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#### < Cautionary Notes >

This material contains forward-looking statements regarding future management strategies or performance forecasts. These statements are based on judgments derived from information that is currently available to Seikagaku and are subject to risk and uncertainty. Actual results and developments may differ significantly from these forward-looking statements due to various factors.

Information about pharmaceutical products or medical devices (including products currently in development) included in this material is not intended to constitute an advertisement or medical advice.



# **Overview for 3Q of FY 2022**

**Net Income per Share** 

	3Q FY2022	Year-o	n-Year	(Refer FY2022 Full Y	
(百万円)	Results	Change	% of Change	FY 2022 Forecasts	Degree of Progress
Net sales	26,162	-1,983	-7.0%	33,500	78.1%
Operating Income	3,407	-2,827	-45.4%	1,700	200.4%
Ordinary Income	4,218	-2,687	-38.9%	2,900	145.5%
Net Income	3,628	-1,735	-32.4%	2,650	136.9%
R&D Expenses (excluding royalty income)	<b>5,355</b> (20.5%)	-500 (-3.3pt)	-8.6%	<b>8,000</b> (23.9%)	66.9%
Average Exchange Rate (1US\$)	¥136.53	+25.43		¥140.00	
		3Q FY2022	3Q FY2021	(Reference)	

Results

¥95.25

Results

¥65.42

FY2022 Forecasts

¥48.12



(1	Millions of Yen)	3Q FY2022 Results	Year-on- Year	% of Change
	Net sales	26,162	-1,983	-7.0%
	Pharmaceuticals	17,953	-3,466	-16.2%
	Domestic Pharmaceuticals	8,850	-323	-3.5%
	Overseas Pharmaceuticals	6,922	+179	+2.7%
	Bulk Products /CDMO	2,178	+225	+11.5%
	Royalty Income	1	-3,548	-100.0%
ı	LAL Business	8,209	+1,483	+22.1%
(C	verseas sales)	15,680	+1,757	+12.6%

<sup>\*</sup> Foreign exchange impact on overall net sales: approx. +2,250million yen

#### **Domestic Pharmaceuticals**

#### ► ARTZ (Joint-function improving agent)

- Market size at the prior-year level (-0.6%)
- Deliveries to medical institutions up due to switching from competing products (+1.7%)
- Market share up as well (+1.5 pt)
- Company sales down because of NHI drug price reductions, despite higher shipment volume due to shipment timing adjustment

#### **► JOYCLU** (Joint-function improving agent)

- Launched in May 2021
- Information provision efforts aimed at ensuring appropriate use
- Company sales up due to longer selling period than in FY2021

# Safety Information on Joint Function Improving Agent JOYCLU

# Blue Letter (rapid safety information) issued in June 2021 Seikagaku is further raising awareness among healthcare professionals and taking measures to identify the cause

<u>Dear Healthcare Professionals Letter of Rapid Safety Communication (Blue Letter)</u>

issued on June 1 in response to multiple reports of anaphylaxis occurring in patients following administration of JOYCLU

- To ensure patient safety by promptly alerting healthcare professionals of the situation to enable the provision of appropriate treatment and measures
- Addition of a WARNING section to the drug package insert and revision of the IMPORTANT PRECAUTIONS section
- Leaflet created to alert patients and their families to the risk of side effects



- Continued gathering of safety information and provision of safety-related information
- Physician-led clinical research to identify the cause initiated in April 2022



Continue gathering of safety information and provision of safety-related information in collaboration with sales partner Ono Pharmaceutical Aim to contribute to appropriate treatment on the basis of clinical research findings

# **Net sales by Business Segment (3Q of FY2022)**

	(Millions of Yen)	3Q FY2022 Results	Year-on- Year	% of Change
	Net sales	26,162	-1,983	-7.0%
	Pharmaceuticals	17,953	-3,466	-16.2%
	Domestic Pharmaceuticals	8,850	-323	-3.5%
	Overseas Pharmaceuticals	6,922	+179	+2.7%
	Bulk Products /CDMO	2,178	+225	+11.5%
	Royalty Income	1	-3,548	-100.0%
	LAL Business	8,209	+1,483	+22.1%
((	Overseas sales)	15,680	+1,757	+12.6%

<sup>\*</sup> Foreign exchange impact on overall net sales: approx. +2,250million yen

#### **Domestic Pharmaceuticals**

#### ► OPEGAN series (Ophthalmic viscoelastic devices)

- Market expanding, gradually returning to the pre-COVID growth trend (+9.2%)
- Deliveries to medical institutions up due to market expansion (+8.8%)
- Share at the prior-year level (-0.2 pt)
- Company sales up, with higher shipments compensating for the impact of NHI drug price reductions

#### ► MucoUp

(Submucosal injection agent for endoscopic surgery)

 Company sales down slightly, reflecting a decline in shipments from a high level in the first nine months of FY2021 and the impact of an NHI reimbursement price revision

#### ► HERNICORE (Treatment for lumbar disc herniation)

- Deliveries to medical institutions at prior-year level
- Company sales up due to shipment timing



(1	Millions of Yen)	3Q FY2022 Results	Year-on- Year	% of Change
	Net sales	26,162	-1,983	-7.0%
F	Pharmaceuticals	17,953	-3,466	-16.2%
	Domestic Pharmaceuticals	8,850	-323	-3.5%
	Overseas Pharmaceuticals	6,922	+179	+2.7%
	Bulk Products /CDMO	2,178	+225	+11.5%
	Royalty Income	1	-3,548	-100.0%
L	AL Business	8,209	+1,483	+22.1%
(0	verseas sales)	15,680	+1,757	+12.6%

<sup>\*</sup> Foreign exchange impact on overall net sales: approx. +2,250million yen

#### **Overseas Pharmaceuticals**

\*Foreign exchange impact on Overseas Pharmaceuticals: approx. +900 million yen

#### ► Gel-One in the U.S. (Single injection)

- Health insurance system change from July 2022
- Local sales volume down because of the system change
- Substantial increase in Company sales due to yen depreciation

#### ► SUPARTZ FX in the U.S. (Multiple injection)

- Local sales volume up slightly
- Company sales at prior-year level due to shipment timing, despite the impact of yen depreciation

#### ► ARTZ in China (Multiple injection)

- Local sales volume down substantially due to limitation of access to outpatient services accompanying the renewed spread of COVID-19
- Company sales down substantially on no 1Q shipments due to a change in packaging material
- Resumption of shipments in August



# **Net sales by Business Segment (3Q of FY2022)**

(1	Millions of Yen)	3Q FY2022 Results	Year-on- Year	% of Change
	Net sales	26,162	-1,983	-7.0%
ı	Pharmaceuticals	17,953	-3,466	-16.2%
	Domestic Pharmaceuticals	8,850	-323	-3.5%
	Overseas Pharmaceuticals	6,922	+179	+2.7%
	Bulk Products /CDMO	2,178	+225	+11.5%
	Royalty Income	1	-3,548	-100.0%
ı	.AL Business	8,209	+1,483	+22.1%
(C	verseas sales)	15,680	+1,757	+12.6%

## **Bulk Products / CDMO**

Bulk products sales at the prior-year level, and CDMO sales at Dalton Pharmaceutical up due to the impact of yen depreciation

\*Foreign exchange impact on Bulk Products/CDMO: approx. +200million yen

## **Royalty Income**

Substantial decline

#### **LAL Business**

Sales up due to the impact of yen depreciation on the results of ACC and steady sales in Japan

> \*Foreign exchange impact on LAL Business: approx. +1.150million yen

#### Overseas Sales Ratio(excluding royalty income)



<sup>\*</sup> Foreign exchange impact on overall net sales: approx. +2,250million yen

<sup>■</sup> Overseas LA, Bulk/CDMO ■ Overseas Pharmaceuticals ■ Domestic sales

# **Income for 3Q of FY2022**

(Millions of Yen)	3Q FY2022 Results	Year-on- Year	% of Change
Net sales	26,162	-1,983	-7.0%
Cost of Sales (excluding royalty income)	<b>11,552</b> (44.2%)	+554 (-0.5pt)	+5.0%
SGA expenses	11,203	+290	+2.7%
R&D Expenses (excluding royalty income)	<b>5,355</b> (20.5%)	-500 (-3.3pt)	-8.6%
Operating Income (to Net sales ratio)	<b>3,407</b> (13.0%)	-2,827 (-9.2pt)	-45.4%
Ordinary Income	4,218	-2,687	-38.9%
Net Income	3,628	-1,735	-32.4%
Depreciation	938	+216	+29.9%

