process.

We have also established the group-wide Energy Conservation Promotion Committee and are engaging in group-level initiatives to save energy, such as information sharing and joint consideration of improvement measures among the Group's business sites.

**Topics**

### Takahagi Plant operational improvement activities (improvement project)

The Takahagi Plant is focusing on operational improvement activities to improve production efficiency and quality. As part of this effort, the Plant undertook capacity utilization improvement and defective product reduction by launching a project bringing in an expert consultant ,and reexamining practices taken for granted. This activity had the added benefit of enabling employees in the Plant to acquire the expertise to objectively analyze and visualize business operations and processes.

In these activities, the improvement project team has actively solicited and listened to employee input, and they work together to progress the improvement activities. Employee feedback such as "Work times have been reduced and work is getting easier" and "Yield has increased" has provided tremendous motivation for the project.

Currently, Seikagaku is setting up a dedicated organization for improvement activities within the Takahagi Plant and striving for further operational improvements. We plan to roll out the activities to the Kurihama Plant and ensure their penetration throughout the entire Production Division and will foster a corporate culture that encourages these activities and develop personnel who will be responsible for them.

Takahagi Plant improvement project team members

## Overview of Production Sites

### Takahagi Plant (Takahagi City, Ibaraki Prefecture)

The Takahagi Plant, located in northern Ibaraki Prefecture, is responsible for manufacturing finished pharmaceuticals and medical devices, including the joint function improvement agents that are Seikagaku's mainstay products. When the plant opened in 1975, it had 28 employees. Since the launch of hyaluronic acid formulations in 1987, it has steadily expanded production scale as a manufacturing plant that specializes in injectable formulations. Today, the Takahagi Plant occupies a site of approximately 86,000 square meters and has five production buildings and some 300 employees.

The Takahagi Plant is one of the world's largest manufacturing sites for hyaluronic acid pre-filled syringe formulations*, producing more than 25 million units per year for the Japanese and overseas markets. Sterility assurance is strictly required for the manufacture of injectable formulations, and the Plant has minimized the risk of contamination by implementing unattended, automated manufacturing processes. The Plant possesses facilities and equipment that can be adapted to optimal sterilization methods suited to the product characteristics and that assures sterility of the products.

* A kit with injectable syringe that has been filled with solution.

### Kurihama Plant (Yokosuka City, Kanagawa Prefecture)

The Kurihama Plant, which manufactures bulk products, opened in 1947 and is Seikagaku's most experienced plant. The plant has some 100 employees and manufactures high-purity hyaluronic acid and chondroitin sulfate for use mainly as active pharmaceutical ingredients.

The most important characteristic of the Kurihama Plant is that it specializes in the manufacturing of bulk products by extraction and fermentation. The plant applies advanced chondroitin sulfate extraction and fermentation technologies nurtured over many years since the founding of Seikagaku and has expertise in the efficient manufacture of high-purity bulk products from chicken combs, the raw material of hyaluronic acid, and shark cartilage, the raw material of chondroitin sulfate.

The Kurihama Plant is also responsible for some of the manufacturing processes for condoliase, the active pharmaceutical ingredient of HERNICORE, a treatment for lumbar disc herniation. The Plant is currently preparing to start up new bulk condoliase manufacturing facilities to further strengthen the production scale.

### Associates of Cape Cod, Inc. (Massachusetts, USA)

Associates of Cape Cod, Inc. (ACC), a wholly owned subsidiary of Seikagaku, was the first FDA-licensed LAL manufacturer. It was established in 1974, became a Seikagaku subsidiary in 1997, and currently plays a central role in the global Bacterial Endotoxin Testing (BET) and clinical glucan detection sectors. ACC employs approximately 230 employees and has operations in the U.K. and Germany.

ACC's reagent production facility, located at their campus in Falmouth Technology Park in Massachusetts, is vertically integrated with an end-to-end manufacturing operation that extends from harvesting horseshoe crab blood cells, a reagent raw material, to manufacturing, testing, packaging/labeling and distributing endotoxin and glucan in-vitro diagnostic agents. From that location, ACC also offers customers in-house contract testing services for BET and clinical glucan product testing.

# MARKETING

**Seikagaku has a unique business model of supplying products through external partnerships in Japan and overseas in collaboration with pharmaceuticals and medical device sales companies. In this way, it intends to focus and develop its business activities without having an in-house pharmaceuticals sales division.**

## Pharmaceuticals and medical devices

Seikagaku manufactures pharmaceuticals and medical devices with, as their main ingredient, glycosaminoglycans (GAG) such as hyaluronic acid, which are the structural components of glycoconjugates, and also products based on enzymes that act on GAG. To deliver these products to patients globally, Seikagaku forms partnerships with pharmaceutical companies that have expertise in each market, including Japan.

Through the activities, our partners, in conformance with laws and regulations on pharmaceutical sales, provide appropriate information on product efficacy, safety, quality, and other matters to physicians on a timely basis. Seikagaku's activities such as sales strategy planning, market analysis, collaborations with academic societies, and product information materials creation are conducted in close cooperation with these partners for promoting market penetration.

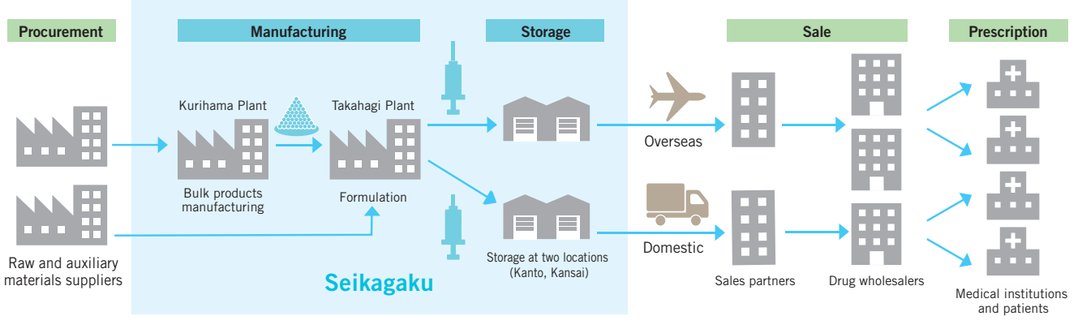
As part of product life cycle management, Seikagaku is implementing product modifications that respond to needs of a changing market. One example is the conversion of the material for syringes used for the joint function improving agent ARTZ, from glass to plastic. Through these efforts, we are adding value of our products.

To accelerate and expand our overseas business, Seikagaku is committed to continuously grow in its current markets, and also develop new markets, by responding to global medical needs with its products.

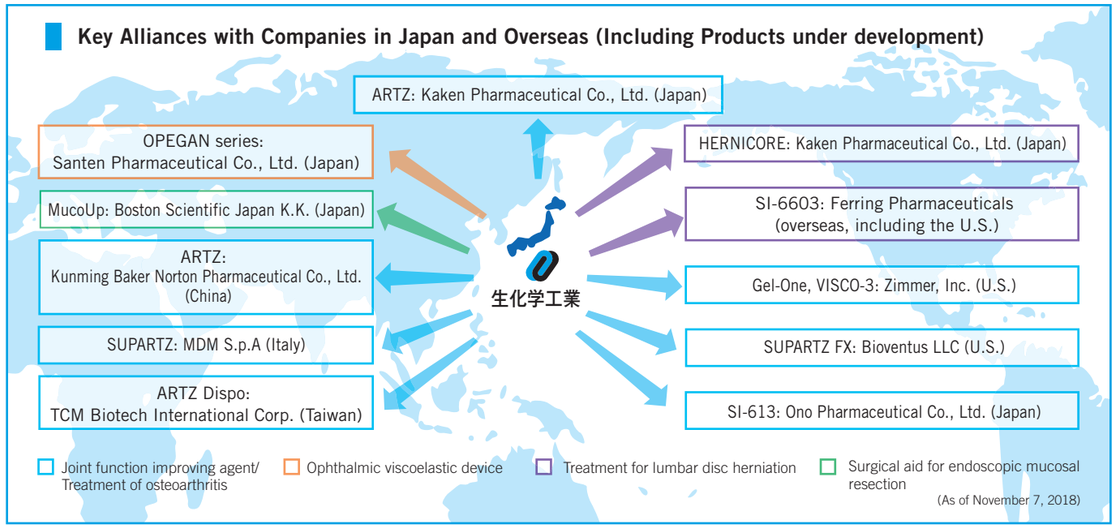
## Bulk products

Seikagaku's business can be traced back to 1950 when it became the first company in the world to successfully produce chondroitin sulfate on a commercial scale. The key to success was its unique extraction and purification technologies. With these technologies, Seikagaku manufactures high-purity and high-quality hyaluronic acid and chondroitin sulfate and sells them to pharmaceutical companies and others globally. The bulk products are widely applied as active pharmaceutical ingredients for orthopedics and ophthalmology. In recent years, those bulk products are also being considered as new application materials in the regenerative medicine area.

