Exploring the Innovative Promise of Glycoscience

Seikagaku Corporation is a pharmaceutical manufacturer with a history of more than 70 years. As a pioneer in glycoscience, a research field with enormous hidden potential in drug discovery, we create innovative pharmaceuticals and medical devices.

Seikagaku contributes to the health, well-being, and improved quality of life for patients around the world in order to create a prosperous future.

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 control 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.

<Reference> It has been found that highly metastatic cancer cells feature an increased amount of giant sugar chains, which are much less prevalent in normal cells.

Our Strengths

Source of Competitiveness

Seikagaku Corporation has developed a unique business model based on specialization in R&D and manufacturing. We contribute to medical care globally by developing and supplying high-quality pharmaceuticals and medical devices that leverage our unique technological capabilities.

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 40%* of our employees are involved in R&D.

*Non-consolidated base

PHILOSOPHY

CORE VALUES

<MOTTO>

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.

Inspiration Behind Our Motto

Creativity

Individual and corporate creativity are important for scientific advancement aimed at pursuit of truth. We can produce novel new products, new technologies, and new use of products by developing and applying unique and creative approaches, thus we can expect to achieve sound and stable corporate growth as a result of these efforts.

Fairness

We will adhere to principles of fairness that are recognized worldwide, and through self-discipline, will ensure we remain a company that is respected by society at large. Our “Creativity” and our “Dreams and Passion” must be built on a foundation of “Fairness.”

Dreams and Passion

We have high ambition, and strive to achieve our dreams by working toward our ideals. This is the ultimate source of growth for our employees and our company.

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≪ Editorial Policy ≫

The Seikagaku Corporate Report 2022 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 2021 (April 1, 2021–March 31, 2022), but it also includes references to activities in fiscal 2022.

OUR HISTORY

Success Based on Steady Pursuit of a Unique Vision

As indicated by the company name, Seikagaku Corporation focuses on research in the field of biochemistry (seikagaku in Japanese). The history of Seikagaku Corporation is a story of growth in step with the development and progress of glycoscience.

Major Product Timeline

1950

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

1960

Start of manufacture and sales of glucide-related research reagents developed in-house

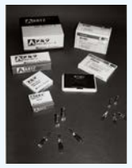
*The research reagent business was terminated in 2012

1981

Start of manufacture and sales of world's first endotoxin colorimetry reagents

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



*The joint function improving agent ARTZ® delisted from the NHI drug price standard on March 31, 2022

1992

Launch of ARTZ®, a joint function improving agent, in Sweden under the name "Artzal®," making the start of full-scale overseas marketing of joint function improving agents

1993

Launch of ARTZ Dispo®, a joint function improving agent

1995

Launch of OPEGAN Hi® (now Sodium Hyaluronate 0.4 Ophthalmic Viscoelastic Preparation 1% SEIKAGAKU), an ophthalmic viscoelastic device

2001

Launch of SUPARTZ®, a joint function improving agent, in the U.S. (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

2019

Launch of HyLink®, an intra-articular single-injection viscosupplement for the treatment of knee osteoarthritis in Italy

2021

Launch of JOYCLU®, a joint function improving agent

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~

Product diversification leveraging cutting-edge glycoscience technology. Toward a new stage.

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

1997

Seikagaku Corporation acquires Associates of Cape Cod, Inc. (U.S.A.), a manufacturer and seller of endotoxin-detecting reagents, etc.

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)

2020

Seikagaku acquires CDMO* business operator Dalton Chemical Laboratories, Inc. (Canada)

*CDMO: Contract Development and Manufacturing Organization
A business that supplies comprehensive services in drug development and manufacturing to pharmaceutical companies, including contract drug manufacturing, pharmaceutical formulation planning at the development stage, manufacturing of investigational drugs, and optimization of manufacturing conditions

2022

SEIKAGAKU NORTH AMERICA CORPORATION is established in Canada to manage pharmaceutical and medical device development in North America

Moved to the Tokyo Stock Market, Prime Market

BUSINESS ACTIVITIES AND PRODUCTS

Seikagaku has two business segments. In the Pharmaceuticals business, we offer a range of original products that leverage technologies and knowledge cultivated over many years as a glycoscience pioneer. In the LAL business, we offer endotoxin-detecting reagents and other products.

LAL Business

Seikagaku engages in the LAL business, manufacturing and selling endotoxin-detecting reagents used in quality control of pharmaceutical and medical device manufacturing processes as well as a beta-glucan-detecting in vitro reagent for the diagnosis of deep fungal infections.

What are endotoxins?

Endotoxins are one of the major components of the outer membrane of gram-negative bacteria and exhibit strong pyrogenic activity even in minute amounts. Since serious side effects can be triggered by endotoxin contamination of injectable pharmaceuticals, biological products, or medical devices, they must be rigorously controlled, especially in directly administered injectable treatments.

What are glucans?

(1→3)-β-D-glucans are structural components of the cell walls of fungi, as typified by molds and yeasts. Measurement of the glucan concentration in blood is widely used in auxiliary diagnosis of deep fungal infections and judgment of the therapeutic effect of antifungal agents.

Endotoxin-detecting reagents and devices

■ ENDOSPECY®, TOXICOLOR®, PYROCHROME®, etc.

Endotoxin-detecting reagents are reagents that measure endotoxins. Made from limulus amebocyte lysate (LAL), a substance extracted from the blood cells of horseshoe crabs, these reagents are used in quality control of injectable pharmaceuticals, biological products, and medical device manufacturing processes and water quality control of dialysate used in artificial dialysis.

Endotoxin-detecting reagents

■ PyroSmart NextGen™

PyroSmart NextGen is an endotoxin-detecting reagent manufactured using genetic recombination technology without the use of blood harvested from horseshoe crabs. Seikagaku has successfully developed the world's first product consisting of recombinant proteins of Factor C, Factor B, and a coagulating enzyme precursor, which are components of horseshoe crab blood cells. Developed together with overseas subsidiary Associates of Cape Cod, Inc., PyroSmart NextGen was launched in Europe and the U.S. in April 2021 and introduced in Japan in May of the same year.

■ 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

Beta-glucan-detecting in vitro reagent

■ Fungitell®

Fungitell is an in vitro diagnostic reagent used in the selection of treatment methods for deep fungal infections and judgment of therapeutic effect. Fungitell was developed by Seikagaku Corporation as the first product of its kind in the world and it is manufactured and sold in markets outside Japan by Associates of Cape Cod, Inc.

Pharmaceuticals Business

The Pharmaceuticals business is Seikagaku Corporation's core business. Seikagaku manufactures and provides pharmaceuticals and medical devices made with GAG, as well as enzymes that act on GAG. GAG stands for glycosaminoglycans such as hyaluronic acid or chondroitin sulfate, the main ingredients in Seikagaku products. GAG is also a structural component of glycoconjugates. Seikagaku contributes to medical care in Japan and around the world by providing global-class high-quality products with its unique technologies.

Joint Function Improving Agents

■ ARTZ Dispo®, SUPARTZ FX®, VISCO-3®

ARTZ Dispo, a prefilled syringe product*1, is a multiple-injection version of ARTZ*2, a joint function improving agent containing hyaluronic acid as its main active pharmaceutical ingredient. When administered directly into the joint cavity, ARTZ Dispo is expected to reduce pain and inflammation. It has been approved and is supplied not only in Japan, but also in overseas markets, including the U.S., Asia, and Europe.

*1 A kit with an injectable syringe that has to be filled with solution.
*2 Delisted from the NHI drug price standard on March 31, 2022.