#### **Operating Income**

3,407 (-2,827)

#### Cost of sales ratio (-0.5pt)

• Ratio at the prior-year level because of change in sales mix, despite NHI drug price reductions

#### SGA Expenses (+290)

- R&D expenses down due to completion of subject enrollment in an additional clinical study in the U.S. for SI-6603 (-500)
- Higher expenses at overseas subsidiaries, including foreign currency translation

# **Ordinary Income**

4,218(-2,687)

## Non-operating Income / Expenses (+140)

• Increase in foreign exchange gain (+211)

#### **Net Income**

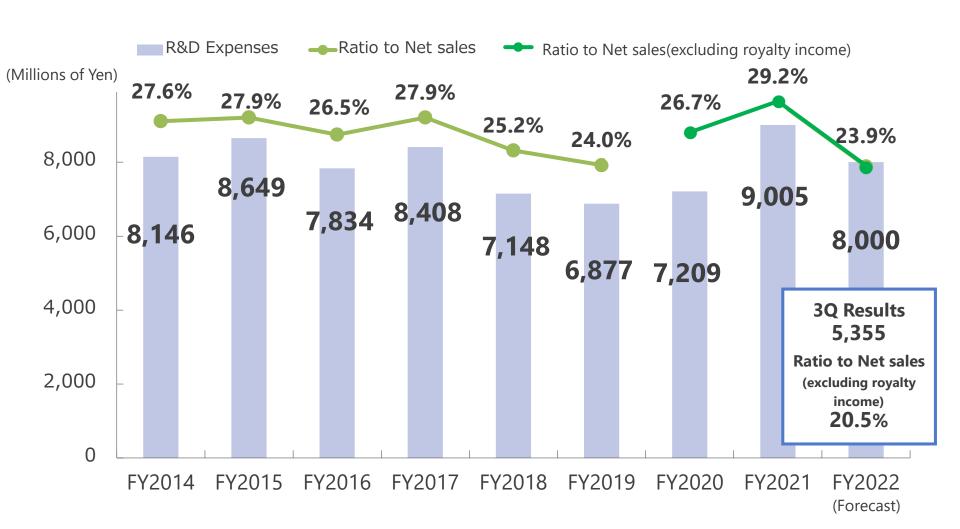
3,628(-1,735)

#### **Income Taxes (-951)**

Decline from high profits in previous fiscal year

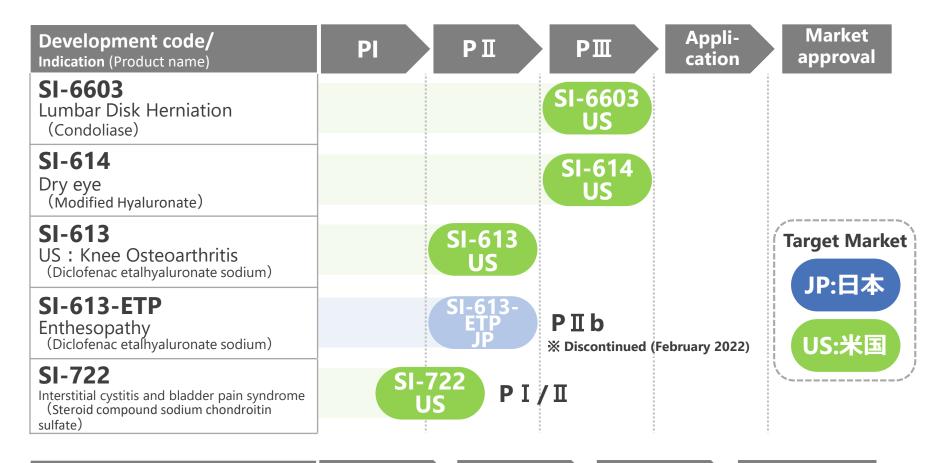


# Continuing to focus on drug discovery specializing in Glycoscience Undertaking improvement in R&D efficiency





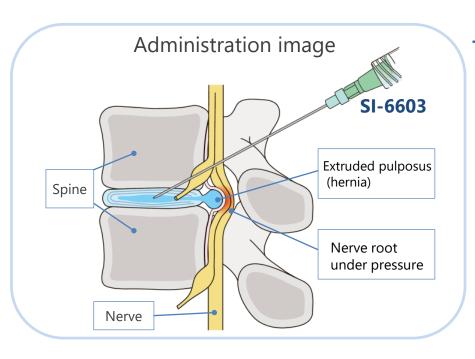
# **Pipeline List**







# Aim to provide new options in lumbar disc hernia treatment and maximize product value through early market penetration



## **Development status**

- ▶ U.S. Phase III : Starting February 2018
  - Subject enrollment complete in March 2022
    - **⇒** Conduct a one-year follow-up observation

## **Expected Features**

- ▶ Relieving symptoms by decreasing intradiscal pressure and reducing the pressure on the nerve root by single injection
- ▶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

<SI-6603 summary>

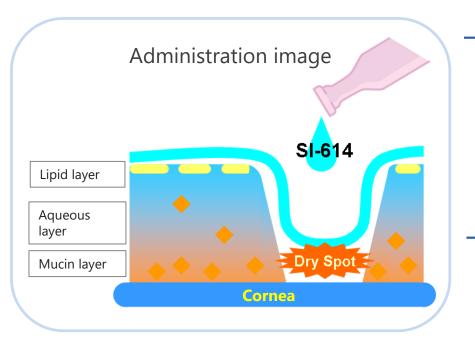
Dev. Code : SI-6603 Generic name : Condoliase

Indication : Lumbar disc herniation

Method of use: Injection into lumbar disc (under X-ray observation)

New patients with lumbar disc herniation: 3 to 5 million per year (Seikagaku estimates)

# Phase III clinical study in the U.S. initiated in May 2022 Subject enrollment completed in February 2023



## **Development status**

- ► U.S.: P III: Starting May 2022

  Subject enrollment completed in Feb. 2023
  - Sales partner selection and second PIII study planned after follow-up observation and results analysis
  - Evaluation of efficacy and safety

#### **Expected Features**

- ►SI-614 Improves symptoms of dry eye by protecting the ocular surface and promoting corneal epithelial wound healing
- ▶ Dry Eye is a multifactorial disease, and Seikagaku aims to provide a treatment option based on a new mechanism unavailable from existing products

<SI-614 summary>

Dev. Code: SI-614 Generic name: Modified Hyaluronate

Product name: Dry eye Formulation: Ophthalmic solution

Estimated U.S. patients: 14 million (Seikagaku estimates)

# SI-613 (Treatment of Osteoarthritis/Enthesopathy)

# Development of SI-613-ETP discontinued Prioritize identification of cause of JOYCLU side effects



## **Development status**

- ► SI-613 (osteoarthritis of the knee) U.S. /China/South Korea
  - Proceeding with preparation of a clinical development plan
- ► SI-613 (Enthesopathy) Japan
  - February 2022: Development discontinued
    - ⇒ Failure of the PII clinical study to meet its primary efficacy evaluation, and to prioritize identification of the cause of shock or anaphylaxis occurring in patients following administration of JOYCLU

<SI-613 summary>

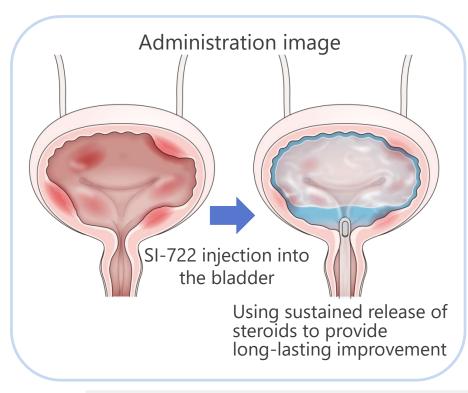
Dev. code: SI-613 Generic name: Diclofenac etalhyaluronate sodium