### Supply Chain for Main Products




### Key Alliances with Companies in Japan and Overseas (Including Products under development)




## Endotoxin-detecting reagents (LAL business)

The endotoxin-detecting reagents that Seikagaku provides are mainly used in quality control of pharmaceutical and medical device manufacturing processes and water quality control of dialysate used in artificial dialysis.

Seikagaku is engaged in the development of the LAL business in Japan, selling endotoxin-detecting reagents and related devices mainly to pharmaceutical companies that manufacture injectable formulations, while wholly owned subsidiary Associates of Cape Cod,Inc. (ACC) handles overseas business development. ACC is the first company in the world to successfully develop endotoxin-detecting reagents from limulus amebocyte lysate (LAL), and it obtained U.S. Food and Drug Administration (FDA) approval in 1977. ACC plays an important role in the overseas business expansion through its global sales network, mainly in the U.S. and Europe, by manufacturing and sales of endotoxin-detecting reagents, as well as beta-glucan-detecting in vitro reagent to diagnose invasive fungal disease.

**Topics**

## Implementing marketing activities in Japan

At Seikagaku, with its unique structure without an in-house pharmaceuticals sales team, the Business Development & Marketing Department is responsible for marketing and promotion activities in Japan. With the aim to improve patients' quality of life (QOL), its activity covers a broad area, such as sales strategy planning together with partners; product information materials creation, academic seminars and workshop arrangements, collection of information at medical institutions, product life cycle management design (including, but not limited to, expansion of indications and product modification), product shipment and inventory control, etc. The Business Development & Marketing Department does engage in direct sales of bulk products in Japan.

To ensure the provision of the new product "HERNICORE" to large numbers of patients from now into the future, we will pursue market penetration with appropriated steps, by gathering safety information and collaborating with academic societies to ensure safety use of the product.


Takahagi Plant has celebrated its first shipment of HERNICORE to the Japanese market.

# QUALITY COMPLIANCE

**Seikagaku's mission is to provide society with a continuous supply of beneficial, high-quality pharmaceuticals and medical devices. We have constructed corporate quality assurance and compliance systems in accordance with laws, regulations, and standards.**

## Quality compliance system

To continuously provide patients and medical professionals with high-quality pharmaceuticals and medical devices, Seikagaku makes maximum effort to ensure quality at every stage, from R&D to post-marketing by complying with the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices ("PMD Act") and a collection of regulations and guidelines called GxP.* In Japan, as a marketing authorization holder, we have developed a system with three key roles (general marketing compliance officer, quality assurance supervisor, and safety management supervisor) and implement appropriate quality management and pharmacovigilance operations.

To continue to reliably provide pharmaceuticals and medical devices required by patients around the world, we will strive to maintain and enhance quality assurance and compliance systems in accordance with global standards.

* GxP is an abbreviation for Good XXX Practice, a collective term for standards established to ensure the efficacy, safety, and quality of pharmaceuticals and medical devices from the R&D stage to post-marketing. (See the diagram to the right.)

## Quality management system based on global standards

To provide a stable supply of high-quality pharmaceuticals and medical devices, according to our Quality Policy, we have developed a quality management system that ensures the reliability of our products worldwide. At the development stage, we ensure reliability under Good Laboratory Practice (GLP) and Good Clinical Practice (GCP). To guarantee quality assurance in accordance with legal and regulatory requirements after product launch, each year we systematically conduct self-inspections and internal audits to confirm the status of operation of the quality management system and promptly take corrective and preventive actions as necessary.

Seikagaku has obtained ISO 13485 certification for the development, manufacture, and distribution of sodium hyaluronate-based viscoelastic products for the treatment of osteoarthritis of the knee and periarthritis of the shoulder. We strictly maintain and control quality at all stages from product design and development to post-marketing in conformance with these manufacturing control and quality assurance systems.

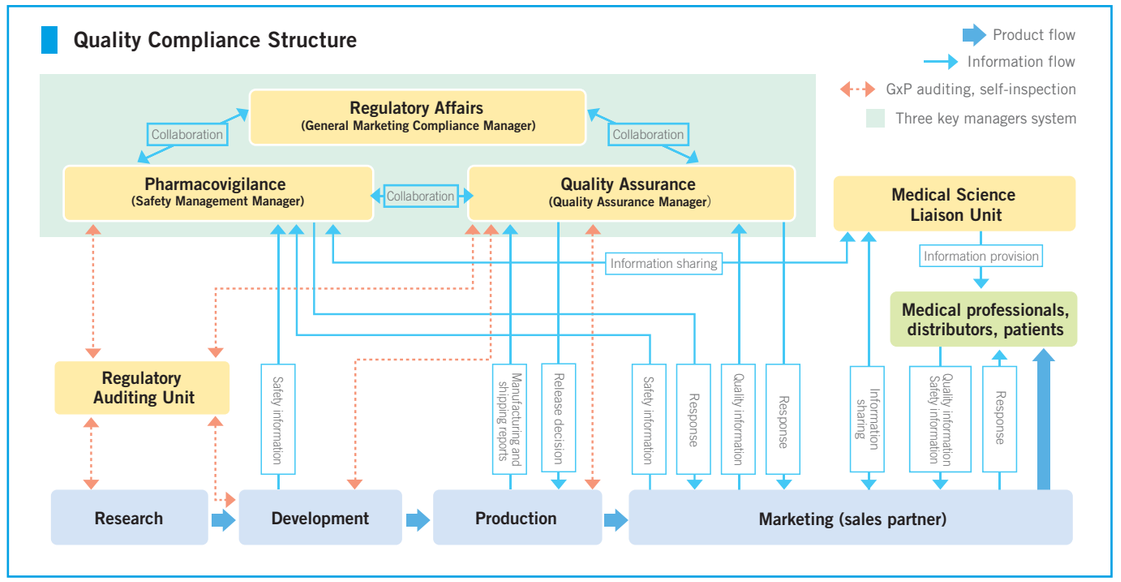
ISO 13485 is an international standard for quality management systems established by the International Organization for Standardization (ISO) that prescribes requirements concerning the design, development, and manufacturing of medical devices. In Japan, ISO 13485 has been adopted as an ordinance on standards for manufacturing control and quality control of medical devices and in vitro diagnostics.

## Laws and Regulations Governing Pharmaceuticals and Medical Devices

| Life cycle | 1 Basic research | 2 Development | 3 NDA | 4 Manufacturing, quality control, information provision, and product provision | 5 Post-marketing |
|---|---|---|---|---|---|
| Laws and Regulations: Pharmaceuticals | ・PMD Act<br>・GLP | ・PMD Act<br>・GLP<br>・GCP<br>・GMP for investigational products | ・PMD Act | ・PMD Act<br>・GMP<br>・GQP | ・PMD Act<br>・GPSP<br>・GVP |
| Laws and Regulations: Medical devices | ・PMD Act<br>・GLP | ・PMD Act<br>・GLP<br>・GCP<br>・QMS | ・PMD Act | ・PMD Act<br>・QMS | ・PMD Act<br>・GPSP<br>・GVP |

・PMD (Pharmaceutical and Medical Device) Act
Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices
・GLP:Good Laboratory Practice
Standards for conducting non-clinical studies on safety
・GCP:Good Clinical Practice
Standards for conducting clinical studies
・GMP:Good Manufacturing Practice
Standards for manufacturing control and quality control in manufacturing
・GVP:Good Vigilance Practice
Standards for post-marketing safety management of drugs, quasi-drugs, cosmetics and medical devices and regenerative medicine products
・GQP:Good Quality Practice
Standards for quality control of products
・GPSP:Good Post-marketing Study Practice
Standards for conducting post-marketing surveys and studies on drugs
・QMS:Quality Management System
Ordinance on Standards for Manufacturing Control and Quality Control of Medical Devices and In Vitro Diagnostic Reagents

## Quality Compliance Structure




## Safety management

Sometimes side effects not observed in the development stage come to light after the launch of a new drug. In accordance with Good Vigilance Practice (GVP) standards, Seikagaku conducts post-marketing pharmacovigilance activities involving promptly and appropriately collecting, evaluating, and sharing feedback information on the side effects of drugs prescribed at medical facilities. Through these activities, we prevent the expansion of side effects and promote safety assurance and appropriate use of new drugs.

