**Exploring the Innovative Promise of Glycoscience** 

# **Financial Results for the 1st Half of Fiscal Year 2018** (April 1, 2018 – September 30, 2018)



http://healthy-knee.com/



(TSE:4548)

## Contents

1H Financial Results	Р3	Research and Development	P15
<ul> <li>Net Sales</li> </ul>	P4-6	<ul> <li>SI-6603 (Lumbar disc herniation)</li> </ul>	P16
• Income	P7	<ul> <li>SI-613 (Osteoarthritis/Enthesopathy)</li> </ul>	P17
Full Year Forecasts	<b>P8</b>	<ul> <li>SI-449 (Adhesion Barrier)</li> </ul>	P18
<ul> <li>Trend in R&amp;D Expenses</li> </ul>	P9	Basic Policy on	P19
Sales by Business Segment Sales by Business Segment	ent	Profit Distribution	. 13
<ul> <li>Domestic Pharmaceuticals</li> </ul>	P10-11		<b>P20</b>
<ul> <li>Overseas Pharmaceuticals</li> </ul>	P12-13	Management Plan	
• LAL	P14	Appendix	P21

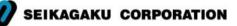
#### < Cautionary Notes >

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 1H of FY2018**

	1H FY2018	Year-o	n-Year	(Reference) FY2018 Full Year Forecasts		
(Millions of Yen)	Results	Change	% of Change	FY 2018 Forecasts	Degree of Progress	
Net sales	14,256	-1,239	-8.0%	28,100	<b>50.7</b> %	
Operating Income	963	-1,255	-56.6%	400	<b>241.0</b> %	
Ordinary Income	2,475	-2,319	-48.4%	2,250	110.0%	
Net Income	1,912	-1,638	-46.1%	1,700	112.5%	
<b>R&amp;D Expenses</b> (Ratio to net sales)	<b>3,287</b> (23.1%)	+82 (+2.4pt)	+2.6%	<b>7,050</b> (25.1%)	<b>46.6</b> %	
Average Exchange Rate (1US\$)	¥110.27	-¥0.80		¥105.00		
		1H FY2018 Results	1H FY2017 Results	(Reference) FY2018 Forecasts		
Net Income per Share		¥ 33.85	¥ 62.73	¥ 30.11		



# Net sales by Business Segment (1H of FY2018)

(	Millions of Yen)	1H FY2018 Results	Year-on- Year	% of Change
	Net sales	14,256	-1,239	-8.0%
	Pharmaceuticals	10,939	-1,620	-12.9%
	Domestic Pharmaceuticals	6,974	-1,478	-17.5%
	Overseas Pharmaceuticals	3,429	-157	-4.4%
	Bulk Products	535	+16	+3.1%
	LAL Business	3,317	+380	+13.0%
((	Overseas sales)	6,224	+203	+3.4%

\*Foreign exchange impact on overall net sales: approx. -100 million yen

#### **Domestic Pharmaceuticals**

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

•Sales down sharply, reflecting the impact of NHI drug price reductions implemented in April 2018 (-14.3%)



ARTZ: Joint function improving agent with hyaluronic acid as its main ingredient

### > OPEGAN series (Ophthalmic surgery aid)

•Sales at the prior-year level, with continued growth from SHELLGAN compensating for NHI drug price reductions(approx. -9%)



SHELLGAN: OPEGAN series product used in cataract surgery (launched July 2016)

## > MucoUp

#### (Submucosal injection agent for endoscopic surgery)

•Sales up, thanks to sales expansion measures by the sales partner

#### HERNICORE (treatment for lumbar disc herniation)

- ·Launched in August 2018
- ·Seikagaku sales small since it is the launch year



# Net sales by Business Segment (1H of FY2018)

(IV	lillions of Yen)	1H FY2018 Results	Year-on- Year	% of Change
	Net sales	14.256	-1,239	-8.0%
F	Pharmaceuticals	10,939	-1,620	-12.9%
	Domestic Pharmaceuticals	6,974	-1,478	-17.5%
	Overseas Pharmaceuticals	3,429	-157	-4.4%
	Bulk Products	535	+16	+3.1%
I	LAL Business	3,317	+380	+13.0%
(C	)verseas sales)	6,224	+203	+3.4%

\*Foreign exchange impact on overall net sales: approx. -100 million yen

#### SEIKAGAKU CORPORATION

#### **Overseas Pharmaceuticals**

\*Foreign exchange impact on Overseas Pharmaceuticals: approx. -10 million yen

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

- ·Both local sales and Seikagaku sales up
- •Growth rate trending down in an increasingly adverse market environment



Gel-One: Single-injection joint function improving agent

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

Seikagaku sales down sharply, reflecting soft local sales and a decline in shipments from a high level in 1H FY2017

#### • ARTZ in China

- ·Local sales on an upward trend
- Seikagaku sales up, partly reflecting a rebound from a local inventory adjustment implemented in 1H FY2017

## Net sales by Business Segment (1H of FY2018)

	1H FY2018 Results	Year-on- Year	% of Change	Bulk Products
Millions of Yen) Net sales		-1,239		<ul> <li>Sales of hyaluronic acid down</li> <li>Overseas sales of chondroitin sulfate up</li> <li>*Bulk Products : High-purity, high-quality hyaluronic acid and chondroitin sulfate for pharmaceutic</li> </ul>
Pharmaceutical	10,939	-1,620	-12.9%	LAL Business
Domestic Pharmaceuticals	6,974	-1,478	-17.5%	*Foreign exchange impact on LAL Business: approx90 million ye Strong sales of endotoxin-detecting reagents and other products in Japan and overseas
Overseas Pharmaceuticals	3,429	-157	-4.4%	*LAL Business : The manufacturing and sales of Endotox detection reagents used in the quality control of pharmaceuticals
Bulk Products	535	+16	+3.1%	<b>Overseas Sales Ratio</b>
LAL Business	3,317	+380	+13.0%	Overseas 12 70 Year-on-Year: Up 4.8pt
(Overseas sales)	6,224	+203	+3.4%	43.7% Up 4.8pt Domestic 56.3%
Foreign exchan		overall net prox100 r		
SEIKAGAKU CO	PORATION			Overseas LAL/Bulk Overseas Pharmaceuticals Domestic sa