ARTZ Dispo®

SUPARTZ FX®

■ JOYCLU®

JOYCLU, a formulation in which hyaluronic acid and diclofenac (an anti-inflammatory drug) are chemically bound, is a joint function improving agent launched in May 2021. Improvement of symptoms of osteoarthritis of the knee joint and hip joint is expected from the administration of JOYCLU into the joint cavity once every four weeks. JOYCLU is the first joint function improvement agent in Japan indicated for the treatment of osteoarthritis of the hip joint.

JOYCLU®

■ Gel-One®, HyLink®

Gel-One is an intra-articular single-injection viscosupplement for the treatment of knee osteoarthritis, which contains cross-linked hyaluronate hydrogel as its main ingredient, originally developed for the U.S. market. Administration of only 3mL provides long-lasting benefits. In March 2019, Seikagaku launched this product in Italy with its brand name "HyLink." Seikagaku is expanding the sales of this unique product with multi-branding strategy. It was launched in Taiwan in August 2021.

Gel-One®

Treatment for Lumbar Disc Herniation

■ HERNICORE®

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

HERNICORE®

Ophthalmic Viscoelastic Devices (OVD)

■ OPEGAN®, SHELLGAN®, Sodium Hyaluronate 0.4 Ophthalmic Viscoelastic Preparation 1% SEIKAGAKU

The OPEGAN series of products allows the creation of appropriate intraocular space by viscoelastic properties of hyaluronic acid 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.

MucoUp®

Bulk Products

■ Sodium hyaluronate, sodium chondroitin sulfate

Based on our unique extraction and purification technology, we manufacture and sell high-quality, high-purity hyaluronic acid and chondroitin sulfate, which are mainly raw materials for pharmaceuticals and cosmetics.

Bulk products

CDMO

■ CDMO services (contract development and manufacturing)

Seikagaku provides services to pharmaceutical companies, including manufacturing of chemical synthetics and pharmaceutical products on a contract basis and manufacturing process development. Seikagaku entered this business by acquiring Dalton Chemical Laboratories, Inc. as a subsidiary in March 2020.

PRESIDENT'S MESSAGE

Our aim is to achieve record-high business results during the term of the new mid-term management plan, which we have positioned as "A period for achieving growth."

President & CEO *Ken Mizutani*

Summary of the previous mid-term management plan

Under the previous mid-term management plan, Seikagaku positioned the three-year period beginning with the fiscal year ended March 31, 2020 (fiscal 2019) as a time for solidifying the profit foundation so as to return Seikagaku to a growth trajectory, and we implemented three important measures: 1) Accelerating new drug discovery to become the pillar of new profits, 2) Solidifying the profit foundation through market expansion of new products, and 3) Productivity improvement reforms.

Although blindsided by the COVID-19 pandemic and other unforeseen crises, and negatively affected by the resulting market stagnation in Japan and overseas, delays in R&D activities, and other consequences of the pandemic, Seikagaku was able to achieve certain positive results with respect to the three measures, notably progress with development pipelines; the launch of new products in Japan, the U.S., and other markets; and profit model diversification through the acquisition and consolidation as a subsidiary of Dalton Chemical Laboratories, Inc. of Canada.

Seikagaku also achieved all of the numerical targets in the plan and believes that during the three-year plan period the Group successfully laid a foundation for the next mid-term management plan.

New mid-term management plan (fiscal 2022–fiscal 2025)

We expect the business environment to remain uncertain due to rapid changes in the pharmaceutical industry, such as National Health Insurance drug price reductions in Japan, healthcare system changes in overseas markets, the increasing sophistication of new drug development, rising development costs, and innovations in medical technologies. Also, fulfillment of social responsibilities, starting with sustainability promotion, is increasingly important for the sustainable development of society and enhancement of corporate value, and responding to this societal trend is a matter of urgent importance.

In this business environment, Seikagaku has formulated a new mid-term management plan, positioning the four-year period beginning with the fiscal year ended March 31, 2023 (fiscal 2022) as "A period for achieving growth." By implementing key measures set out in the plan on the basis of a profit foundation solidified during the period of the previous management plan, Seikagaku will aim to maintain a constant growth trajectory and achieve record-high business results in the final year of the plan.

Seikagaku Corporation Group will work to achieve further enhancement of corporate value by implementing five key measures set out In the new mid-term management plan: 1) Accelerate R&D utilizing unique drug-discovery technologies, 2) Maximize the product value of SI-6603 (treatment for lumbar disc herniation), 3) Maintain and enhance the business value of joint function improving agents, 4) Construct a global production system, and 5) Expand the LAL business through recombinant technologies.

R&D is the source of growth for pharmaceutical companies, and Seikagaku is no exception. We focus on R&D as an important pillar of the business to be prioritized in preparation for future business development. Two key points of the management plan are steady advancement of existing pipelines, notably SI-6603, a treatment for lumbar disc herniation, and maximization of product value. In parallel with this effort to create next-generation products, we will actively revise the existing business structure, carrying out cost structure improvement targeting mainstay joint function improving agents and reinforcing our stable supply structure by constructing a global supply system. Gathering and providing safety information on the joint function improving agent JOYCLU remains a high priority, and we will seek to contribute to appropriate prescription on the basis of clinical research findings.

We expect to achieve record-high business results by implementing these key measures, as reflected in the numerical targets for net sales and operating income for fiscal 2025 in the management plan.

We consider enhancement of employee engagement along with organizational strengthening and human resource development to be the critical factors for carrying out these key measures. We introduced a new HR system in October 2022, erecting a framework for cultivating and fostering the growth of our human talent, which forms the nucleus of the business. We will continue to implement measures to enhance employee engagement and work to strengthen and improve the foundation for achieving sustained growth.
(For details, please refer to the section "Mid-term Management Plan FY2022 to FY2025" beginning on Page 17.)

Sustainability initiatives

Seikagaku considers the pursuit of sustainability to be an important priority. We have identified six material issues that should be addressed on a priority basis in the interest of achieving sustainable development of society and enhancement of corporate value. By continuing to focus on these material issues, which will become the foundation for the key measures in the mid-term management plan, we will strengthen development of medical-related businesses as well as ESG (Environment, Social, Government) initiatives, and aim to contribute to solving social issues through close communication with supply chain partners and stakeholders.
(For details, please refer to the section "Sustainability Progress" beginning on Page 32.)

Forecast of financial results for fiscal 2022

The forecast of financial results for fiscal 2022 anticipates a sales decrease to result from a decline in royalty income from a high prior-year level coupled with strong impact from an NHI drug price decrease in Japan, which will offset a volume increase for pharmaceuticals in Japan and strong performance from pharmaceuticals overseas fueled by a strong yen.

We forecast a decrease in operating income to result from higher expenses at overseas subsidiaries, including foreign currency translation, despite a projected decrease in R&D expenses accompanying completion of subject enrollment in an additional clinical study underway in the U.S. for SI-6603, a treatment for lumbar disc herniation. Ordinary income and net income attributable to owners of parent are expected to decline less steeply than operating income because of expected foreign exchange gains related to valuation of foreign currency-denominated assets.