## Medical information collection and provision activities(Medical Science Liaison)

Seikagaku has established the Medical Science Liaison (MSL) Unit, which engages in activities to provide current scientific knowledge to external professionals independently from the marketing division. As scientific experts with sufficient ethical perspective, the MSL Unit contributes to medical progress by creating and disseminating medical evidence relating to disease information and products in the fields in which Seikagaku focuses, such as orthopedic disorders and ophthalmic diseases.

**Topics**

### HERNICORE post-marketing surveys

The Pharmacovigilance Department is conducting post-marketing surveys of HERNICORE, the treatment for lumbar disc herniation launched in August 2018, in cooperation with sales partner Kaken Pharmaceutical Co., Ltd. We are surveying and examining safety and efficacy, and what factors affect them, after the administration of HERNICORE at medical facilities.

HERNICORE is the first drug to be classified as intradiscal enzyme injection therapy in Japan, and this is the largest survey project ever undertaken by Seikagaku, involving more than 3,000 patients for three years after administration. For this reason, we are mounting a concerted effort to reliably conduct the survey in collaboration with numerous physicians of related academic societies and patients as well as with our sales partner.. By feeding back the safety and efficacy information obtained through surveys to medical facilities, we promote appropriate use of HERNICORE and contribute to post-marketing drug development.

HERNICORE post-marketing survey team members

# HUMAN RESOURCES

**Seikagaku aims to develop self-driven and self-disciplined employees who can contribute to sustainable growth.**

## Development of human resources

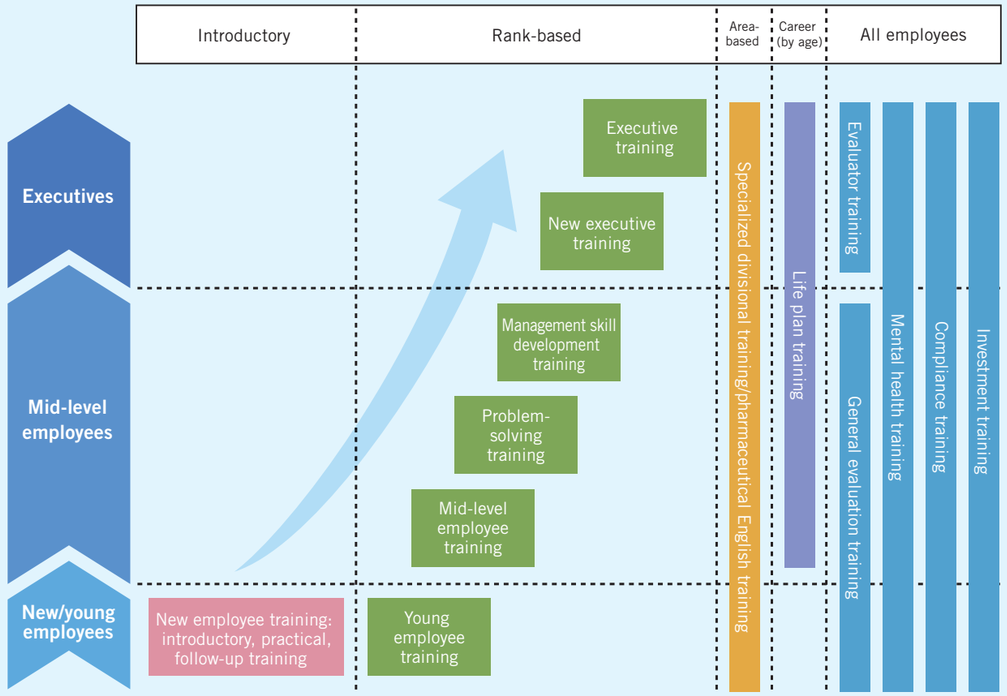
Seikagaku Corporation considers human resources to be an important corporate asset and seeks people who understand and put into practice our core values “creativity,” “fairness,” and "dreams and passion” and are capable of self-growth while fulfilling their roles with a sense of responsibility.

Seikagaku also strives to provide fields for each person to grow and thrive.

We endeavor to cultivate autonomous employees who go about their work with enthusiasm and pride and produce results. We promote upskilling and career development of individuals through a combination of systematic education in various training programs, personnel training in the workplace through day-to-day work, and job rotation.

In addition, to develop the human resources required by each division and department, we conduct age-specific and level-specific training for everyone from rank-and-file employees to executives.

### Training Systems




## Work-life balance

To help its employees achieve a good work-life balance, Seikagaku has introduced flex-time at all of its business sites except for a few production operations and established a weekly “no overtime day” to encourage employees to leave work at the normal finishing time. To help employees balance the demands of their personal lives with their work activities, Seikagaku encourages employees to develop their own workstyles. For example, we are introducing a reduced working hours system to help employees to take care of childcare and nursing care duties, and there is also a system that allows employees to accumulate lapsed annual paid leave for use during prolonged illnesses or to cope with extended childcare and nursing care responsibilities. In the fiscal year ended March 2018, employees used an average of 77.5% of their paid leave.

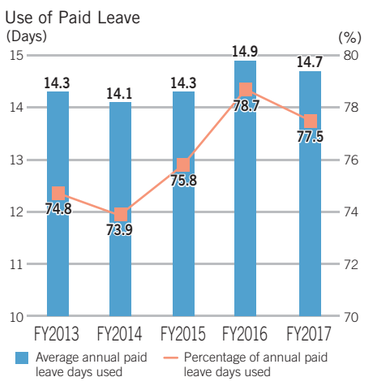
In the period from fiscal 2007 to fiscal 2017, 100% of staff who left work for childcare reasons returned to work. The number of male employees taking childcare leave has also increased in recent years.

Seikagaku will continue to consider systems to meet workstyle needs as part of its efforts to improve working environments.

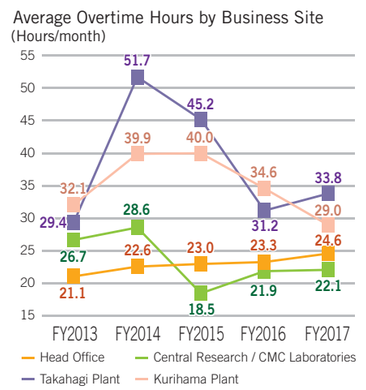
## Career development for female employees

Career development for female employees is an important aspect of diversity management at Seikagaku. Related measures include the creation of environments, systems, and structures that allow female employees to achieve their full potential, and support for career advancement. Specifically, we have set a target of increasing the percentage of executive positions held by women to 10% by the end of March 2019. A variety of initiatives have been implemented since April 2016 under an in-house project led by female employees and the Human Resources Department. Activities include interviews with and surveys of all female employees, a study concerning improvements to internal systems, and workshops and seminars designed to foster a culture of success for female employees. In addition, female employees have been sent to outside executive training programs specifically for women. As of March 31, 2018, 8.9% of executive positions were held by women.

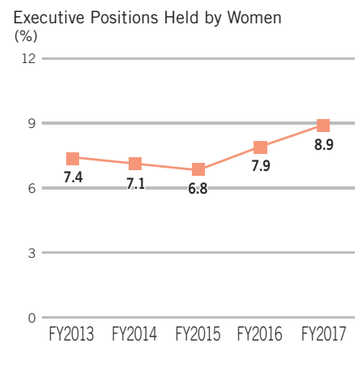
Use of Paid Leave




Average Overtime Hours by Business Site




Executive Positions Held by Women




*The figures provided on this page are all on a non-consolidated basis.

**Topics**

## Participation in J-Win

Seikagaku is helping to promote diversity by sending female employees to participate in the activities of the Japan Women's Innovative Network (J-win), a non-profit organization established to support networking and reciprocal learning among female executives and candidate executives from various companies.