Indication: Osteoarthritis/Enthesopathy Method of use: Injection into joint cavity

Estimated patients: 24 million (U.S.) / 47 million (China) 3.7 million (South Korea)



# Subject enrollment for PI/PII studies in the U.S. completed Analysis of study results to proceed



## **Development status**

- ▶ **U.S. Phase I/II**: Starting November 2019
  - Subject enrollment complete in January 2021
  - **⇒Tolerability confirmed (a primary objective)**Will consider the next-phase study

## **Expected Features**

- Designed for sustained release by bonding steroids to chondroitin sulfate
- ➤ Anti-inflammatory effects of steroids under sustained release should provide sustainable relief of frequent urination and bladder pain

<SI-722 summary>

Dev. Code: SI-722Generic name: Steroid conjugated with chondroitin sulfate

Indication: Interstitial cystitis and bladder pain syndrome

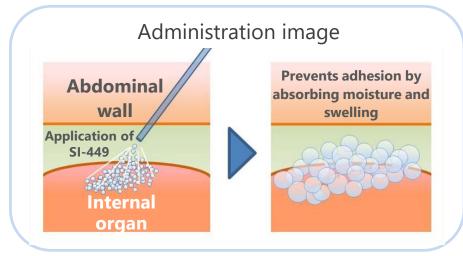
Method of use: Injection into the bladder

Estimated U.S. patients: 1.3 million (Seikagaku estimates)



# SI-449 (Adhesion Barrier / Medical Device)

# Subject enrollment for pivotal study completed in September 2022 Carrying out observation period for both studies and results analysis



# **Expected Features**

► Leveraging pulverized characteristics to respond to healthcare needs through the spreading use of laproscopic surgery

# **Development status**

- ► Japan pivotal study(field of gastroenterological surgery)
  Starting May 2020
  - Evaluated for effectiveness, safety, and usability
  - ⇒Subject enrollment complete in Sept. 2022
- ► Japan pilot study (field of gynecology) Starting November 2021
  - Confirming operability and safety
  - Aiming to expand range of applications
  - ⇒Subject enrollment complete in May 2022
- Proceed with development with a view to global development; Start of U.S. study under review

<SI-449 summary>

Dev. Code: SI-449 Generic name: Cross-linked chondroitin sulfate

Product name: Adhesion barrier

Method of use: Intra-abdominal application (powdered formulation)

Adhesion barrier market: Japan: ¥14 billion, Global: ¥100 billion (Seikagaku estimates)

# **Dividends from Surplus and Treasury Stock Acquisition**

# Board resolution to pay dividends in accordance with the dividend policy in the mid-term management plan Acquisition of treasury shares completed

#### FY2022

**Annual dividend:** ¥26 per share (including an interim dividend of ¥13)

	FY2018	FY2019	FY2020	FY2021	FY2022 (forecast)
Net profit per share	¥39.76	-¥192.15	¥75.54	¥66.32	¥48.12
Annual dividend per share	¥26.00	¥26.00	¥24.00	¥30.00 <sup>*2</sup>	¥26.00
Dividend payout ratio	65.4%	_	31.8%	45.2%	54.0%

<sup>\*1</sup> Includes JOYCLU approval commemorative dividend of ¥4

# **Treasury Stock Acquisition**

Total number of shares to be acquired: 2,000,000 shares (maximum)

Total value of shares to be acquired: ¥1.5 billion (maximum)

Acquisition period: May 16, 2022 to December 30, 2022

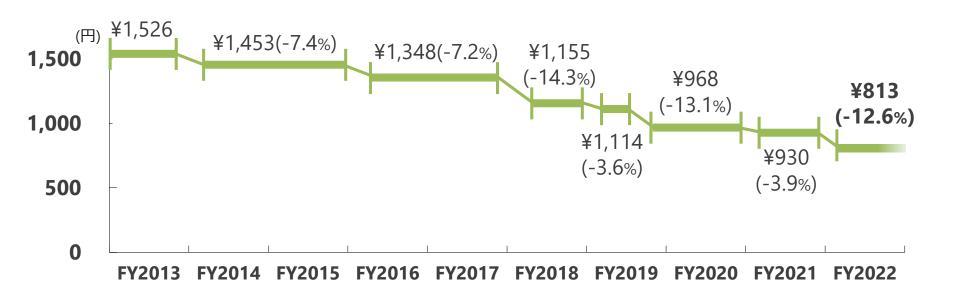
Acquisition result (acquisition completed on Dec. 23, 2022)

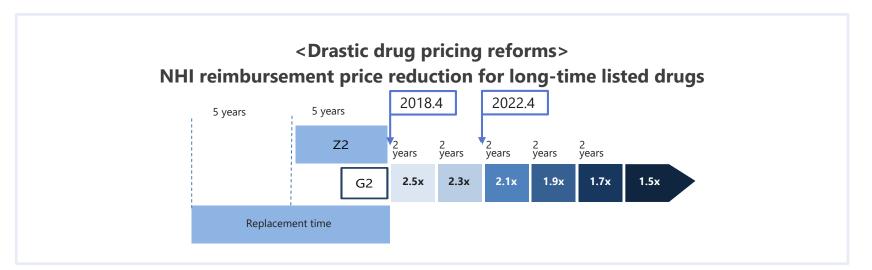
Total number of shares acquired: 1,725,700 shares Total amount of acquisition cost: ¥1,499,994,100

<sup>\*2</sup> Includes JOYCLU launch special dividend of ¥10



# **Trend in NHI Reimbursement Price of ARTZ to Domestic**







# Trend in Deliveries of ARTZ / OPEGAN to Domestic Medical Institutions

#### Joint-function improving agent

#### **ARTZ**



- The first HA joint function improving agent in the world
- Knee osteoarthritis (OA) pain relief
- Distributor: Kaken Pharmaceutical

#### Trend in unit deliveries to medical institutions



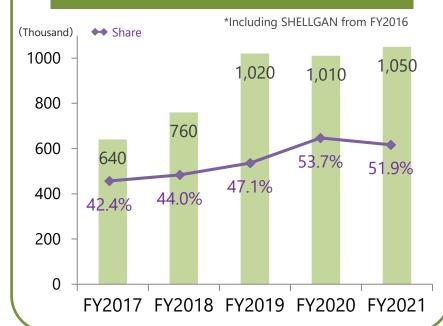
#### Ophthalmic viscoelastic devices

#### **OPEGAN**



- The first domestically HA formulation
- Used in cataract surgery to anterior chamber expansion
- Distributor: Santen Pharmaceutical

#### Trend in unit deliveries to medical institutions



# **Overview of Forecasts in FY2022**

	FY2022		FY2021 Results		Degree of
(Millions of Yen)	Forecasts	Results	Change	% of Change	Progress
Net sales	33,500	34,851	-1,351	-3.9%	51.5%
Operating Income	1,700	4,495	-2,795	-62.2%	153.6%
Ordinary Income	2,900	5,395	-2,495	-46.2%	124.2%
Net Income	2,650	3,733	-1,083	-29.0%	118.6%
R&D Expenses (Ratio to net sales excluding royalty income)	<b>8,000</b> (23.9%)	<b>9,005</b> (29.2%)	-1,005 (-5.3pt)	-11.2%	42.6%
Average Exchange Rate (1US\$)	2Q forecast <b>¥140.00</b>	¥112.38			

	FY2022 Forecasts	FY2021 Results
Net Income per share	¥48.12	¥66.32
Dividend per share	¥26.00	¥30.00
<b>Dividend Payout ratio</b>	54.0%	45.2%

Exchange Rate Sensitivity (Impact of a change of ¥1against the US\$)				
Net sales Approx. ¥45 million				
Operating income	Approx. ¥15 million			

# Forecasts (Net sales) in FY2022

	FY2022 Forecasts	Year-on-Year	
(Millions of Yen)		Change	% of Change
Net sales	33,500	-1,351	-3.9%
Pharmaceuticals	22,500	-3,196	-12.4%
Domestic Pharmaceuticals	10,850	-597	-5.2%
Overseas Pharmaceuticals	8,650	+997	+13.0%
Bulk Products /CDMO	3,000	+392	+15.1%
Royalty income	1	-3,988	-100.0%
LAL Business	11,000	+1,844	+20.2%
(Overseas sales)	20,650	+2,731	+15.2%

<sup>\*</sup> Foreign exchange impact on overall net sales: approx. +3,100million yen

#### **Net sales**

Forecasting a sales decrease to result from steep decline in royalty income and impact of NHI drug price reductions, despite higher pharmaceutical sales volumes in Japan and positive impact of yen depreciation

## **Pharmaceuticals**

#### **Domestic pharmaceuticals:**

Sales decrease to result from NHI price reductions

#### Overseas pharmaceuticals:

Sales increase due to yen depreciation

#### **Bulk products/CDMO:**

CDMO sales increase due to yen depreciation

#### **Royalty income:**

Substantial decline

#### **LAL Business**

Expected sales increase due to the impact of yen depreciation on overseas sales



<sup>\*</sup> There is no change in forecast announced on November 8, 2022.