Summary of the forecast of financial results for fiscal 2022

(Millions of yen)

	Forecast for Fiscal 2022	Fiscal 2021 Results	Change	% of Change
Net Sales	33,500	34,851	-1,351	-3.9%
Operating Income	1,700	4,495	-2,795	-62.2%
Ordinary Income	2,900	5,395	-2,495	-46.2%
Net Income	2,650	3,733	-1,083	-29.0%
R&D Expenses (Overseas sales ratio excluding royalty income)	8,000 (23.9%)	9,005 (29.2%)	-1,005 (-5.3pt)	-11.2%

To our shareholders and other stakeholders

The entire Seikagaku Corporation Group will implement the key measures set out in the newly formulated mid-term management plan in order to nurture the capability to maintain a growth trajectory and will work to achieve the targets in the plan. It is Seikagaku's mission to contribute to the health and well-being of people around the world through the wider provision on a global scale of new pharmaceuticals that patients truly need, and in so doing, we aim to enhance our value to society as a pharmaceutical company.

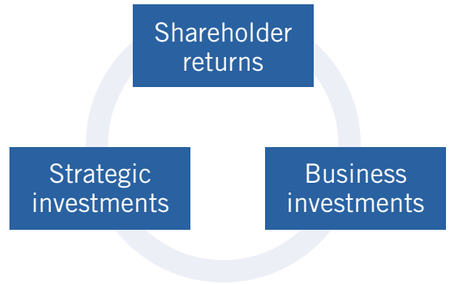
We will also strive to strengthen corporate governance on the basis of high ethical standards by rigorously practicing honest corporate activities and ensuring management transparency.

We request the continued understanding and support of our shareholders and other stakeholders in the coming years.

Basic policy on profit distribution

Seikagaku believes that sustained profit growth and enhancement of corporate value contribute to the common interests of the shareholders. Management regards the return of profits to shareholders as an important priority and, while taking an annual dividend of ¥26 per share as the basis, will consider dividend increases, taking into account the trend in business performance, the financial position, and other factors. Also, while taking into consideration future business expansion and the total return ratio, Seikagaku will consider the purchase of treasury stock when appropriate.

In addition, in order to solidify the business foundation and improve capital efficiency, the Company will make efficient and active business investments in R&D for creating new value, in production system development, and in sustainable activities and will flexibly make strategic investments offering prospects for future growth and synergy effects.



Shareholder returns	• Consider dividend increases, while taking an annual dividend of ¥26 per share as the basis, taking into account business performance and other factors. • Consider the purchase of treasury stock when appropriate.
Business investments	• Continue efficient investments in R&D and production. • Make active business investments in sustainable activities.
Strategic investments	• Flexibly consider strategic investments with prospects for future growth and synergy effects.

	Forecast for Fiscal 2022	Fiscal 2021 Results
2nd Quarter	¥13.00	¥15.00 (including a special dividend of ¥5.00)
Fiscal Year-end	¥13.00	¥15.00 (including a special dividend of ¥5.00)
Annual Total Dividend	¥26.00	¥30.00 (including a special dividend of ¥10.00)
Dividend Payout Ratio	54.0%	45.2%

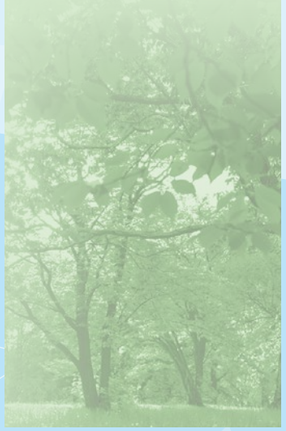
VALUE CREATION

Innovating Novel Contributions and Approaches

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 and the external environment

- Response to unmet needs
- Increased incidence of locomotive syndrome
- Super-aging society
- Increased healthcare access
- Declining probability of success in new drug development
- Protracted new drug development periods and soaring costs
- Contraction of the Japanese market, expansion of the global market
- Aggravation of environmental problems, environmental consideration (ESG), environmental conservation initiatives



Forms of capital advantageous for R&D and domestic and international alliances

Financial capital
- A stable financial base that provides the source of funds for continuous new drug creation

Manufacturing capital
- Manufacturing and quality management systems for the stable provision of high-quality pharmaceuticals

Intellectual capital
- Accumulated glycoscience-related chemical compound library
- Drug creation capabilities focused on target substances and high-priority target diseases

Human capital
- People capable of creating new value by applying a high level of expertise in a challenge-driven corporate culture

Social capital
- Relationships of trust with stakeholders for realization of a sustainable society

Natural capital
- Low-environmental-impact business activities as a life sciences company
- Corporate management that gives consideration to biodiversity

An original business model of specializing in R&D and manufacturing

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

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

Mid-term Management Plan

Ⅰ Accelerate R&D utilizing unique drug-discovery technologies

Ⅱ Maximize the product value of SI-6603 (treatment for lumbar disc herniation)

Ⅲ Maintain and enhance the business value of joint function improving agents

Ⅳ Construct a global production system

Ⅴ Expand the LAL business through recombinant technologies

P17

Output

Provision of innovative, high-quality pharmaceuticals and medical devices, etc.
- Ethical pharmaceuticals, medical devices
- Bulk product
- CDMO services (contract development and manufacturing)
- LAL-related products

P07

Business flow

R&D P23 → Production P31 → Marketing (through sales partners) P29

Quality compliance P28

Material Issues

1. Creation of truly useful pharmaceuticals and medical devices
2. Provision of a stable supply of pharmaceuticals and medical devices of guaranteed quality
3. Expansion of healthcare access and appropriate provision of high-quality medical information
4. Fair and ethical business activities and strengthening of corporate governance
5. Promotion of diversity and development of human resources
6. Engagement in environment-friendly corporate activities

Creation of economic value and social value

Medical institutions and patients
- Contribution to QOL improvement
- Creation of truly useful pharmaceuticals
- Provision of a stable supply of pharmaceuticals and other products of guaranteed quality

Shareholders
- Stable shareholder returns provided through sustained growth
- Fair information provision
- Enhancement of shareholder value

Employees
- Provision of growth opportunities
- Provision of an environment, systems, programs, and mechanisms to enable all employees to fully demonstrate their capabilities

Society
- Contribution to realization of a sustainable society
- Further development and refinement of glycoscience research technologies

Resolution of social issues and actualization of the management philosophy

Glycoscience for Human Well-being

SIX MATERIAL ISSUES

Seikagaku Corporation has identified six material issues on the basis of assessment of important issues that should be addressed on a priority basis in the interest of achieving sustainable development of society and enhancement of corporate value, in light of both their importance to the company and the expectations of society, including diverse stakeholders. By promoting initiatives related to these material issues, Seikagaku will contribute to achievement of the Sustainable Development Goals (SDGs) adopted by the United Nations.

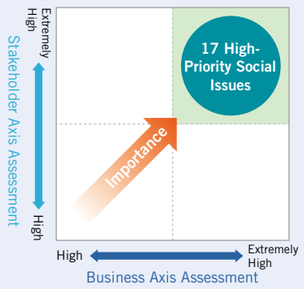
Material Issue Identification Process

Step 1 Identification and organization of social issues

To identify material issues, we identified social issues based on factors including non-financial information disclosure guidelines; international frameworks, principles, and guidelines; and survey items from ESG assessment organizations. Furthermore, we closely examined issues specific to the pharmaceutical industry. On that basis, we compiled a list of 39 social issues.

Step 2 Prioritization of social issues

Using the list of 39 social issues identified in Step 1, we assessed the importance of issues to Seikagaku in light of its Corporate Philosophy, management strategies, and financial situation. Also, an external consultant scored, analyzed, and organized the issues from an outside perspective to assess the expectations of society, including diverse stakeholders. Based on the results of this assessment process, we prepared a social issues assessment matrix and shortlisted 17 high-priority social issues of importance to both Seikagaku and society.