During the year I participated, we ran several projects and implemented problem-solving activities, including lectures by J-Win member presidents, training camps in Japan, and overseas training programs. One of the most stimulating aspects of the activities was the opportunity to discover and discuss issues and find solutions with women working in various industries, and to rethink our ideas based on direct advice from J-Win executives. Repetitions of this process led to accelerating changes in my awareness, and I was able to broaden my horizons and perspectives. I believe that changes in the awareness of individual women are vital to the development of a culture in which women can succeed. I am determined to maintain my sense of mission so that I can inspire others to raise their awareness.

Medical Science Liaison Unit
Miwako Sato

# CORPORATE GOVERNANCE (As of November 7, 2018)

## Members of the Board

President & CEO
Ken Mizutani

Executive Vice President
Toshiyuki Okada

Executive Vice President
Yosuke Funakoshi

Executive Vice President
Takayuki Akita

Outside Member of the Board
Eiji Katayama

Outside Member of the Board
Izumi Hayashi

Audit & Supervisory Board Member
Toru Takeda

Audit & Supervisory Board Member
Shigeru Kawahara

Outside Audit & Supervisory Board Member
Nobuhiro Takeuchi

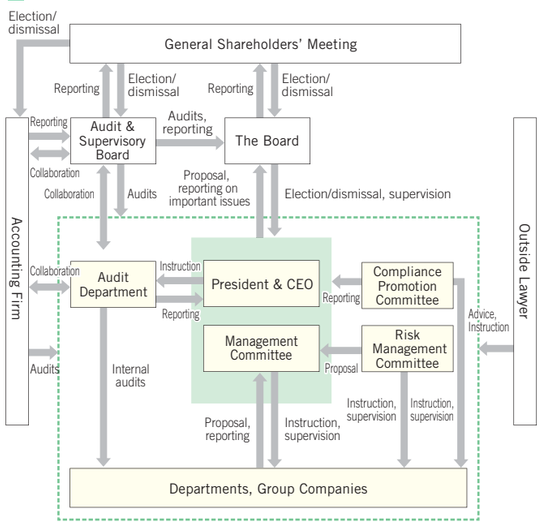
Outside Audit & Supervisory Board Member
Yoshihito Shibata

Outside Audit & Supervisory Board Member
Mie Fujimoto

## Basic policy of corporate governance

Seikagaku Corporation views corporate governance as a core management priority, and endeavors to gather information accurately and adequately, speed up decision-making, and strengthen the supervisory function of business execution. We are profoundly aware of our social mission and responsibilities as a pharmaceutical company, and are committed to always earning the confidence of stakeholders, including our shareholders. In addition to establishing internal control systems, such as for compliance and risk management, we are enhancing our corporate governance through mutual collaboration among departments within the company in order to create a management environment that meets the expectations of society.

## Corporate Governance Structure




## Concrete approach and measures for corporate governance

### The Board

- The Board holds regular monthly meetings to make decisions on tasks stipulated in laws, the Articles of Incorporation and rules for the Board, such as basic management policy, mid-term management plan, annual management plan, and executive functions. The Board decides on important business, and supervises the performance of business operations. If necessary, additional meetings of the Board are convened.
- The term of office for members of the Board is one year with the aim of creating a management structure that would be able to adapt quickly and flexibly to changes in the business environment.
- The Board comprises four full-time and two outside members. We enhance management oversight from an independent standpoint by appointing outside members of the Board to one-third of the Board seats.
- The outside members of the Board are responsible for oversight from an objective standpoint, a perspective that incorporates the common interests of shareholders, and is based on expert knowledge and insights into corporate management. The outside members of the Board also attend meetings held among the President & CEO, Audit & Supervisory Board members, and vice presidents to share views of business issues and the external environment.
- The two outside members of the Board each act as an independent officer under the TSE (Tokyo Stock Exchange) listing rules.
- The documents and supplemental materials on the agenda are generally distributed to the members three days before the date of the Board meetings in order to ensure review time for ample discussions.
- In the procedure for determining compensation for members of the Board and selecting candidates for members of the Board and Audit & Supervisory Board members, President & CEO implement prior explanations and exchange of opinions with the outside members of the Board.
- The Outside Officers meeting, comprising the outside members of the Board and outside Audit & Supervisory Board members, analyzes and evaluates the effectiveness of the Board periodically, and reports the evaluation results to the Board.

### Business operations

- We operate an executive vice president system for enhancing the corporate governance. Under this system, executive functions are separated from the Board, the functions of which are limited to decision-making and the supervision of business operations. We endeavor to build up an internal system, which is quickly able to respond to changes in the management environment, by improving the flexibility and efficiency of executive functions, expanding the executive vice president system, and promoting the transfer of authority.
- We hold weekly meetings of the Management Committee. At the Committee, full-time members of the Board and executive vice presidents confer on and decide the agenda of executive functions they have been tasked with implementing by the Board, based on the basic policy of the Board.
- We have established the Risk Management Committee with the aim of strengthening the internal control framework. The Committee, chaired by the member of the Board in charge of Corporate Strategy, Human Resources, Finance & Accounting and Corporate Staff, comprises primarily members of the Board and executive vice presidents of various functions.

### The Audit & Supervisory Board

- The Audit & Supervisory Board comprises five members, two full-time and three outside members, and each member audits the execution of duties by members of the Board.
- Among the five Audit & Supervisory Board members, one full-time and one outside member have appropriate knowledge of finance and accounting.
- The outside members suitably perform supervision of the execution of duties by members of the Board from a perspective that incorporates the common interests of shareholders, based on expertise of company management and professional knowledge etc.
- The three outside Audit & Supervisory Board members each act as an “independent officer” under the TSE (Tokyo Stock Exchange) listing rules.
- To strengthen the oversight function, Audit & Supervisory Board members attend meetings of the Board, and the full-time members attend important meetings of the Management Committee, Compliance Promotion Committee, Risk Management Committee, and other management bodies and receive reports concerning the status of management and business execution.
- The Audit & Supervisory Board increases audit effectiveness and efficiency by holding regular meetings with the President & CEO, accounting auditor and the Corporate Audit Department and by interviewing members of the Board and executive vice presidents, in charge of divisions.

### Internal audit and accounting audit framework

- Internal audits include audits performed by the Corporate Audit Department. The Corporate Audit Department mainly verifies and ensures the reliability of financial reporting by all departments and subsidiaries. Quality audits and GCP audits are carried out by the Quality Assurance Department and the Regulatory Auditing Unit, respectively.
- We employ Deloitte Touche Tohmatsu LLC as the accounting firm. The firm performs audits on the Company as the need arises, even during a fiscal year, not being limited to the fiscal year closing.
- The certified public accountants responsible for carrying out financial audit duties for Seikagaku are Ms. Keiko Hayashi and Ms. Masumi Nakagawa of Deloitte Touche Tohmatsu LLC. Four certified public accountants and six others assist execution of the financial auditing duties.

### Compliance

- We institute a compliance program, based on the management beliefs and code of conduct outlined in the corporate principles, in order to act as a socially ethical company and achieve compliance with the stringent regulations that surround the pharmaceutical industry. The Seikagaku Compliance Program Handbook is compiled and distributed to increase the awareness and understanding of employees.
- The Compliance Promotion Committee is chaired by the President & CEO and shares the same members as the Management Committee. There are also various programs to promote compliance on a company-wide basis.
- We control subsidiaries adequately by stipulating the rules for regularly reporting important events, such as compliance and risk status, in addition to financial condition, ensuring adequate and efficient operation of subsidiaries.
- We ensure that management decisions and daily business execution are in compliance with laws and regulations by receiving advice and instructions from outside lawyers.

## Coordination between Audit & Supervisory Board members, accounting auditors, and internal audits

The Audit & Supervisory Board members and the Corporate Audit Department met 17 times during fiscal 2017 to review audit results related to internal controls at each internal division, and share information and views on the audit plan and the status of audits conducted by the Corporate Audit Department. We also aim to reach a mutual understanding through spontaneous communications.

Regarding the state of coordination between the Audit & Supervisory Board members and the accounting auditors, information exchange was provided for on 12 occasions during the fiscal year, and the year's plan for the auditing firm and the results of the financial audit were received at a hearing where views on these matters were also exchanged.