# Forecasts (Income) in FY2022

	FY2022	Year-on-Year	
(Millions of Yen)	Forecasts	Change	% of Change
Net sales	33,500	-1,351	-3.9%
OperatingIncome (Ratio to net sales)	<b>1,700</b> (5.1%)	-2,795 (-7.8pt)	-62.2%
Ordinary Income	2,900	-2,495	-46.2%
Net Income	2,650	-1,083	-29.0%
Cost of Sales ratio (excluding royalty income)	47.2%	+0.8 <sub>pt</sub>	-
R&D Expenses	8,000	-1,005	-11.2%
R&D Expenses ratio (excluding royalty income)	23.9%	-5.3 <sub>pt</sub>	-
Depreciation	1,300	+248	+23.6%

# **Operating Income**

#### **SGA** expenses

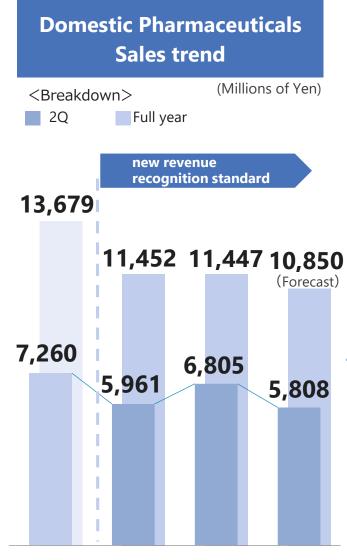
- Decrease in R&D expenses accompanying completion of subject enrollment in an additional clinical study in the U.S. for SI-6603
- Higher expenses at overseas subsidiaries, including foreign currency translation

# **Ordinary Income**

#### **Non-operating Income/Expenses**

 Increase in foreign exchange gains related to valuation of foreign currency-denominated assets

# **Domestic Pharmaceuticals (Year-on-Year)**



**2Q FY2022 Results -14.7**%

(Sales)

Sales down, reflecting concentration of JOYCLU shipments in 1H FY2021 due to launch coupled with impact of NHI drug price reductions

#### **Joint-function improving agent** (Unit deliveries to medical institutions)

**Market** (+1.1%)

Signs of recovery from the impact of COVID-19

**ARTZ** (+3.4%)

 Volume and market share expansion due to market recovery and 1Q promotion of switching from competing products (63.7%/+1.4pt)

#### **JOYCLU**

Information provision efforts to ensure correct use

#### **Ophthalmic viscoelastic devices** (Unit deliveries to medical institutions)

**Market** (+12.5%)

• Expansion due to COVID-19 recovery and market growth trend **OPEGAN series** (+11.5%)

- Volume increase accompanying market expansion
- Market share at the prior-year level (51.7%/-0.5 pt)

#### Treatment for lumbar disc herniation (Unit deliveries to medical institutions)

#### **HERNICORE**

Sales at the prior-year level

FY2019 FY2020 FY2021 FY2022

24

# **Domestic Pharmaceuticals (FY2022 Forecast Year-on-Year)**



FY2022 Forecast
-5.2%
(Sales)

Substantial sales decrease, with NHI drug price reductions offsetting an expected volume increase from domestic pharmaceuticals

#### Joint-function improving agent (Unit deliveries to medical institutions)

#### **Market**

• Trending toward recovery from the impact of COVID-19

#### **ARTZ**

• Sales at prior-year level thanks to switching from competing products

#### **JOYCLU**

Information provision efforts to ensure correct use

#### **Ophthalmic viscoelastic devices** (Unit deliveries to medical institutions)

#### **Market**

Return to the pre-COVID-19 growth trend

#### **OPEGAN** series

Increase accompanying market expansion

#### **Treatment for lumbar disc herniation** (Unit deliveries to medical institutions)

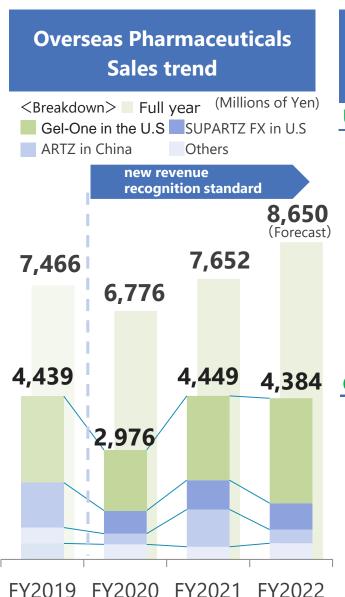
#### **HERNICORE**

- Forecasting sales at the prior-year level
- Continuation of promotion of correct use and patient awareness activities

FY2019 FY2020 FY2021 FY2022

SEIKAGAKU CORPORATION

# **Overseas Pharmaceuticals (Year-on-Year)**



#### 2Q FY2022 Results

- 1.5%

(Sales)

Sales at the prior-year level, with the impact of yen depreciation compensating for ARTZ inventory adjustment in China

# U.S. (Value basis) Market in the U.S.

\* Foreign exchange impact: approx. + 500million

Health insurance system change relating to price disclosure implemented in July 2022

#### **Gel-One**

(approx. -15% on a volume basis)

Local sales: Decrease due to the impact of the system change Seikagaku sales: Substantial increase due to yen depreciation

#### **SUPARTZ FX**

Local sales: At the prior-year level

Seikagaku sales: Decrease due to shipment timing

# China, Other Regions. (Value basis)

#### **Market in China**

Lockdowns in major cities due to renewed spread of COVID-19

#### **ARTZ in China**

Local sales: Substantial decrease due to impact of lockdowns Seikagaku sales: Substantial decrease because of shipment adjustments due to a packaging material change

## **Other Regions**

Seikagaku sales: Increase in Italy, now starting to recover from impact of COVID-19

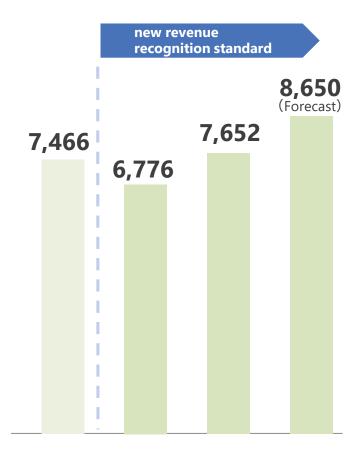
<sup>\*</sup> There is no change in forecast announced on November 8, 2022.

# **Overseas Pharmaceuticals (FY2022 Forecast Year-on-Year)**



<Breakdown> Full year

(Millions of Yen)



FY2019 FY2020 FY2021 FY2022

FY2022 Forecast +13.0%

(Sales)

Sales increase, with impact of yen depreciation compensating for impact of system changes in the U.S. and ARTZ shipment adjustments in China

U.S. (Value basis)

Market in the U.S.