Step 3 Identification of material issues through validation and grouping of issues

To validate the social issues assessment matrix prepared in Step 2, following discussion and careful examination of the matrix together with involved Seikagaku divisions and departments and an external consultant, the Board performed grouping of the 17 high-priority social issues and identified six material issues relevant to Seikagaku. The Board articulated reasons for selection and a future vision and determined objectives, initiatives, and monitoring indicators for each identified material issue and organized and confirmed their relevance to SDGs. The material issues were then deliberated and approved by the Board.

SUSTAINABLE DEVELOPMENT GOALS

Material Issues	Future Vision
1 Creation of truly useful pharmaceuticals and medical devices	Seikagaku increases its value to society by utilizing knowledge of glycoscience to continuously create pharmaceuticals and medical devices that are truly needed by society, and contribute to the health and well-being of people around the world. Seikagaku also considers intellectual property to be an important management resource and implements a global intellectual property strategy to contribute to the continuous creation of pharmaceuticals and medical devices. R&D P23
2 Provision of a stable supply of pharmaceuticals and medical devices of guaranteed quality	Seikagaku strengthens its compliance and production systems to ensure uninterrupted access to reliable pharmaceuticals and medical devices for patients and medical institutions. Also, we manage risks associated with raw materials procurement and other business processes and take all possible measures to prevent risks from materializing. Quality compliance P28 Production P31
3 Expansion of healthcare access and appropriate provision of high-quality medical information	Seikagaku promotes global distribution of pharmaceuticals and medical devices that address medical needs and, as a pharmaceutical manufacturer, strives to enhance information provision in order to achieve appropriate awareness of the safety and efficacy of our pharmaceuticals and medical devices and of diseases related to our products. Marketing P29
4 Fair and ethical business activities and strengthening of corporate governance	Seikagaku engages in business management to ensure that each employee not only complies with laws and regulations, but also behaves on the basis of high ethical standards. Seikagaku also continuously works to develop a highly effective corporate governance system. Corporate governance P41 Compliance and risk management P51
5 Promotion of diversity and development of human resources	Seikagaku considers human resources to be an important corporate asset and works to develop people capable of creating new value. We develop an environment, systems, programs, and mechanisms to enable all employees to fully demonstrate their capabilities so that the contributions and successes of diverse employees are the driver of Seikagaku's sustained growth. Human Resources P39
6 Engagement in environmentally friendly corporate activities	As a member of society, Seikagaku aims to achieve balance between environmental protection measures and business growth and engages in business activities with low environmental impact in addition to obeying environment-related laws and regulations. Environmental impact reduction initiatives P34 Initiatives for biodiversity P37

Mid-term Management Plan FY2022 to FY2025

Seikagaku has positioned the four-year period beginning with the fiscal year ended March 31, 2023 (fiscal 2022) as “A period for achieving growth” and formulated a new mid-term management plan. By implementing key measures set out in the plan on the basis of a profit foundation solidified during the period of the previous management plan, Seikagaku will aim to maintain a constant growth trajectory and achieve record-high business results in the final year of the plan.

Summary of Previous Mid-term Management Plan

Seikagaku was able to achieve positive results with respect to important measures set out in the management plan and solidified the foundation for returning to a growth trajectory by achieving the numerical targets in the plan.

Ⅰ Accelerating new drug discovery to become the pillar of new profits

- Joint function improving agent JOYCLU launched
- SI-722 (treatment for interstitial cystitis) and SI-449 (adhesion barrier) advanced to the next stage of development
- Enrollment for SI-6603 (treatment for lumbar disc herniation) completed
- SEIKAGAKU NORTH AMERICA CORPORATION established

Ⅱ Solidifying the profit foundation through market expansion of new products

- HyLink (intra-articular single-injection viscosupplement for the treatment of knee osteoarthritis) launched in Taiwan
- Alliance agreement concerning SI-613 concluded with Eisai (China, South Korea)
- PyroSmart NextGen Recombinant LAL Reagent launched

Ⅲ Productivity improvement reforms

- DALTON CHEMICAL LABORATORIES, INC. made a subsidiary
- Business continuity system developed in response to the impact of COVID-19
- Progress with review of procurement costs and sales-related expenses

Numerical Targets

	FY2021 results*1	FY2021 target	Percentage achievement
Net sales	¥31.2 billion	¥28.3 billion	+10.5%
Ordinary income	¥5.39 billion	¥4.5 billion	+19.9%
SKK EBITDA*2	¥5.54 billion	¥5.0 billion	+10.9%
Overseas sales ratio (excluding royalty income)	56.6%	50.0%	+6.6pt

*1 Converted to previous presentation categories
*2 SKK EBITDA: A profit indicator that adds depreciation and royalty income to operating income

Overview of Key Measures

We expect the business environment to remain uncertain due to rapid changes in the pharmaceutical industry, such as National Health Insurance drug price reductions in Japan, healthcare system changes in overseas markets, the increasingly sophisticated demands of new drug development, rising development costs, and innovations in medical technologies. Also, fulfillment of social responsibilities, starting with sustainability promotion, is increasingly important for the sustainable development of society and enhancement of corporate value, and responding to this societal trend is a matter of urgent importance. (Information on sustainability initiatives is available in the section beginning on page 32.)

In this business environment, Seikagaku will implement the five key measures in the management plan to develop the ability to maintain a constant growth trajectory.

In addition, enhancement of employee engagement along with organizational strengthening and human resource development will be critical factors for carrying out the above five key measures. Seikagaku will work to solidify and improve the foundation for achieving sustained growth by stepping up investment to create an environment that promotes development and growth of human resources, the heart and soul of the Group’s businesses.

Ⅰ	Ⅱ	Ⅲ	Ⅳ	Ⅴ
Accelerate R&D utilizing unique drug-discovery technologies	Maximize the product value of SI-6603 (treatment for lumbar disc herniation)	Maintain and enhance the business value of joint function improving agents	Construct a global production system	Expand the LAL business through recombinant technologies
P19	P20	P20	P21	P21

Business foundation

Enhancement of employee engagement/
Organizational strengthening and human resource development

Numerical Targets

Seikagaku aims to achieve record-high business results in fiscal 2025, the final year of the management plan.

	FY2021 results	FY2025 target
Net sales	¥34.8 billion	¥40.0 billion
Operating income	¥4.4 billion	¥7.0 billion

<Assumptions>

- U.S. market introduction of SI-6603 (treatment for lumbar disc herniation)
- Profit expansion from joint function improving agents in Japan
- Expansion of the overseas pharmaceutical and LAL business
- Ratio of R&D expenses to sales (excluding royalty income): target of 25%
- Exchange rate: ¥135/US$1

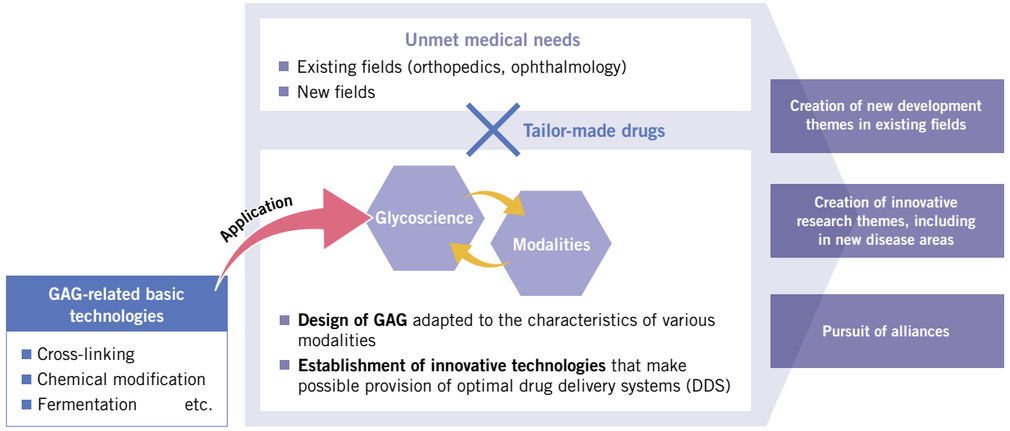
Summary of the Key Measures

Ⅰ Accelerate R&D Utilizing Unique Drug-Discovery Technologies

Create products that patients need utilizing Seikagaku's own GAG-related technologies and aim for steady advancement of the pipeline list.