Coordination between the Corporate Audit Department and the accounting auditors took place at one meeting held during the fiscal year. At this event, information was shared and views exchanged on the audit plans and audit procedures concerning internal controls for ensuring the reliability of the Company's financial reporting.

In addition, through attendance and participation at important meetings including those of the Management Committee, the Compliance Promotion Committee, and the Risk Management Committee, the full-time Audit and Supervisory Board members coordinate with the Corporate Audit Department and the financial auditors to ensure that the framework for internal controls is an appropriate one.

## Outside members of the Board and outside Audit & Supervisory Board members

### Number of outside members of the Board and outside Audit & Supervisory Board members

- The Company has two outside members of the Board and three outside Audit & Supervisory Board members for a total of five names reported as independent officers as specified by the Tokyo Stock Exchange.

### Interests including those having a personal relationship, capital relationship, or transactional or other business relationship with the company

- The Company has established a compensation system linked to the company's stock price as a source of funds for a certain amount of officer compensation. The system consists of continual monthly purchases of company stock through an officers' shareholding association.
- Concerning relationships between our company and another company in which the same person serves, or has served, as an outside member of the Board or an outside Audit & Supervisory Board member, there are no interests that would be affected by a personal relationship, a capital relationship (except for the holding of our company stock through a compensation system linked to the stock price), a business relationship, or performance of other work duties.

### Functions and roles carried out in corporate governance

- Using insights from specialized expertise and corporate management, the outside members of the Board supervise business execution and contribute to the enhancement of the corporate governance system by offering advice and suggestions from an objective standpoint, including a viewpoint of shared profits with shareholders.
- Using insights from specialized expertise and corporate management, the outside Audit & Supervisory Board members fulfill their supervisory function with respect to the performance of duties by members of the Board by asking questions from the members' respective specialized viewpoints and offering advice and suggestions, as needed, at Board meetings from an objective standpoint, including a viewpoint of shared profits with shareholders.

### Standards and guidelines of appointment with respect to the independence from the company for the appointment, and approach concerning appointment status

- The Company stipulates that in order to fulfill the criteria for independence, an outside officer must not fall under any of the following:

A. A person who executes business of the Company and its group companies (the "Group").
B. A party who provides the Group with products or services whose transactions with the Group accounted for at least 2% of their consolidated net sales in the most recent fiscal year, or a person who executes business thereof.
C. A party to whom the Group provides products or services whose transactions with the Group accounted for at least 2% of the Company's consolidated net sales in the most recent fiscal year, or a person who executes business thereof.
D. A consultant, an accounting expert, or a legal expert who received ¥10 million or more of monetary consideration or other property from the Group in the most recent fiscal year (or if the entity receiving such property is an organization, such as a corporation or an association, a person belonging to such entity which received at least 2% of its total annual income from the Group).
E. A party who received donations of ¥10 million or more from the Group in the most recent fiscal year, or a person who executes business thereof.
F. A shareholder who held at least 10% of the total voting rights of the Company at the end of the most recent fiscal year, or a person who executes business thereof.
G. A person who fell under any of the above criteria (A) to (F) within the past three years.
H. A relative who is within the second degree of kinship or who is living together with a person falling under any of items (A) to (G) above.
I. A party who is deemed to have any other significant interest in the Group, or a person who executes business thereof.

- From the candidates for outside member of the Board, we select well-qualified persons who apply insight from specialized expertise and corporate management and who can exercise appropriate supervision of business execution from an objective standpoint, including a viewpoint of shared profits with shareholders. From the candidates for outside Audit & Supervisory Board member, we select well-qualified persons who apply insight from specialized expertise and corporate management and who can exercise appropriate supervision of the Board's performance of duties from an objective standpoint, including a viewpoint of shared profits with shareholders.
- Because they fulfill the standards of independence for outside officers set by the Company and the standards of independent officers set by the Tokyo Stock Exchange, we believe that the outside members of the Board and the outside Audit & Supervisory Board members hold sufficient independence from the management that executes the Company's business.

### Mutual coordination with supervision and auditing for internal audits, audits by the Audit & Supervisory Board, and accounting audits and relationship between the internal control department

- Because they share recognition of the Company's business challenges and an appreciation of its external environment, the outside members of the Board hold meetings with the President & CEO, the Audit & Supervisory Board, and individual department heads.

  In addition, along with sharing information with the full-time Audit & Supervisory Board members, the outside Audit & Supervisory Board members strive to improve the supervisory function by holding meetings with the President & CEO, the outside members of the Board, and individual department heads, and others and by coordinating with the Corporate Audit Department and the accounting auditors.

## Officers' compensation

### Details of the policy and the method of determination for the amount of officer compensation and the decision process for the method of determination

#### a. Policy for determining the amount of officer compensation

The Company has set a basic policy on officer compensation that raises incentives for officers to act in alignment with the expectations of shareholders and which facilitates persistent earnings improvement.

In the determination of compensation, consideration is given to balancing compensation with social standards, business operation, and employees' pay. While compensation is basically set as fixed-amount compensation, for members of the Board other than the outside members of the Board, the Company has introduced an earnings-linked compensation system in which a portion of the compensation is calculated as the product of the previous fiscal year's net income and a coefficient for the grade of officer. In addition, all officers contribute a set amount from their compensation in accordance with their officer grade to make continual monthly purchases of company stock through the officers' shareholding association. As a rule, the shares acquired shall be held during the officer's term of office. In this way, creating a linkage between a portion of compensation for all officers and the stock price strengthens the linkage between compensation and shareholder profits and establishes a compensation system that helps clarify management responsibility with respect to earnings and raises corporate value.

The 60th Ordinary General Shareholders' Meeting held on June 23, 2006, resolved that the Company shall dissolve the officers' retirement benefit plan.

#### b. Method for determining the amount of officer compensation

Officer compensation for members of the Board is set at the Board meeting, and compensation for Audit & Supervisory Board members is set by consultation with the Audit & Supervisory Board. The amount of this compensation is determined in accordance with the basic policies laid out in "a." above and set within the limits of the respective total compensation as determined by a general shareholders' meeting. Also, in order to enable suitable contribution and advice from the independent outside members of the Board, the motion is explained and views are exchanged before a meeting of the Board at which compensation is deliberated. As a result of these activities, sufficient review is provided at the Board meeting before the resolution is approved.

## Total amount of compensation for each category of officer, total amount by type of compensation, and the number of relevant officers (fiscal year ended March 2018)

| Officer category | Total compensation (Millions of yen) | Total by type of compensation (Millions of yen) | | Number of officers |
|---|---|---|---|---|
| | | Basic compensation | Other | |
| Members of the Board (excluding outside officers) | 216 | 216 | — | 5 |
| Audit & Supervisory Board members (excluding outside officers) | 45 | 45 | — | 3 |
| Outside officers | 47 | 47 | — | 5 |
| Total | 309 | 309 | — | 13 |

Notes:
1. Based on the status at the time of adjournment of the 71st Ordinary General Shareholders' Meeting held on June 20, 2017, one retired member of the Board and one retired Audit & Supervisory Board member are included in the table above.
2. The amount of pay for a member of the Board does not include the employee portion of salary of someone who is concurrently an employee and a member of the Board.
3. The total amount of compensation paid to all members of the Board was resolved at the 61st Ordinary General Shareholders' Meeting held on June 22, 2007, to be no more than ¥400 million per year (of which the outside Board member proportion shall be no more than ¥50 million per year).
4. The total amount of compensation paid to all Audit & Supervisory Board members was resolved at the 61st Ordinary General Shareholders' Meeting held on June 22, 2007, to be no more than ¥80 million per year.