\* Foreign exchange impact: approx. + 1,200million

Expected impact from system change relating to price disclosure

#### **Gel-One**

Local sales: Decrease due to impact of system change Seikagaku sales: Increase because of impact of yen depreciation

#### **SUPARTZ FX**

Local sales: Decrease due to trend toward preference for products requiring few injections

Seikagaku sales: Increase because of impact of yen depreciation

# **China, Other Regions. (Value basis)**

#### **Market in China**

Expected impact from lockdowns due to new outbreaks of COVID-19

#### **ARTZ in China**

Local sales: Substantial decline due to lockdowns

Seikagaku sales: Decrease because of shipment adjustments due to a packaging material change

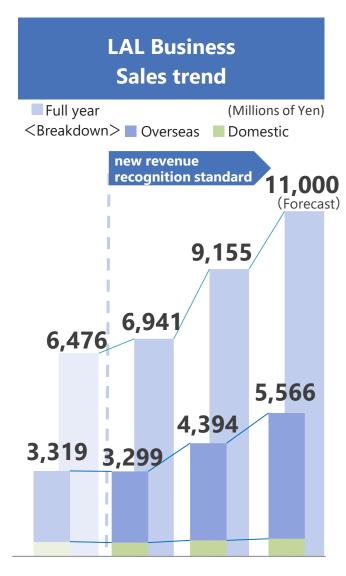
## **Other Regions**

Seikagaku sales: Increase in Italy, now starting to recover from impact of COVID-19

27

<sup>\*</sup> There is no change in forecast announced on November 8, 2022.

# Sales of LAL Business (year-on-year / value basis)



FY2019 FY2020 FY2021 FY2022

#### 2Q FY2022 Results: +26.7% (Year-on-Year)

\* Foreign exchange impact: approx. + 630million

\* Foreign exchange impact: approx. + 1,650million

#### **Overseas**

Sales increase on growth from Bacterial Endotoxin Testing (BET) reagents, Clinical Diagnostic (Fungitell) reagents, and contract testing services at overseas subsidiary ACC

#### **Domestic**

Sales increase on solid sales of reagents and other products

# FY2022 Forecasts: +20.2% (Year-on-Year)

Sales increase due to the impact of yen depreciation

#### **Overseas**

#### .

#### **Domestic**

Forecast of steady sales

LAL Business:

The manufacturing and sales of Endotoxin detection reagents\* used in the quality control of pharmaceuticals and medical devices

\*Endotoxin detection reagents are reagents whose main ingredient is Limulus Amebocyte Lysate (LAL).



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# Manufacturing and marketing approval in Japan obtained in March 2021 For the indication of osteoarthritis (knee joint and hip joint) May 19 NHI drug price listing and launch



Product name	JOYCLU®30mg Intra-articular Injection
Generic name	diclofenac etalhyaluronate sodium
Indication	Osteoarthritis (knee joint and hip joint)
Dosage and administration	The usual adult dosage is 1 syringe per dose (30 mg of diclofenac etalhyaluronate sodium) injected intra-articularly every 4 weeks.

#### **Overview of JOYCLU**

# Improvement of symptoms expected by administration once every 4 weeks First joint function improvement agent in Japan indicated for the treatment of osteoarthritis of the hip joint

#### **Features**

- ► Hyaluronic acid and diclofenac chemically bound using a proprietary technology
- ▶ Diclofenac released by hydrolysis in the joint
- ► Improvement of symptoms of osteoarthritis (knee joint and hip joint) expected by administration once every four weeks
- ► First joint function improvement agent in Japan indicated for the treatment of osteoarthritis of the hip joint

## **Expected positioning**

► Establishment as a new base drug in the treatment of osteoarthritis alongside existing hyaluronic acid formulations and NSAIDs

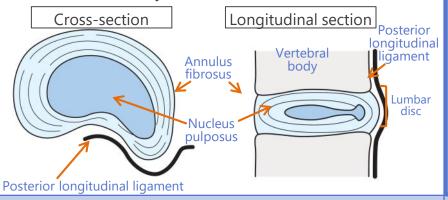
#### <Target Patients>

- People for whom existing hyaluronic acid formulations are insufficiently effective
- People who want to avoid NSAIDs, such as oral drugs or patches, in consideration of side effects
- People for whom frequent hospital visits are a hardship
- Provision of a new treatment option for osteoarthritis of the hip joint

# Four types of lumbar disc herniation

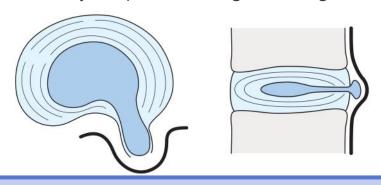
# 1. Protrusion

The hernia does not extend beyond the outermost layer of the annulus fibrosus



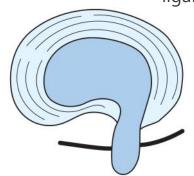
# 2. Subligamentous extrusion

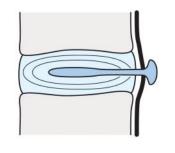
Although the hernia extends beyond the outermost layer of the annulus fibrosus, it is covered by the posterior longitudinal ligament



# 3. Transligamentous extrusion

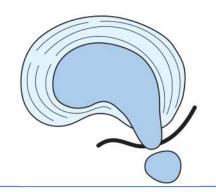
The hernia perforates the posterior longitudinal ligament

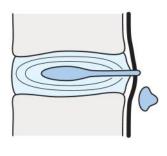




# 4. Sequestration

The hernia migrates outside the dura mater





# Physician and Facilities Requirements for HERNICORE Use

# Setting of physician and facility requirements for HERNICORE use to promote appropriate use and ensure safety

#### **[Physician requirements]**

#### [Japanese Society for Spine Surgery and Related Research]

: Physicians under the following conditions (as of April 2019)

- 1. Supervisory physicians or certified physicians of the Japanese Society for Spine Surgery and Related Research (JSSR) or who are supervised under the JSSR, or who participated in the this clinical study
- 2. Physicians having experience with performing intradiscal puncture or at least 50 surgeries for lumbar disc herniation

#### 【 Neurospinal Society of Japan 】: Physicians under the following conditions(as of April 2019)

- 1. Supervisory physicians or certified physicians of the Neurospinal Society of Japan
- 2. Physicians having experience with performing intradiscal puncture or at least 50 surgeries for lumbar disc herniation

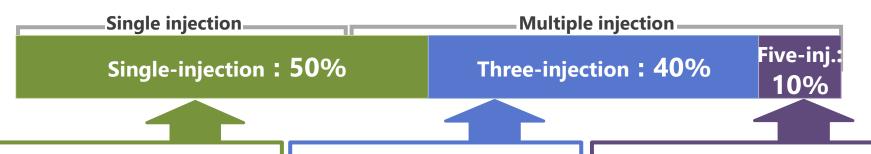
## **Facility requirements** : Facilities under the following conditions

- **1.** Facilities equipped with an X-ray fluoroscopic system (C-arm, etc.) capable of administering HERNICORE using clean technique
- 2. Facilities capable of treating shock and anaphylaxis
- **3.** Facilities capable of performing urgent spine surgery or facilities that cooperate with facilities capable of performing spine surgery
- 4. Facilities with hospitalization equipment
- X Among those who meet the physician requirements, supervisory physicians in the JSSR may be used at non-fulltime work facilities that meet the facilities requirements (as of November 2019)



# Market size of US\$950 mil. in 2021 (+8.3% year-on-year)

■ U.S. market share by number of injections (Value basis, including competitors)



# single-injection product **Gel-One**

- Full-scale sales since 2012
- September 2016: Efficacy extension label change (13weeks⇒26weeks)

Gel-One® Cross-linked Hyaluronate the only 3 mL single injection, cross-linked hyaluronate gel

# three-injection product VISCO-3

- December 2015 : Market approval
- November 2016:
   Conclusion of an exclusive sales
   agreement with Zimmer Biomet

VISCO-3<sup>TM</sup>
SODIUM HYALURONATE 25 mg
2,5 mL intra-articular injection.