Apply Seikagaku's own GAG*-related basic technologies to create new drugs that patients truly need, with an emphasis on unmet medical needs, by focusing on creation of new development themes in existing fields and creation of innovative research themes, including in new disease areas. Also, to increase the probability of success of these efforts, pursue various alliances aimed at making early progress.

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



Pipeline List (Research and Development themes)

Advance existing pipelines with the aim of obtaining approval and introducing in the U.S. SI-6603 (a treatment for lumbar disc herniation), completing a Phase III clinical study in the U.S. of SI-614 (a treatment for dry eye), and obtaining approval in Japan and initiating a clinical study in the U.S. of SI-449 (an adhesion barrier).

[Pharmaceuticals]

(As of September 30, 2022)

Development code/Product name		Indication	Developed in	Phase I	Phase II	Phase III	Application	Market approval
SI-6603	Condoliase	Lumbar Disk Herniation	USA					
SI-614	Modified Hyaluronate	Dry eye	USA					
SI-613	Diclofenac etalhyaluronate sodium	Knee Osteoarthritis	USA					
SI-613-ETP	Diclofenac etalhyaluronate sodium	Enthesopathy	Japan		Phase I/II b (Discontinued (February 2022))			
SI-722	Steroid compound sodium chondroitin sulfate	Interstitial cystitis and bladder pain syndrome	USA		Phase I/II			

[Medical Devices]

Development code/Product name		Product name	Developed in	Pilot study	Pivotal study	Application	Market approval
SI-449	Cross-linked Chondroitin Sulfate	Adhesion Barrier	Japan				
SI-449	Cross-linked Chondroitin Sulfate	Adhesion Barrier	USA				

➡ Planned progress as of the end of fiscal 2025

Ⅱ Maximize the Product Value of SI-6603 (treatment for lumbar disc herniation)

Aim for an NDA, approval, and market introduction during the period of the mid-term management plan.

Take maximum advantage of SEIKAGAKU NORTH AMERICA CORPORATION, established in Canada for the purpose of obtaining approval in the U.S. and launching SI-6603, a treatment for lumbar disc herniation, to ensure a prompt and accurate NDA and response to regulatory review. Also proceed with sales preparations and pursue maximization of product value through early penetration at medical institutions in close cooperation with the sales partner. (For information on the development status and characteristics of SI-6603, please refer to the section "Research and Development" beginning on page 23.)

<Steps leading up to market introduction>

Follow-up observation period (1 year) → NDA preparations → NDA → Approval obtained → Market approval

March 2022 Subject enrollment for a Phase III additional clinical study in the U.S. completed

- Cooperation with SNA in prompt and accurate NDA and response to regulatory review to obtain approval
- Timely, close communication with the regulatory authorities

- Sales preparations in cooperation with the sales partner
- Construction of a stable supply system

Ⅲ Maintain and Enhance the Business Value of Joint Function Improving Agents

Seek to enhance business value through maximization of Seikagaku products in the market for joint function improving agents and cost structure improvement.

Strive to maintain and enhance the business potential of the core products that support business management by increasing the presence of Seikagaku products in the mainstay domestic market for joint function improving agents. Since the domestic pharmaceuticals business is greatly affected by NHI drug price reductions, cost structure improvement is essential. Seikagaku will further proceed with product material specification changes, which help ensure continuity of product supply, manufacturing process efficiency improvement, and other measures. Seikagaku will also continue gathering and providing safety information on the joint function improving agent JOYCLU with the aim of contributing to appropriate prescription on the basis of clinical research findings.

Maximization of Seikagaku products in the market for joint function improving agents

ARTZ
- Share expansion through switching from competing products

JOYCLU
- Conduct of clinical research to identify the cause of shock and anaphylaxis
- Continuation of information provision to ensure appropriate treatment and measures

Cost structure improvement
- Packaging material specification change
- Manufacturing process efficiency improvement

Maintenance and enhancement of business value that supports business management

Ⅳ Construct a Global Production System

Undertake construction of a global production system with Japan and North America as dual production bases, including transfer of production of some products.

Further reinforce a stable supply of products on the basis of an appropriate and efficient production system by making Dalton Chemical Laboratories, Inc. (Toronto, Canada) and the Seikagaku Takahagi Plant (Ibaraki Prefecture, Japan) dual production bases.

Seikagaku Corporation Takahagi Plant
(Ibaraki Prefecture, Japan)

▶ Please refer to “Overview of Production Sites” on page 31.

DALTON CHEMICAL LABORATORIES, INC.
(Toronto, Canada)

▶ Please refer to “Overseas Subsidiaries” on page 58.

Ⅴ Expand the LAL Business Through Recombinant Technologies

Accomplish a transformation necessary from a long-term perspective in addition to continuation of current businesses and product improvement.

Further reinforce a stable supply of products on the basis of an appropriate and efficient production system by making Dalton Chemical Laboratories, Inc. (Toronto, Canada) and the Seikagaku Takahagi Plant (Ibaraki Prefecture, Japan) dual production bases, including transfer of production of some products.

▶ Please refer to “Overseas Subsidiaries” on page 58.

For details on the mid-term management plan:

https://www.seikagaku.co.jp/en/ir/management/midtermplan.html

Endotoxin-detecting reagent
PyroSmart NextGen®

Business Progress

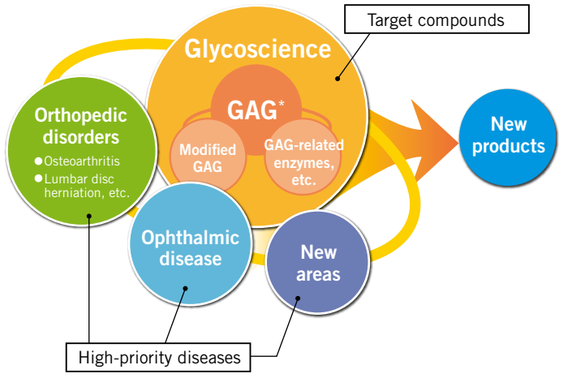
Research and Development

Seikagaku engages in research and development of innovative drugs in our specialty field of glycoscience. And we contribute to the health and well-being 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, where we have expertise through the development of such products as ARTZ Dispo joint function improving agent and OPEGAN ophthalmic viscoelastic device.



*GAG: Glycosaminoglycans
(One of the constituents of complex carbohydrates)

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 continue to focus on drug discovery for orthopedic disorders and ophthalmic diseases and have also begun utilizing GAG-related technology to expand new fields. At the same time, we make efforts to maximize the value of our products on the market or themes in development through expansion of indications, additional formulations, changes in dosage and administration, etc.