## Main activities of the outside members of the Board and the outside Audit & Supervisory Board members (fiscal year ended March 2018)

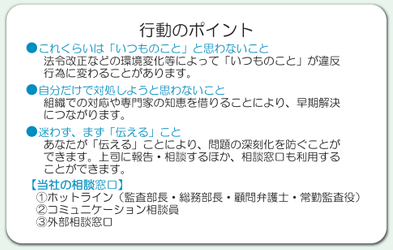
| Officer category | Last/First name | Independent officer | Board meetings | Audit & Supervisory Board meetings |
|---|---|---|---|---|
| Outside member of the Board | Eiji Katayama | ○ | Attended 13 of 13 meetings | — |
| | Izumi Hayashi | ○ | Attended 13 of 13 meetings | — |
| Outside Audit & Supervisory Board members | Nobuhiro Takeuchi | ○ | Attended 13 of 13 meetings | Attended 14 of 14 meetings |
| | Yoshihito Shibata | ○ | Attended 13 of 13 meetings | Attended 14 of 14 meetings |
| | Mie Fujimoto | ○ | Attended 13 of 13 meetings | Attended 14 of 14 meetings |

## Compliance promotion activities

In order to ensure a strong sense of ethics across all of its corporate activities, Seikagaku Corporation strives as a pharmaceuticals company, not simply to comply with relevant laws and regulations, but also "to regulate its own conduct in accordance with a moral understanding (proper thinking on what human beings ought to do intrinsically) and to have the courage to rectify the misdeeds of others," positioning sincere and fair conduct this as a basis of all activities.

To embody these principles, we have established a Compliance Program that, among other things, has promulgated a Code of Conduct for the Group. In addition, in order for the program to proceed better in an appropriate manner and without obstruction, we have established a Compliance Promotion Committee and develop an annual action plan. Through these actions, we promote greater compliance awareness on an all-company scale and increase its effectiveness.

We have also distributed to all employees and publicized a Compliance Program Handbook that describes the contents of this program and a Compliance Card that summarizes the key points of conduct.



Compliance Card

In the fiscal year ended March 2018, we established a policy of "promoting an understanding of the revisions to related laws and regulations and ensuring deep and thorough awareness of compliance." To this end, we have carried out awareness activities centered on training and e-learning.

In addition, so that employees' compliance consultations can be handled anonymously, we have established multiple consultation liaisons, including outside lawyers, and have put in place a system for the rapid discovery and prompt resolution of problems. There were four consultations in fiscal 2017, and all received an appropriate response.



# SOCIAL CONTRIBUTION ACTIVITIES

**Seikagaku pursues respect for learning by engaging in global research assistance and sponsoring activities that support the development of glycoscience.**

## Glycoforum, a website for comprehensive information on glycoscience research

http://www.glycoforum.gr.jp/indexJ.html

Since 1997, Seikagaku has operated "Glycoforum," an academic website that shares information about research findings to contribute the development of glycoscience, which is one of Seikagaku's areas of specialization.

As a portal site for glycoscience information, the website promptly disseminates science paper information, including commentary from global leading researchers and academic conference information. The site enjoys strong support from researchers in Japan and overseas, and was selected as one of the recommended websites by the worldwide scientific journal *Nature Reviews*.

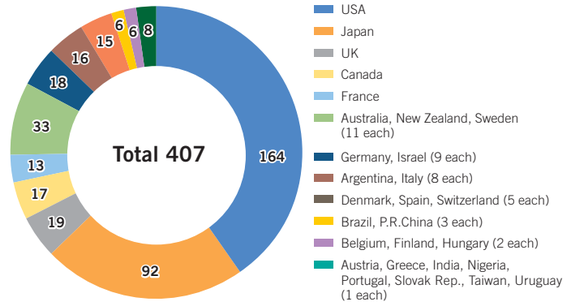

## Support for the Mizutani Foundation for Glycoscience

http://www.mizutanifdn.or.jp/indexj.html

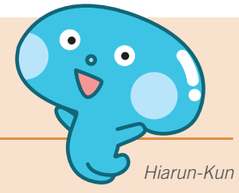
The Mizutani Foundation for Glycoscience was established in 1992 with an endowment from the late Masakane Mizutani, former president of Seikagaku Corporation, for the purpose of contributing to the welfare of humanity through the advancement and development of glycoscience. The Foundation provides research grants to glycoscience researchers in Japan and overseas and supports conferences. In fiscal 2018, the Foundation provided research grants totaling approximately ¥75.6 million to 20 grant recipients.

Seikagaku endorses the purpose of the Foundation and has continuously supported its activities since its founding.

**Number of Grant Recipients by the Mizutani Foundation for Glycoscience** (By country and area: 1993–2018)




## Promoting early treatment of knee osteoarthritis *Hiza Ikiiki* (Sprightly Knees), a website for provision of information concerning knee osteoarthritis to the general public


*Hiarun-Kun*

https://www.ehiza.jp

Some 30 million patients* in Japan are said to suffer from knee osteoarthritis, a disorder marked by knee joint strain due to aging, excessive exercise, or weight increase causing the cartilage gradually wear away. The *Hiza Ikiiki* website explains basic knowledge concerning knee osteoarthritis, diagnosis, and treatment methods in an easy to understand way and gives information on nearby medical institutions that operate outpatient clinics and provide treatment for knee pain. Visitors can also download a pamphlet "Exercise therapy of knee osteoarthritis."

We will provide correct knowledge to people with knee pain and further enhance website content to enable greater numbers to promptly obtain appropriate treatment.


*Locomotive Disorder Countermeasures to Promote Preventive Care," a report from the Ministry of Health, Labour, and Welfare" issued in 2008

# BUSINESS RISKS

The following are the principle risks that could have a material effect on the operating results and the financial situation of the Seikagaku Corporation.

## Legal restrictions

Most of the Seikagaku Group's products affect people's lives and health and, consequently, are subject to legal restrictions for ensuring the quality, efficacy, and safety of pharmaceuticals and other products imposed by regulatory authorities in each country. Actions taken by regulatory authorities, such as amendments to these related laws and regulations, could affect our business results.

## Time and expense required for new product development

In pharmaceutical product development, the core of Seikagaku's business, various clinical trials to confirm efficacy and safety are required from the time of basic research to new drug approval. Even if the Company bears enormous Research and Development (R&D) expenses over long periods of time, there is risk that products under development will not progress to launch. R&D expenses vary according to R&D progress, and this could affect our business results.

## Revisions to the National Health Insurance Drug Price Standard to contain medical costs

The National Health Insurance Drug Price Standard in Japan, which establishes drug prices at the time of payment from medical insurance to health insurance medical care institutions and health insurance pharmacies, is periodically revised. Also, with the aim of reducing medical costs, the use of inexpensive generics is promoted, and additional price reductions are implemented for long-listed drugs (original drugs with generic equivalents). Similarly, overseas, the use of generics is being promoted, and price reductions are implemented as medical cost reduction measures. These trends could affect our business results.

## Reliance on specific distributors

We have entered into exclusive distributorship agreements with sales partners for the pharmaceuticals and medical devices that are our mainstay products, which limits the number of distributors. In Japan, we have entered into exclusive distributorship agreements with Kaken Pharmaceutical Co., Ltd. for the joint function improving agents ARTZ and ARTZ Dispo and with Santen Pharmaceutical Co., Ltd. for OPEGAN, OPEGAN Hi, and SHELLGAN. Overseas, we have entered into exclusive agreements that cover specific countries or regions for distributorship of our products. Changes to the business relationships with these companies due to changes in circumstances, depending on the nature of the changes, could affect our business results.

## Reliance on specific products

Joint function improving agents and ophthalmic viscoelastic devices account for more than 90% of the net sales of the pharmaceuticals business in Japan and overseas markets in the fiscal year ended March 31, 2018. Consequently, any unforeseen material side effects or other events that have a material effect on the manufacturing and sale of these mainstay products could affect our business results.

## Reliance on specific suppliers

Various restrictions apply to the manufacture of pharmaceuticals, and some raw materials require the approval of regulatory authorities. Therefore, the number of raw materials suppliers is limited, and we perform on-site audits and strive to maintain quality in order to establish a stable supply system. We rely on singlesupply sources for certain raw materials. Consequently, any change in circumstances that makes it difficult to procure raw materials could disrupt the manufacture of products and affect our business results.

## Use of animal-derived ingredients as raw materials

Many of the Seikagaku Group's products are made using ingredients derived from animals, namely chickens, sharks, and horseshoe crabs, as raw materials. Consequently, any restrictions on the use of animal-derived ingredients as raw materials or difficulty in procuring these ingredients could affect our business results.

## Exchange rate fluctuations

Revenues from sales of intra-articular injection agents for the treatment of knee osteoarthritis in the U.S. and the sales of U.S. consolidated subsidiary Associates of Cape Cod Inc. are denominated in U.S. dollars. Although we endeavor to reduce exchange risks by denominating a portion of R&D expense payments in foreign currencies and other means, recently the overseas sales ratio has been increasing. Consequently, exchange rate trends could affect our business results.