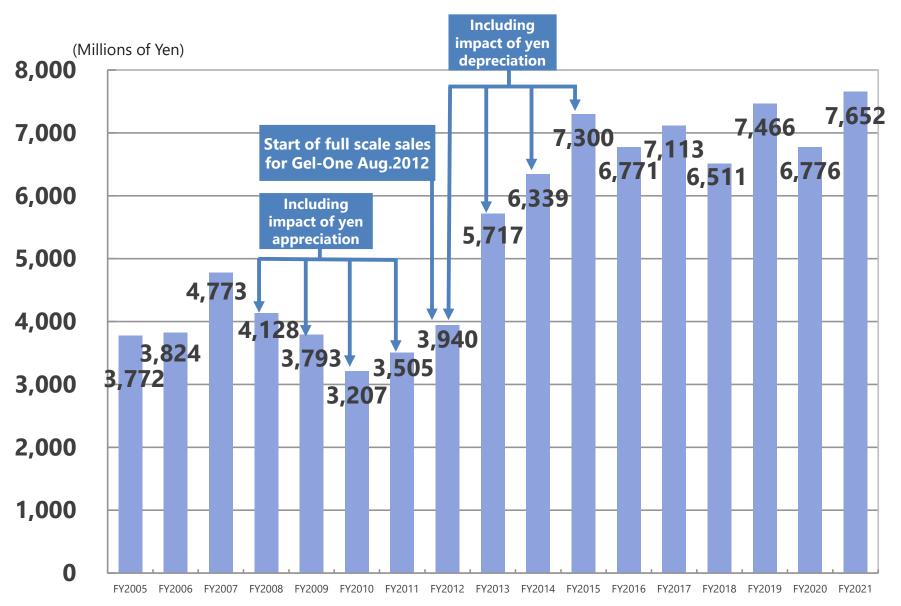
# five-injection product SUPARTZ FX

- Sales since 2001
- October 2015:
   Brand name changed
   from SUPARTZ



\*Figures for 2021, Seikagaku estimates

# Trend in Overseas Sales of Hyaluronic Acid Products





# Recombinant LAL reagent 「PyroSmart NextGen」

# April 2021 launch at ACC Product to be marketed globally, with a launch in Japan planned for May or later in 2021



#### **Product Features**

- ▶ Product manufactured using recombinant technology without using blood harvested from horseshoe crabs, a raw material used in traditional products
  - → Ensures continuous product supply
- ► Ability to utilize the same test methods and instruments as naturally sourced products
  - → Ensures consistency with endotoxin-testing reagents
  - → A next-generation BET reagent designed to deliver highly reliable quantitation of endotoxins



# **Endotoxin detection reagents** (Seikagaku Corporation, ACC)

- Manufacture and sale of reagents for detecting endotoxins\* in the manufacturing process of pharmaceuticals, etc. (Japan, USA, Europe, etc.)
- Used mainly at pharmaceutical companies
- Launch of PyroSmart NextGen, a recombinant endotoxin detection reagent, in April 2021
- Accelerated global expansion of recombinant reagents

\*Since endotoxins exhibit strong pyrogenic activity even in minute amounts, they must be rigorously controlled pursuant to regulations in the manufacture of pharmaceuticals and medical devices.

►Global market: Approx. ¥2.5 mil

(Seikagaku estimate / including related equipment)

# Glucan detection in vitro diagnostic agents (ACC)

- Manufacture and sales of in vitro diagnostic agents for measuring the glucan\* concentration in blood for use in the diagnosis of deep fungal infections (USA, Europe, etc.)
- Since symptoms of deep fungal infections can be similar to those of COVID-19, the products are used together with COVID tests as necessary to ensure appropriate diagnosis and treatment
- Used mainly at hospitals and testing centers
- Market expansion into additional countries

\*(1→3) - $\beta$ -D-glucans are structural components of the cell walls of fungi, as typified by molds and yeasts.





## 受託試験サービス(ACC社)

- Contract testing for endotoxin and glucan contamination
- Contributes to quality control at pharmaceutical companies and medical institutions



### **Outline of Associates of Cape Cod, Inc.**

## Developed the world's first endotoxin detection reagent and obtained FDA approval in 1977 / Sales network spanning 80 countries

### Associates of Cape Cod, Inc. (ACC社)

- Headquarters: Massachusetts, U.S.A.
- Established: 1974 (became a Seikagaku subsidiary in 1997)
- Business areas: Manufacture and sale of endotoxin detection reagents and glucan detection in vitro diagnostic agents, provision of contract test services
- Number of employees: 263 (as of March 31, 2022)



Recombinant LAL reagent PyroSmart NextGen®



Endotoxin detection reagents PYROCHROME®

Exterior of the ACC office



## Dalton, a Canadian CDMO, becomes a subsidiary Acquiring a pharmaceuticals manufacturing base compliant with US/Canadian GMP

### **Outline of acquisition**

- Name: Dalton Chemical Laboratories, Inc.
- Acquisition cost: Up to CAD 41 million
- Acquisition method : Acquired all issued shares

### **Dalton Chemical Laboratories, Inc.**

- Location: Toronto, Ontario Province, Canada
- Established: 1986
- Business description:
   Contract manufacturing services (CDMO\*), including the manufacturing of chemosynthesis products and active pharmaceutical ingredients (API) and API process development for pharmaceutical companies



Exterior of the Dalton offices

- Employee number: 147 (2022.3)
- \*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.



## Established new company in Canada, promoting development of Seikagaku pharmaceuticals and medical devices in North America

### SEIKAGAKU NORTH AMERICA CORPORATION

Location : Toronto, Ontario Province, Canada

Established : January 25, 2022

Capital : CAD10

Business description: Development of pharmaceuticals and medical devices in

North America

### **Purpose of establishment**

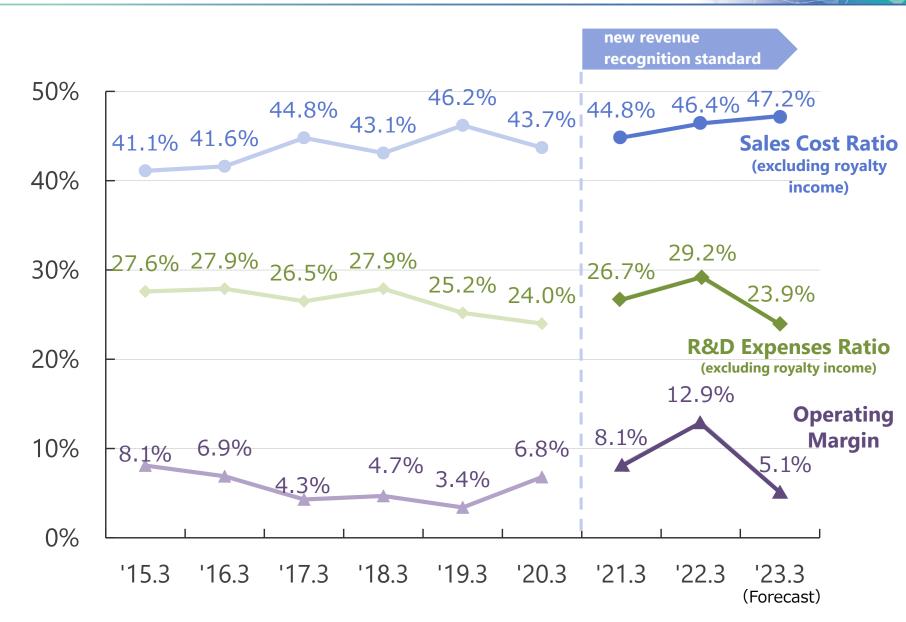
- Enable responses with fewer constraints on time differences or distance by operating a development base in North America
  - Formulate development plans more closely aligned with local medical environment
  - Create smooth communications with U.S. Food and Drug Administration (FDA) and clinical trial sites



Strengthening the development system in North America.