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 designing GAG for various modalities—not only low-molecular compounds, but also so-called middle molecules, such as peptides and nucleic acids, and high polymers, such as proteins—and providing Seikagaku's own DDS.

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.

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.

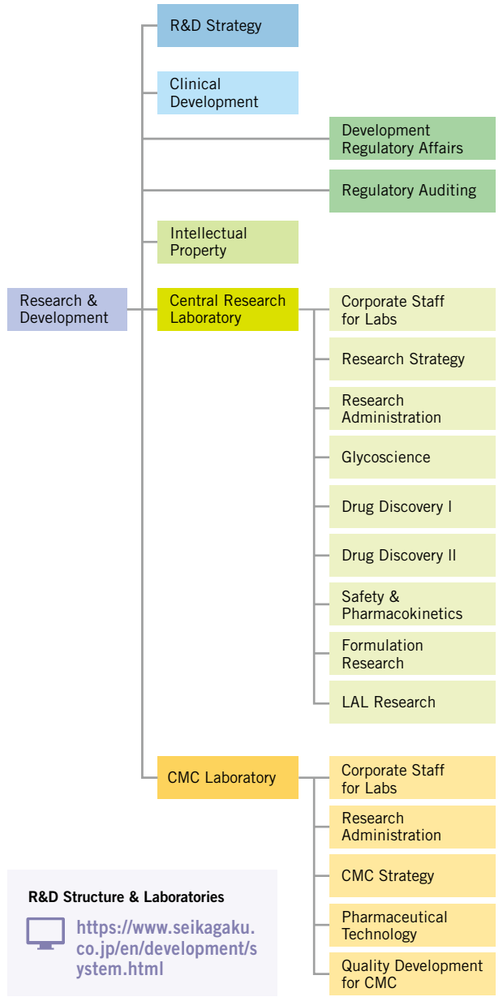
A Phase I clinical study, the initial phase, is ordinarily conducted for the main purpose of examining the pharmacokinetics (absorption, distribution, metabolism, and excretion) and safety (adverse events and side effects) of investigational drugs in a small number of healthy subjects.

A Phase II clinical study examines efficacy, safety, and pharmacokinetics and confirms optimal dosage and usage in a small number of patients.

A 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.

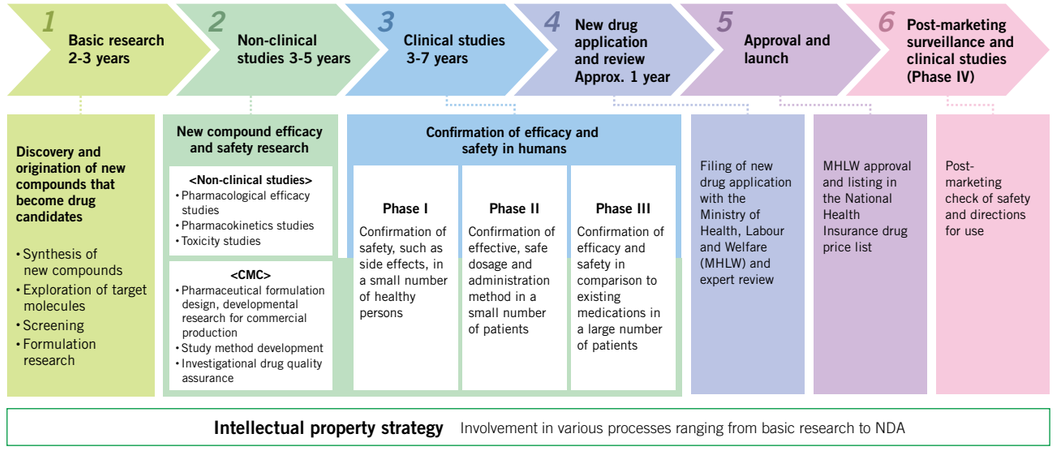
Ordinarily, more than ten years is required from discovery of a candidate substance until its approval as a new drug. Within the long, difficult new drug development process, clinical development is considered to hold the key to whether an NDA can be filed.

[Research & Development Division Structure]
(As of April 1, 2021)



R&D Structure & Laboratories
https://www.seikagaku.co.jp/en/development/system.html

[The Drug Research and Development Process]



Research and Development

Development Pipeline

[Pharmaceuticals]

(As of September 30, 2022)

Development code/Product name		Indication	Developed in	Phase I	Phase II	Phase III	Application	Market approval
SI-6603	Condoliase	Lumbar Disk Herniation	USA			●		
SI-614	Modified Hyaluronate	Dry eye	USA			●		
SI-613	Diclofenac etalhyaluronate sodium	Knee Osteoarthritis	USA		●			
SI-613-ETP	Diclofenac etalhyaluronate sodium	Enthesopathy	Japan		Phase IIb (Discontinued (February 2022))			
SI-722	Steroid compound sodium chondroitin sulfate	Interstitial cystitis and bladder pain syndrome	USA		Phase I/II			

[Medical Devices]

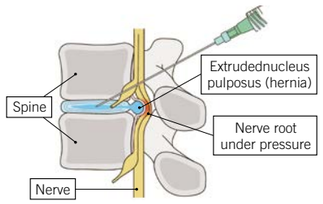
Development code/Product name		Indication	Developed in	Pilot study	Pivotal study	Application	Market approval
SI-449	Cross-linked Chondroitin Sulfate	Adhesion Barrier	Japan		●		

SI-6603 (treatment for lumbar disc herniation)

SI-6603, which contains condoliase as its active pharmaceutical ingredient, is a treatment for lumbar disc herniation directly injected into the intervertebral disc. It has the special characteristic of not requiring general anesthesia and being less invasive to patients than surgical treatment. Since a single injection is expected to improve the symptoms of lumbar disc herniation by reducing intervertebral disc pressure and relieving pressure on the nerve root, SI-6603 can contribute to improving patients' quality of life as a new treatment option.

In Japan, marketing approval was obtained from the Ministry of Health, Labour and Welfare in March 2018, and SI-6603 was launched on August 1, 2018 as HERNICORE 1.25 units for intradiscal injection.

Subject enrollment for an additional Phase III clinical study being conducted in the U.S. since February 2018 was completed in March 2022. Following a one-year observation period, Seikagaku plans to analyze the results and prepare for an NDA.

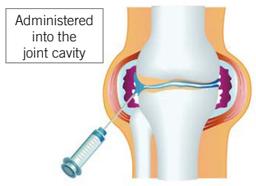


Administration of SI-6603

SI-613 (treatment for osteoarthritis)/SI-613-ETP (treatment for enthesopathy)

SI-613 is a formulation in which hyaluronic acid and diclofenac (an anti-inflammatory drug) are chemically bound using a drug binding technology proprietary to Seikagaku. By releasing diclofenac through hydrolysis, relief for osteoarthritis and enthesopathy can be expected.

In Japan, marketing approval was obtained for SI-613 for its efficacy and effect on osteoarthritis (knee joint and hip joint) on March 23, 2021, and it was launched as joint function improvement agent JOYCLU® 30mg Intra-articular Injection in May of the same year. It is the first joint function improving agent in Japan indicated for osteoarthritis.



Administration of SI-613

Since shock or anaphylaxis has occurred in Japan, to promote appropriate use, Seikagaku is conducting a clinical study to identify the cause of the side effects.

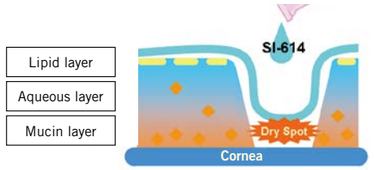
The Company will consider the future direction for development in the U.S., China, and South Korea while assessing progress with identification of the cause of shock or anaphylaxis.