## Price fluctuations of holdings of marketable securities

We invest cash reserves in marketable securities for the purpose of applying them to future R&D and capital expenditures. Although we endeavor to reduce risks through diversification of investments and other means, price fluctuations of marketable securities and other investments could affect our business results.

## Litigation

Initiation of litigation relating to pharmaceutical side effects, product liability, patents or other intellectual rights, labor problems, depending on the details, could affect our business results.

## Occurrence of large-scale disasters

Any stagnation of business activities or disruption of product supply as a result of extensive damage to the Seikagaku Group's business sites due to an earthquake, a typhoon or other natural disaster, fire or other accident, or an epidemic of a new influenza virus or other infectious disease could affect our business results. Also, any major expenses for the repair of facilities damaged in a disaster could affect our business results.

## Status of development and operation of risk management regulations and systems

### Regulations and other systems related to the management of risk of losses

- We have established business risk management regulations and developed a system to ascertain and manage risks pertaining to business execution.
- The divisions engage in risk management pertaining to their respective operations.
- We have established the Risk Management Committee, chaired by the chief risk management officer (the member of the Board in charge of Corporate Strategy, Human Resources, Finance and Accounting, and Corporate Staff) and comprising the executive vice presidents in charge of various departments. The Committee deliberates risk prevention measures and, when a material business risk event occurs, establishes a response headquarters and takes measures to minimize damage.

### Status of operation of risk management systems

The Risk Management Committee met twice in the fiscal year ended March 31, 2018 and deliberated major issues such as strengthening of the confidential information management system, confirmed the status of progress with groupwide risk prevention measures, and sought to prevent risk events from occurring.

In addition, we strove to reduce risks relating to our business by conducting simulation drills in accordance with accident procedure manuals for the purpose of increasing the effectiveness of the rapid business recovery response, developing regulations on an inspection system and handling of electronic data for the purpose of preventing information leakage, and amending regulations relating to appropriate disposal of documents whose retention deadlines have passed.

# FINANCIAL / NON-FINANCIAL HIGHLIGHTS

## Basic Policy on profit distributions

The improvement of shareholder value is an important management priority. Our goal is to enhance shareholder returns while achieving sustainable growth through balanced business investment, including investment in R&D and the improvement of production structures.

Our policy on shareholder returns is to maintain dividend stability from a medium- to long-term perspective by continuing to pay an annual dividend of ¥26 per share. We will also continue to consider share buy-back schemes, while giving due consideration to future business development and the overall payout ratio.

In the year ended March 2018, we set the final dividend at ¥13 per share. Together with the interim dividend of ¥13 per share, this resulted in an annual dividend of ¥26 per share for the year ended March 31, 2018, equivalent to a payout ratio of 37.5%.

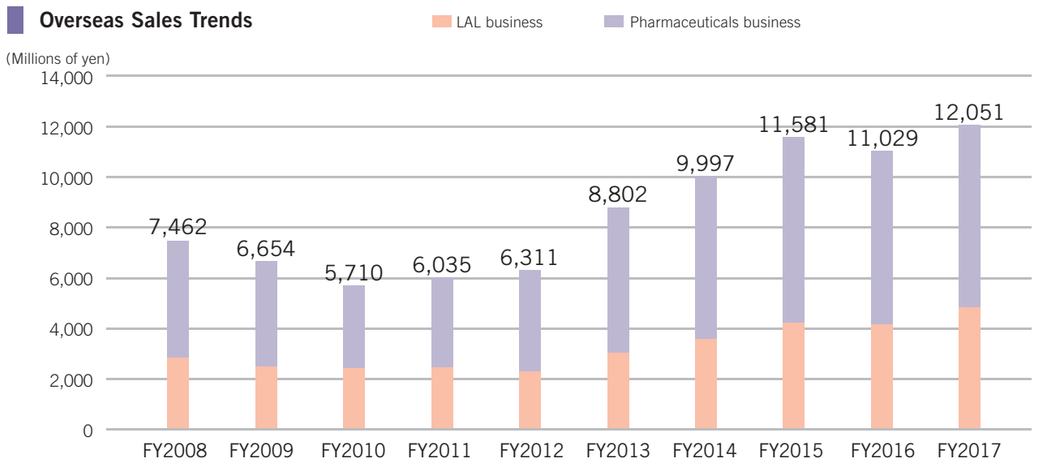
### Consolidated Business Performance

(Millions of yen)

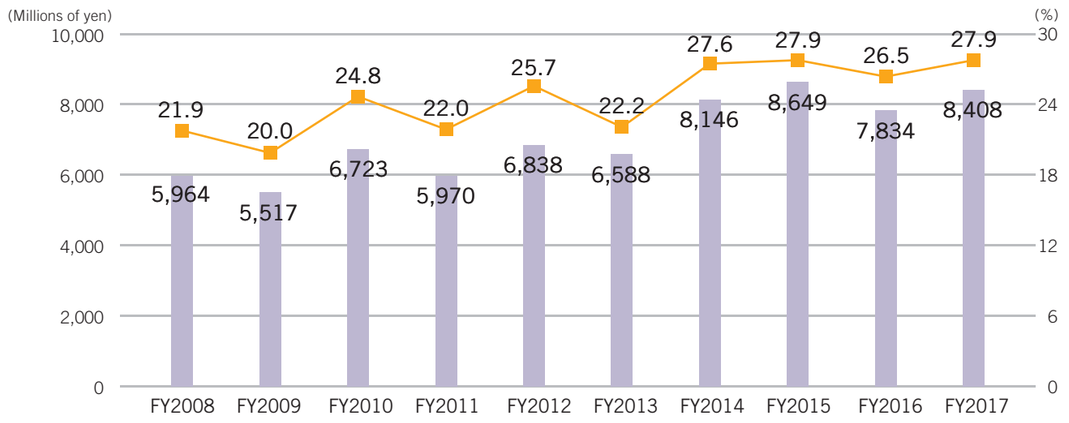
| | FY2013 | FY2014 | FY2015 | FY2016 | FY2017 |
|---|---|---|---|---|---|
| Net Sales | 29,614 | 29,522 | 30,962 | 29,589 | 30,175 |
| Overseas Sales | 8,802 | 9,997 | 11,581 | 11,029 | 12,051 |
| Overseas Sales Ratio (%) | 29.7 | 33.9 | 37.4 | 37.3 | 39.9 |
| Cost of Sales | 11,223 | 12,130 | 12,871 | 13,247 | 13,008 |
| Gross Profits | 18,390 | 17,391 | 18,091 | 16,341 | 17,166 |
| R&D Expenses | 6,588 | 8,146 | 8,649 | 7,834 | 8,408 |
| Operating Income | 4,937 | 2,383 | 2,144 | 1,282 | 1,421 |
| Operating Income Ratio (%) | 16.7 | 8.1 | 6.9 | 4.3 | 4.7 |
| Ordinary Income | 5,878 | 4,008 | 3,500 | 2,477 | 5,327 |
| Net Income | 4,745 | 3,650 | 2,578 | 1,787 | 3,922 |
| Net Income Ratio (%) | 16.0 | 12.4 | 8.3 | 6.0 | 13.0 |
| Total Equity | 64,785 | 70,410 | 69,815 | 70,646 | 73,945 |
| Return on Equity (ROE) (%)※1 | 7.5 | 5.4 | 3.7 | 2.5 | 5.4 |
| Total Assets | 73,826 | 80,889 | 80,218 | 80,048 | 84,749 |
| Return on Assets (ROA) (%)※1 | 8.1 | 5.2 | 4.3 | 3.1 | 6.5 |
| Dividend Payout Ratio (%) | 31.1 | 40.5 | 57.3 | 98.3 | 37.5 |
| Net Income per Share (yen) | 83.55 | 64.27 | 45.39 | 31.55 | 69.30 |
| Total Equity per Share (yen) | 1,140.48 | 1,239.51 | 1,229.05 | 1,248.07 | 1,306.37 |
| Dividends per Share (yen) | 26.00 | 26.00 | 26.00 | 31.00※2 | 26.00 |
| Number of Employees (persons) | 639 | 649 | 663 | 687 | 718 |

※1 Total Equity and Total Assets are average amounts of the numbers for the end of previous fiscal year and the end of current fiscal year, respectively.
※2 Including a 70th anniversary commemorative dividend of 5 yen per share.