Aiming to accelerate pharmaceutical and medical device development as well as obtaining of approvals

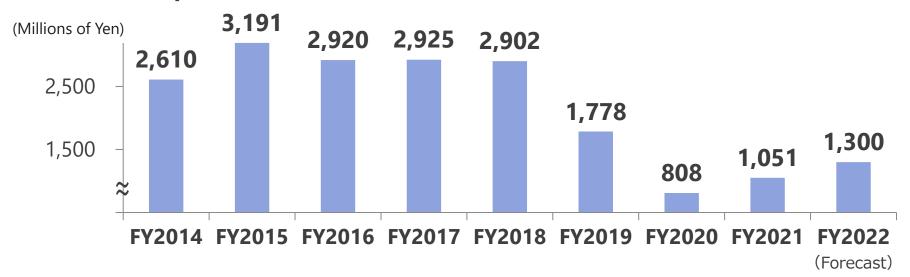
### **Trend in Financial Index**





## Impairment loss taken in FY2019 Depreciation will trend toward ¥1.0 billion

### **■** Trend in Depreciation



### ■ Trend in Capital Investments (Millions of Yen)

FY2014	FY2015	FY2016	FY2017	FY2018	FY2019	FY2020	FY2021	FY2022 (Forecast)
2,095	1,975	1,173	1,591	1,310	2,109	2,127	2,194	3,000



### **Overview of Current Mid-term Management Plan**

FY2025 numerical targets

Net sales ¥40.0 billion

Operating income ¥7.0 billion

Next mid-term management plan

**Next Stage** 

Current mid-term management plan Fiscal 2022 to Fiscal 2025

Previous mid-term management plan

Solidification of the profit foundation

A period for achieving growth

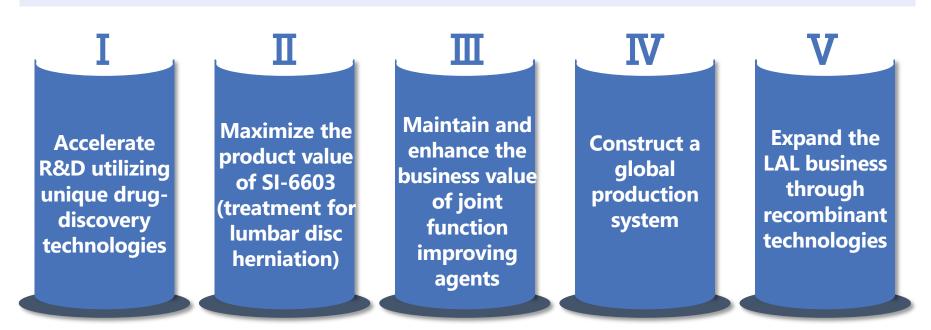
Based on a solidified profit foundation, nurture the capability to maintain a constant growth trajectory by energetically implementing the key measures

Aim to achieve record-high business results in the final year of the plan



### **Overview of Key Measures**

## **Five Key Measures** (Strategic Pillars)



### **Business foundation**

Enhancement of employee engagement/
Organizational strengthening and human resource development



### **Accelerate R&D Utilizing Unique Drug-Discovery Technologies**

## Aim to leverage Seikagaku's GAG-related technologies to create products needed by patients

### **Unmet medical needs**

- Existing fields (orthopedics,ophthalmology)
- New fields



Creation of new development themes in existing fields

Glycoscience

**Modalities** 

Application

### GAG-related basic technologies

- Cross-linking
- Chemical modification
- Fermentation etc.

- Design of GAG adapted to the characteristics of various modalities
- Establishment of innovative technologies that make possible provision of optimal drug delivery systems (DDS)

Creation of innovative research themes, including in new disease areas

#### **Pursuit of alliances**

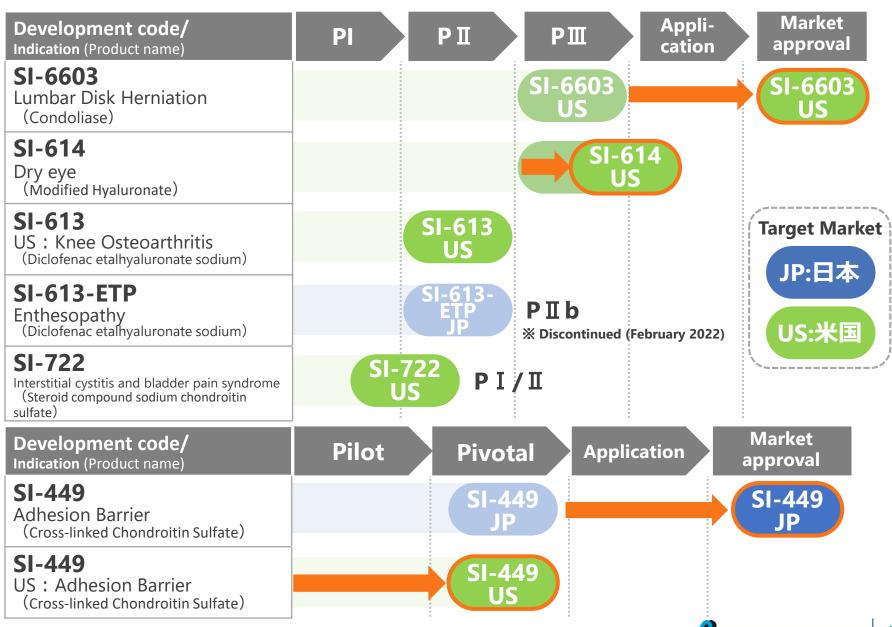
\*GAG: Glycosaminoglycans, such as hyaluronic acid and chondroitin sulfate, which are structural components known as glycoconjugates.



## A

### I . Accelerate R&D Utilizing Unique Drug-Discovery Technologies

### **Pipeline List (Research and Development themes)**



### Obtain clinical study findings during FY2025 Aim for an NDA and approval during the period of the current mid-term management plan



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

<sup>\*</sup> SEIKAGAKU NORTH AMERICA: Established in January 2022 in Canada with the aim of accelerating development of pharmaceuticals and medical devices and obtaining regulatory approval



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

## Pursue corporate value enhancement through maximization of Seikagaku products in the market for joint function improving agents and cost structure improvement

### 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



### **Construct a Global Production System**

## Further reinforce a stable supply of products on the basis of a GMP-compliant, appropriate governance system



Seikagaku Corporation Takahagi Plant (Ibaragi Prefecture, Japan)



### DALTON CHEMICAL LABORATORIES, INC. (Toronto, Canada)



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



### **Strategic Direction for the LAL Business**

## Aim to be a leading company in the market for recombinant endotoxin detection reagents and glucan detection in vitro diagnostics

### **Pursuit of Unique Value**

Refine the joint development system on the basis of further collaboration with ACC.\*

► Next-generation products (recombinant technologies, new reagents, new measurement systems)

### **Collaboration with Affiliated Companies**

Create value from business models and operating systems that cannot be created independently

► Automatic measurement devices



\* Associates of Cape Cod: Overseas subsidiary responsible for overseas expansion of the LAL business

## Creation of unique value that competitors cannot imitate in a market with strong customer needs





### **Initiatives for Expansion of the LAL Business**

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

### 1. Endotoxin detection reagent business

- Acceleration of global expansion of endotoxin detection reagents leveraging recombinant technologies
- Accumulation of reliable scientific data utilizing PyroSmart NextGen Recombinant LAL Reagent (launched in 2021) and market penetration and sales promotion through support for early adopters

### 2. Diagnostics business

- Increase in the number of countries where glucan detection in vitro diagnostics are sold and acceleration of new expansion into the hospital market
- Progress in development of recombinant glucan detection in vitro diagnostics and product portfolio expansion

### 3. Measurement equipment and software business

 Promotion of development and improvement of automatic measurement equipment and software in Japan and overseas in collaboration with an affiliated company



### **Materiality**

## Seikagaku has identified important issues that should be addressed on a priority basis in the interest of achieving sustainable development of society and enhancement of corporate value

1	Creation of truly useful pharmaceuticals and medical devices	17 /i=13-0-070
2	Provision of a stable supply of pharmaceuticals and medical devices of guaranteed quality	12 268 ME
3	Expansion of healthcare access and appropriate provision of high-quality medical information	3 #ATOME
4	Fair and ethical business activities and strengthening of corporate governance	16 ##£@46
5	Promotion of diversity and development of human resources	10 A>BOARB  €60€5
6	Engagement in environmentally friendly corporate activities	14 %0 # h t t t t t t t t t t t t t t t t t t



Seikagaku will focus on initiatives related to these material issues, which will become the foundation for the key measures in the mid-term management plan



### **Mid-term Management Plan: Sustainability**

### **Sustainability-Related Initiatives**

### **Healthcare**

- Acceleration of multinational expansion and new drug development.
- Strengthening and utilization of original GAG-related basic technologies
- Product improvement and post-marketing product development aligned with medical needs