The primary efficacy endpoint in a late-stage Phase II clinical trial in Japan of SI-613-ETP for the treatment enthesopathy was not met, and the Company will prioritize identification of the cause of shock or anaphylaxis. For these reasons, development of SI-613-ETP was discontinued in February 2022.

SI-614 (treatment for dry eye)

SI-614, an ophthalmic solution, is a modified hyaluronate produced using Seikagaku's proprietary technology. Instilling this solution as an eyewash is expected to improve dry eye symptoms by stabilizing the tear film and promoting corneal wound healing.

Clinically beneficial effects were confirmed in a Phase II/III clinical study in the U.S. Accordingly, in May 2022 Seikagaku initiated a Phase III clinical study with the objective of evaluating efficacy and safety.

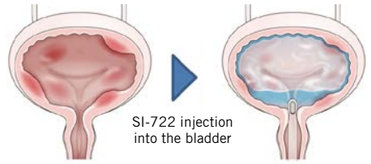


Administration of SI-614

SI-722 (treatment for interstitial cystitis and bladder pain syndrome)

SI-722 is a novel chemical compound in which a steroid is conjugated with chondroitin sulfate using Seikagaku's proprietary glycosaminoglycan modification technology and drug delivery systems. SI-722 injected into the bladder is thought to demonstrate an improvement effect in symptoms such as of frequent urination and bladder pain, by releasing a steroid with an anti-inflammatory effect.

While a Phase I/II clinical trial in the U.S. experienced delays in the trial schedule due to the spread of COVID-19, subject enrollment was completed in January 2021, and tolerability in the patients of this trial has been confirmed. Currently, we are exploring the next phase of trials based on the data we have obtained.

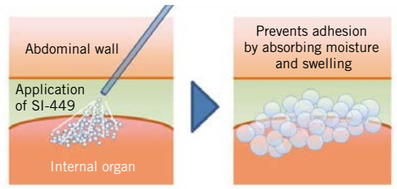


Using sustained release of steroids to provide long-lasting improvement

Administration of SI-722

SI-449 (adhesion barrier)

SI-449 is a powdered adhesion barrier whose main ingredient is cross-linked chondroitin sulfate developed using Seikagaku's own glycosaminoglycan cross-linking technology. 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. Development of this subject is progressing with an eye not only on domestic development, but also globally.



Use of SI-449

Subject enrollment for a pivotal study in the field of gastroenterological surgery was completed in September 2022. The study is being conducted to confirm efficacy (prevention of adhesion formation), safety, and usability in gastroenterological surgery. Also, subject enrollment for a pilot study in the field of gynecology aimed at expanding the scope of application of SI-449 was completed in May 2022. Following the observation periods of both studies, the Company will aim for an NDA based on the data obtained.

Research and Development

Seikagaku and glycoscience

Seikagaku's Management Creed states: "We create safe and useful products for human well-being with basic research 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 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). Sugar chains are known in the life sciences as the third biological chain, along with nucleic acids and proteins, but they have complex chemical structures because they are molecules that handle various kinds of information within living organisms. In research in areas such as structural analysis, automatic synthesis, and large-scale synthesis, this complexity poses characteristic difficulties not found in other biological materials.

However, long-term efforts in the industry and academia have advanced the structural analysis and synthesizing technologies of sugar chains. In addition, the genes of sugar-chain synthesizing enzymes and degrading enzymes have been comprehensively identified, and our understanding of the homeostasis of sugar chains in living organisms and their pathological function is advancing.

This progress in glycoscience technologies is closely linked with Seikagaku's drug discovery research.

Intellectual property strategy

Appropriate protection of intellectual property relating to Seikagaku's technologies, products, and other assets is essential not only for maintaining corporate competitiveness, but also for continuing to create and supply unique, high-quality pharmaceuticals and medical devices. Seikagaku views intellectual property as an important management resource and engages in global intellectual property-related activities.

The Intellectual Property Department engages in activities related to acquisition of intellectual property rights (patents, designs, trademarks, copyright, know-how, etc.) and their protection. It works closely with the Research & Development Division involved in drug discovery as well as with Business Development & Marketing Division, Production Division, and other relevant Company organizations.

Fair R&D activities

In the interest of conducting fair R&D activities, Seikagaku has established the Ethical Review Committee for Research Using Human Specimens and the Animal Experimentation Ethics Committee. Through comprehensive examination of the appropriateness of clinical studies and research using human specimens and animal experimentation in these committees, including ethical and scientific perspectives, Seikagaku strives to rigorously ensure ethical consideration in R&D activities.

Ethical considerations concerning research using human biological materials

https://www.seikagaku.co.jp/ja/development/research/research01.html (Japanese only)

Ethical considerations in non-clinical studies

https://www.seikagaku.co.jp/ja/development/research/research02.html (Japanese only)

Quality Compliance

Seikagaku's mission is to provide patients with a continuous supply of safe, 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

Seikagaku places quality first, from R&D to post-marketing by complying with overseas pharmaceutical laws and regulations, including GxP* regulations and guidelines. In Japan, as a marketing authorization holder, Seikagaku operates a legal compliance system under the officer responsible for pharmaceutical matters (Responsible Officer) in accordance with the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices ("PMD Act"). And, the general marketing compliance officer, quality assurance supervisor, and safety management supervisor oversee appropriate quality management and pharmacovigilance operations.

To reliably provide pharmaceuticals and medical devices to patients around the world, we will continue to operate in accordance with global standards.

* GxP stands for Good XXX Practice, a collective term for standards established to ensure the efficacy, safety, and quality of pharmaceuticals and medical devices from R&D to post-marketing.

Quality compliance system

https://www.seikagaku.co.jp/en/corporate/activities/quality.html

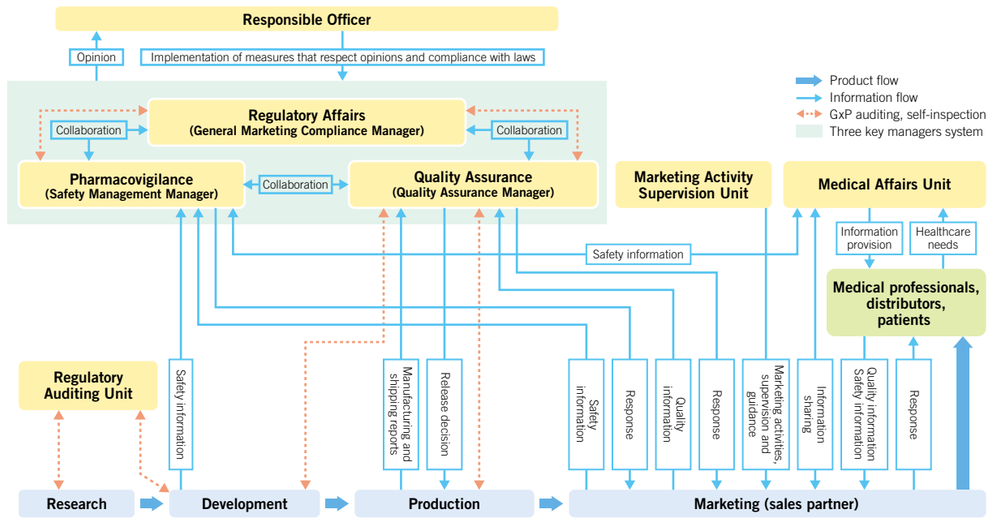
Safety management

Sometimes side effects not observed in the development stage come to light after the launch of a new pharmaceutical product. 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 pharmaceuticals 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

Seikagaku has established the Medical Affairs 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 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.