### Overseas Sales Trends

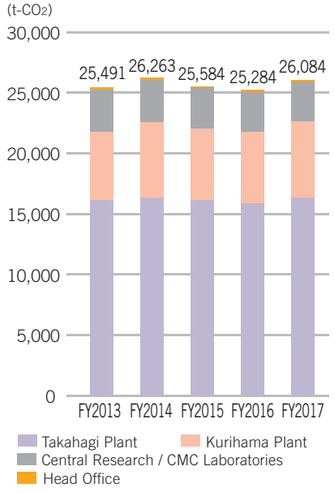



### R&D Expense Trends

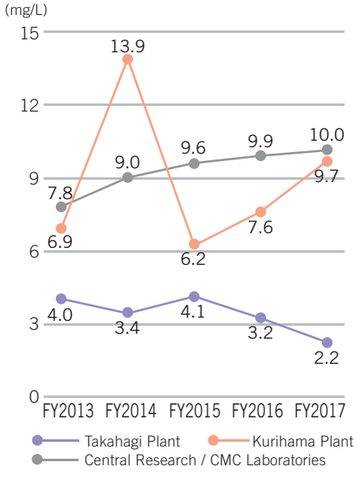



### Non-financial Highlights (Non-consolidated Basis)

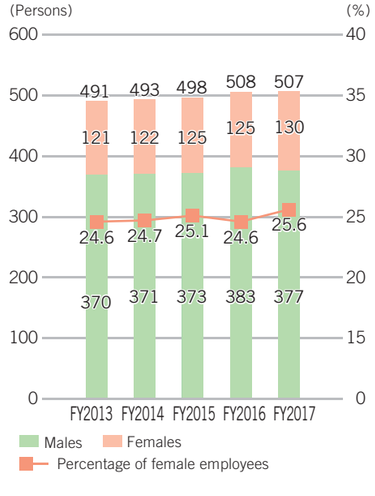
#### $CO_2$ Emissions




#### Water Pollution Load (COD)




#### Composition of Work Force



# CORPORATE DATA

## Overview (As of March 31, 2018)

| | |
|---|---|
| Company Name | SEIKAGAKU CORPORATION |
| President | Ken Mizutani |
| Establishment | June 2, 1947 |
| Business Activities | Manufacturing and sales of pharmaceuticals and medical devices specifically related to glycoconjugates |
| Stock Exchange Listing | Tokyo Stock Exchange, First section (Stock code:4548) |
| URL | http://www.seikagaku.co.jp |
| Number of Employees | 718 (Consolidated) |
| Paid-in Capital | ¥3,840 million |
| Net Sales | ¥30,175 million |

## Members of the Board (As of June 20, 2018)

| | |
|---|---|
| President & CEO | Ken Mizutani |
| Executive Vice President | Toshiyuki Okada |
| Executive Vice President | Yosuke Funakoshi |
| Executive Vice President | Takayuki Akita |
| Outside Member of the Board | Eiji Katayama |
| Outside Member of the Board | Izumi Hayashi |
| Audit & Supervisory Board Member | Toru Takeda |
| Audit & Supervisory Board Member | Shigeru Kawahara |
| Outside Audit & Supervisory Board Member | Nobuhiro Takeuchi |
| Outside Audit & Supervisory Board Member | Yoshihito Shibata |
| Outside Audit & Supervisory Board Member | Mie Fujimoto |
| Executive Vice President | Aisuke Nii |
| Executive Vice President | Mikako Torii |
| Executive Vice President | Yuji Shimojima |

## Locations

| | |
|---|---|
| Head Office | Marunouchi Center Building<br>6-1, Marunouchi 1-chome, Chiyoda-ku<br>Tokyo 100-0005, Japan<br>Tel: (81) 3-5220-8950 |
| Central Research Laboratory · CMC Laboratory | 1253, Tateno 3-chome, Higashiyamato-shi<br>Tokyo 207-0021, Japan<br>Tel: (81) 42-563-5811 |
| Kurihama Plant | 3-1, Kurihama 9-chome, Yokosuka-shi<br>Kanagawa 239-0831, Japan<br>Tel: (81) 46-835-3311 |
| Takahagi Plant | 258-5, Aza-Matsukubo, Oaza-Akahama<br>Takahagi-shi, Ibaraki 318-0001, Japan<br>Tel: (81) 293-23-1181 |

## Major Subsidiary

ASSOCIATES OF CAPE COD, INC.

124 Bernard E. Saint Jean Drive, East Falmouth
MA 02536-4445 U.S.A.
Tel: (1) 508-540-3444

| | |
|---|---|
| Paid-in Capital | $2,080 |
| Ownership Ratio | 100% |
| Business | Manufacturing and sales of endotoxin-detecting reagents |
| URL | http://www.acciusa.com |



# STOCK INFORMATION

## Stock Information (As of March 31, 2018)

| | |
|---|---|
| Authorized Shares | 234,000,000 |
| Authorized Outstanding Shares | 56,814,093 |
| Number of Shareholders | 9,792 |

## Shareholder Registry Administrator

Mitsubishi UFJ Trust and Banking Corporation

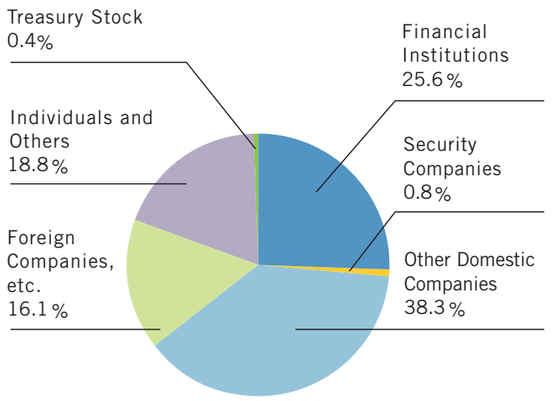
《Contact》
Mitsubishi UFJ Trust and Banking Corporation
Securities Agency Division
PO Box 29,New Tokyo Post Office,Tokyo 137-8081
Tel: 0120-232-711(Domestic toll-free)

## Major Shareholders (As of March 31, 2018)

| | Name of Shareholders | Number of Shares Held (Thousands of Shares) | Percentage of Outstanding Shares (%) |
|---|---|---|---|
| 1 | Shingyo KK | 7,843 | 13.9 |
| 2 | KK Kaiseisha | 7,293 | 12.9 |
| 3 | The Master Trust Bank of Japan, Ltd. (Trust account) | 2,737 | 4.8 |
| 4 | Trust & Custody Services Bank, Ltd. as Trustee for Mizuho Bank, Ltd. Retirement Benefit Trust Account re-entrusted by Mizuho Trust and Banking Co, Ltd. | 1,973 | 3.5 |
| 5 | Japan Trustee Services Bank, Ltd. (Trust account 9) | 1,919 | 3.4 |
| 6 | MUFG Bank, Ltd. | 1,536 | 2.7 |
| 7 | Japan Trustee Services Bank, Ltd. (Trust account) | 1,242 | 2.2 |
| 8 | Kaken Pharmaceutical Co., Ltd. | 1,207 | 2.1 |
| 9 | State Street Bank and Trust Company 505001 | 1,067 | 1.9 |
| 10 | The Bank of New York Mellon (International) Limited 131800 | 1,066 | 1.9 |

※Treasury stock (209 thousand shares) is excluded from the calculations of the percentage above.

## Breakdown of Shareholders by Type (As of March 31, 2018)




## Corporate Logo

The main motif of Seikagaku's corporate logo is a chain, which symbolizes our decades-long commitment to sugar chain R&D. The closely interlocked links represents the strong bonds that exist between science and industry, between people and people, and between a rich natural environment and an enriching life. The links also symbolize Seikagaku's emphasis on partnership with society.

The overall shape of the logo as an oval stretched toward the upper right represents Seikagaku's corporate stance of aiming for infinite growth.

The blue brand color in the corporate logo symbolizes creativity and innovation, while the black projects an impression of strength.

**SEIKAGAKU CORPORATION**

Marunouchi Center Building
6-1, Marunouchi 1-chome, Chiyoda-ku
Tokyo 100-0005, Japan
TEL: (81)3-5220-8950
FAX: (81)3-5220-8951
URL: http://www.seikagaku.co.jp

2019.3(150)
Printed in Japan