Related material issues: 1, 2, 3

### **Environment**

- CO2 emissions reduction (33.6% reduction from the reference year by FY2030)
- Zero waste emissions and promotion of use of recycled raw materials
- Biodiversity preservation activities, including reduction or elimination of use of animal-derived materials in products

Related material issues: 6

### Society

• Strengthening of initiatives for respect of human rights in the supply chain

 Boosting of employee motivation through strengthened HR systems and introduction of diversity measures and work-life balance measures that lead to employee retention

Related material issues: 5

### Governance

- Development and operation of a highly effective corporate governance system
- Fostering of compliance awareness and a quality culture
  - Enhancement of preventive maintenance activities for a stable supply of products

Related material issues: (4)

Numerical	

	FY2021 results	FY2025 target
Net sales	¥34.8 billion	¥40.0 billion
<b>Operating income</b>	¥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 businesses
- Ratio of R&D expenses to sales (excluding royalty income): target of 25%
- Exchange rate: ¥135/US\$1



### Aim to achieve record-high business results



### **Basic Policy on Profit Distribution**

### Make investments for sustained profit growth and corporate value enhancement and pay stable dividends



**Strategic** investment

**Business** investment

### Shareholder returns

- Consider dividend increases with ¥26 per share as a guideline, taking into account business performance, etc.
- Consider treasury stock purchases as appropriate.

### **Business investment**

- Continue efficient investments related to R&D and production. Make active business investments in
- sustainable activities.

### Strategic investment

Flexibly consider strategic investments offering prospects for future growth and synergy effects.



### **Mid-term Management Plan Summary**



### **Business foundation**

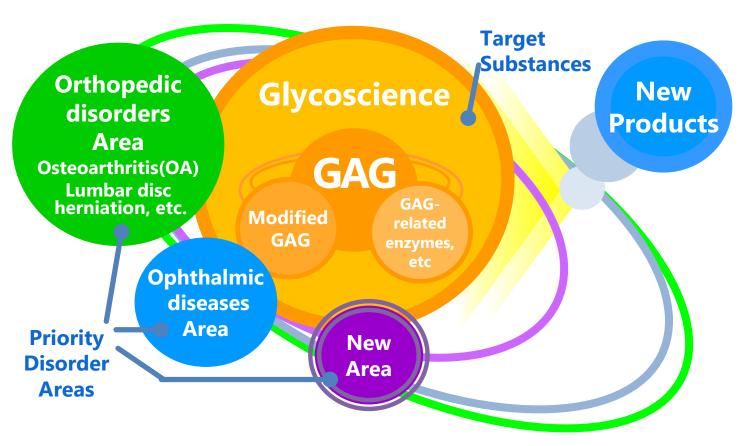
Enhancement of employee engagement/
Organizational strengthening and human resource development



Nurture the capability to maintain a constant growth trajectory by energetically implementing the key measures



## Continue Our R&D policy to make the most of our technology and knowledge



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



### **Clinical Study Information**

Development code/ Indication	Develop- ment Location	Clinical Study Title (Study ID)	Target Enroll- ment	Estimated Period	Primary End Point (Primary Follow-up period)
SI-6603 Lumbar Disk Herniation	U.S.	Phase III additional study (NCT03607838)	320	May. 2018 – Nov. 2022	Leg pain (13 weeks)
SI-613-ETP Enthesopathy	Japan	Late-stage Phase II clinical study (JapicCTI-173758)	240	Oct. 2017 – Oct. 2018	Pain in motion (4 weeks)
SI-613 Knee Osteoarthritis	U.S.	Phase II clinical study (NCT03209362)	80	Oct. 2017 – Nov. 2018	WOMAC(Knee pain) (12 weeks)
SI-614 Dry eye	U.S.	Phase III clinical study	240	May. 2022 – Jan. 2023	
SI-722 Interstitial cystitis and bladder pain syndrome	U.S.	Phase I / II clinical study (NCT04208087)	32	Mar. 2020 – Jan. 2021	Maximum observed plasma concentration
SI-449 Adhesion Barrier	Japan	Pivotal study (Field of gastroenterological surgery) (JapicCTI-205343)	130	Jun. 2020 – Dec. 2022	Efficacy
<b>SI-449</b> Adhesion Barrier	Japan	Pilot study (Field of gynecology) (jRCT2072210100)	10	Dec. 2021 – Sep. 2022	Usability, Safety

Note: The table shows data registered (or planned to be registered) on clinical trial information websites.

The information is updated from time to time. Refer to the websites for details and the latest information. (The websites can be accessed from the trial ID links.)

- · Japan Pharmaceutical Information Center(JAPIC) http://www.clinicaltrials.jp/user/cteSearch\_e.jsp
- University hospital Medical Information Network (UMIN) Center <a href="http://www.umin.ac.jp/ctr/index.htm">http://www.umin.ac.jp/ctr/index.htm</a>
- ClinicalTrials.gov <a href="https://clinicaltrials.gov/ct2/search">https://clinicaltrials.gov/ct2/search</a>



## Planned receipt of milestone royalties in accordance with future progress in development and marketing

Development Code Indication	Develop- ment Location	Sales Partner	Total Amount of Milestone Royalties ( of which, in upfront payment )
SI-6603 Lumbar Disk Herniation	U.S.	Ferring Pharmaceuticals (Switzerland)	Max. US \$95 million (US \$5 million)
	Japan	Ono Pharmaceutical Co., Ltd.	Max. ¥12.0 billion (¥2.0 billion)
SI-613	U.S.	Searching	_
Japan: Osteoarthritis U.S.: Knee Osteoarthritis	China	Eisai Co., Ltd.	_
	Korea	Eisai Co., Ltd.	_
SI-613-ETP Enthesopathy	Japan	Ono Pharmaceutical Co., Ltd.	*included in the above
SI-614 Dry eye	U.S.	Searching	_
SI-722 Interstitial cystitis	U.S.	_	_
SI-449 Adhesion Barrier	Japan	_	_

### Seikagaku's vision

	Our vision	A company that is valued by the world through its innovative drug discovery
	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	<ul> <li>We create a corporate environment of mutual trust and communication using individual abilities.</li> <li>We create innovative and useful products through in-depth cooperation between industrial and academic circles.</li> <li>We assure the highest quality and safety of our products.</li> <li>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.</li> </ul>
N	Aission statement	"Glycoscience for human well-being"

### **Special Profile**



### **Specialization in Glycoscience**

- Niche field, market not big enough for the major pharmaceutical companies to penetrate
- Focusing on this field more than 70 years

# 2

### State-of-the-art technology related to GAG

- Drug discovery expertise using modified-GAG, GAG-related enzymes, etc.
- Extraction, Purification, Fermentation, etc. technology to manufacture GAG related products



### **Unique business model**

- ■Concentration on **R&D** and **manufacturing**
- R&D staff comprising **40%** of our employees (Non-consolidated base)
- Allocation of **25%** of net sales to R&D investment



### **Our Business Segment**



### **Pharmaceutical** Business **73.7**%

**Domestic Pharmaceuticals** 

**⇒** 32.8%



Joint Function Improving Agents



Treatment for lumbar disc herniation

**Overseas Pharmaceuticals → 22.0**%



Joint Function Improving Agents





**Ophthalmic** Surgical Aids

**Bulk Products/ CDMO** 

**→ 7.5**%



**Bulk Products** 

**Net Sales** 

34,851 million

(FY2022 Results)

**Royalty income** 11.4%



**LAL Business** 26.3%

**Endotoxin-detecting reagents** 

(used mainly for quality control of pharmaceuticals and medical devices)











### **ARTZ**<sup>®</sup> Joint function improving agent by multiple injections

- The first HA joint function improving agent in the world
- Main distributors:

Kaken Pharmaceutical (Japan): ARTZ

Bioventus (U.S.): SUPARTZ FX

Kunming Baker Norton

Pharmaceutical (China): ARTZ



### **Gel-One**<sup>®</sup> Intra-articular single-injection viscosupplement for the treatment of knee osteoarthritis

- Requires only 3ml to be as effective as multiple injections
- Full-scale sales since August 2012
- Distributor: Zimmer (U.S.)