[Research & Development Division Structure]



Marketing

Seikagaku has a 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

To efficiently deliver these products to patients globally, Seikagaku forms partnerships with pharmaceutical companies that have expertise in each market, including Japan, rather than selling directly to pharmaceutical wholesalers and medical institutions. Through their 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, in close cooperation with sales partners, formulates sales strategies, supports preparation of product information materials, analyzes the market environment, including information on competing products, and collaborates with academic societies. Through these activities, we support sales partner activities and appropriately promote market penetration for our products.

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 Dispo, from glass to plastic. Through these efforts, we are adding value to our products.

Furthermore, we have been accelerating overseas business expansion in recent years. We are working to increase sales in countries where we already do business, and to meet global medical needs, we are implementing a plan to introduce existing products and products in development into new markets.

Bulk products

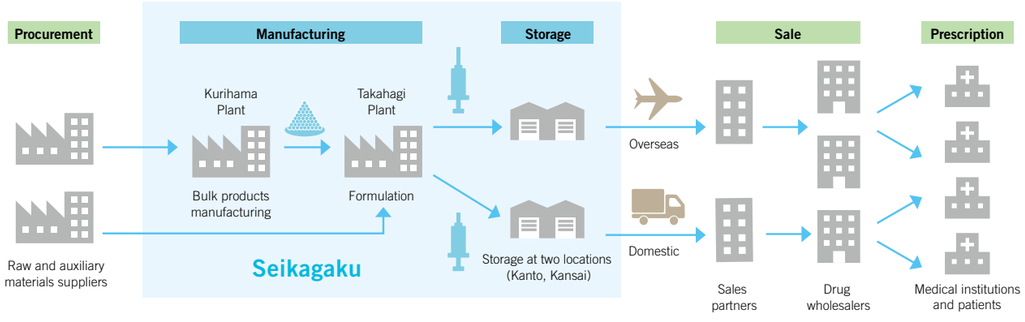
Using proprietary extraction and purification technologies, Seikagaku manufactures high-purity and high-quality hyaluronic acid and chondroitin sulfate and sells them to pharmaceutical and cosmetic companies, and others globally.

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.

Contract development and manufacturing organization (CDMO)

A contract development and manufacturing organization (CDMO) is a business that supplies comprehensive services in drug development and manufacturing to pharmaceutical companies, including contract drug manufacturing, pharmaceutical formulation planning at the development stage, manufacturing of investigational drugs, and optimization of manufacturing conditions. In March 2020, we added to our business by acquiring Dalton Chemical Laboratories, Inc. as a subsidiary.

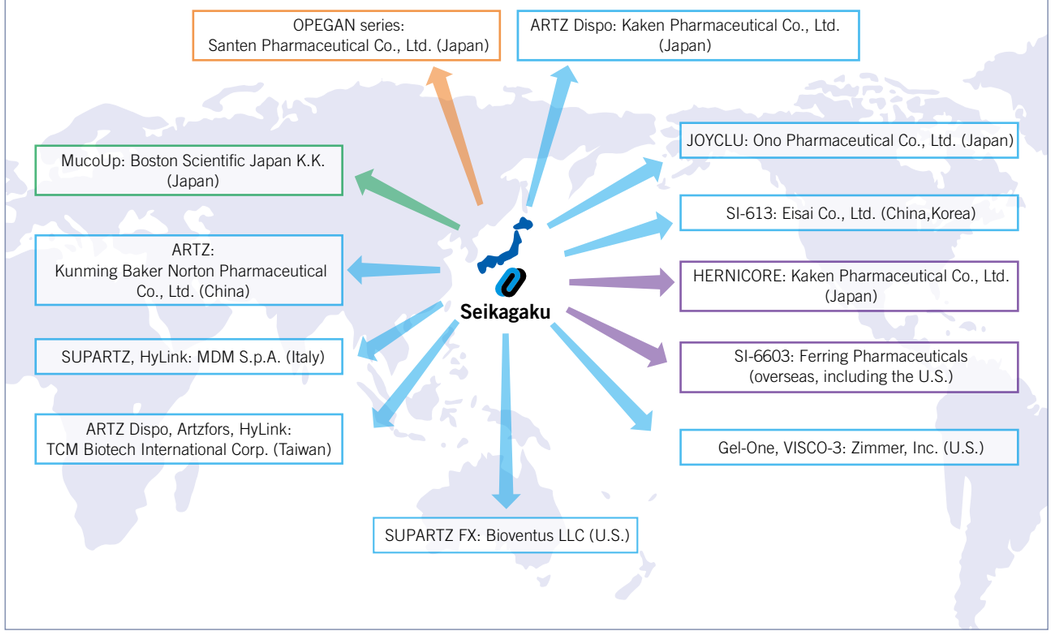
[Supply Chain for Main Products]



[Key Alliances with Companies in Japan and Overseas (Including Products under Development)]

Joint function improving agent/ Treatment of osteoarthritis | Ophthalmic viscoelastic device | Treatment for lumbar disc herniation | Surgical aid for endoscopic mucosal resection

(As of September 30, 2022)



LAL business

Seikagaku is engaged in the development of the LAL business in Japan, which is mainly used in quality control of injectable pharmaceuticals and medical device manufacturing processes and water quality control of dialysate used in artificial dialysis.

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, through the manufacturing and sales of endotoxin-detecting reagents, as well as beta-glucan-detecting in vitro reagent to diagnose invasive fungal disease.

Furthermore, Seikagaku has successfully developed the world's first product consisting of recombinant proteins of Factor C, Factor B, and a coagulating enzyme precursor, which are components of horseshoe crab blood cells. We launched gene-recombinant endotoxin-detecting reagent PyroSmart NextGen through ACC and in Japan in 2021.

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. and plant related to CDMO business in Canada.

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.

Also, in the area of manufacturing control and quality control, we use computer systems to improve the completeness of records and work to improve production efficiency through rigorous regular checks, elimination of human error, and improvement of manufacturing processes. We will continue to pursue continuous improvement so as to manufacture and supply high-quality products that comply with global standards.

Ensuring a stable supply of products

It is important for pharmaceutical companies to provide stable supplies. Seikagaku prepares for major disasters and other risks by diversifying raw materials suppliers and maintaining appropriate inventory levels. At the Takahagi Plant, responsible for manufacturing the finished products, we have introduced a quake-absorbing structure that helps isolate the main production buildings from earthquakes. Through these measures, we now have a system capable of stable, reliable product production even in an emergency.

Furthermore, to cope with product supply risk from disruption of distribution in a disaster, we maintain a certain level of product inventory and have pharmaceutical warehouses in two separate locations: at the Takahagi Plant in Ibaraki Prefecture near Tokyo and in Hirakata City, near Osaka.

[Overview of Production Sites]

Takahagi Plant (Takahagi City, Ibaraki Prefecture)

The Takahagi Plant is responsible for manufacturing finished pharmaceuticals and medical devices, including the joint function improvement agents that are Seikagaku's mainstay products. Today, the Takahagi Plant occupies a site of approximately 86,000 square meters and has five production buildings and some 200 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.

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

Kurihama Plant (Yokosuka City, Kanagawa Prefecture)

The Kurihama Plant, which manufactures bulk products, 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.

Information on U.S.-based Associates of Cape Cod, Inc. and Canada based Dalton Chemical Laboratories, Inc. is provided in the section "Overseas Subsidiaries" on page 58.