# Income for 1H of FY2018 (Year-on-Year)

	1H FY2018		% of	Operating Income
(Millions of Yen)	Results	Year	Change	Cost of Sales Ratio (+3.6pt):
Net sales	14,256	-1,239	-8.0%	Increase due to the impact of NHI drug price reductions
Cost of Sales (Cost of Sales ratio)	<b>6,518</b> (45.7%)	+ <b>0</b> (+3.6 <sub>pt</sub> )	+0.0%	<ul> <li>SGA Expenses (+14):</li> <li>Decrease at Seikagaku due to expense cutting</li> </ul>
SGA expenses	6,774	+14	+0.2%	<ul> <li>Increase at the overseas subsidiary accompanying stepping up of overseas sales activities in the LAL business</li> </ul>
<b>R&amp;D Expenses</b> (to Net sales ratio)	<b>3,287</b> (23.1%)	+82 (+2.4pt)	+2.6%	<ul> <li>At the prior-year level on a consolidated basis</li> </ul>
Operating Income (to Net sales ratio)	<b>963</b> (+6.8%)	<b>-1,255</b> (-7.5pt)	-56.6%	Net Income
Ordinary Income	2,475	-2,319	-48.4%	<ul> <li>Non-operating Income / Expenses (-1,064)</li> <li>Increase in gain on sale of investment securities (+576)</li> </ul>
Net Income	1,912	-1,638	- <b>46.1</b> %	<ul> <li>Year-on-year decrease in royalty income (-1,491)</li> </ul>
				Income Taxes (Tax Rate: 22.7%):
Depreciation	1,446	-21	- <b>1.5</b> %	Impact of a tax decrease in the U.S. (-3.2pt)



# **Overview of Forecasts in FY2018**

* There is no change in forecast announced on May 11, 2018.											
	FY	2018		F	Y201	.7 Re	esult	S		(Reference)	
(Millions of Yen)		ecasts	Re	esults	CI	Change		% of Chang	je	Degree of 1H progress	
Net sales	2	8,100		30,175	-2,075		)75	- <b>6.9</b> %		<b>50.7</b> %	ó
Operating Income		400		1,421		-1,0	)21	-71.9	%	241.0%	6
Ordinary Income		2,250		5,327	-3,077		)77	-57.8%		110.0%	6
Net Income		1,700		3,922 -2,22		222	<b>22</b> - <b>56.7</b> %		% 112.5%		
<b>R&amp;D Expenses</b> (to Net sales ratio)		<b>7,050</b> (25.1%)		<b>8,408</b> (27.9%)		- <b>1</b> ,3 (-2	<b>358</b> .8pt)	-16.2	%	46.6%	6
Average Exchange Rate (1US\$)		¥105.00		¥110.86	¥-5.86		5.86	5			
		FY201 Foreca	-	FY2017 Results			Exchange Rate (Impact of a change of				
Net Income per share ¥30.1		80.11	¥(	69.30			Net sales	Appro	Approx. ¥110 million		
Dividend per sha	ire	¥26.00		¥26.00					x. ¥55 million		
Dividend Payout r	atio	8	6.4%				Oper	ating income	Applo	×. +55 minor	
											8

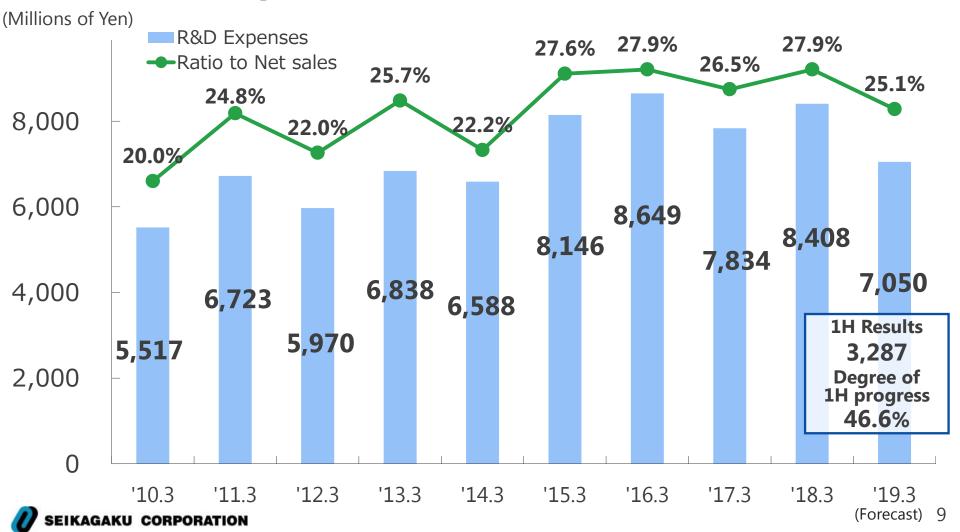


SEIKAGAKU CORPORATION

## **Trend in R&D Expenses**

\* There is no change in forecast announced on May 11, 2018.

# Specializing in glycoscience and engaging in prioritized, efficient R&D



## **Domestic Pharmaceuticals**

(Unit deliveries to medical institutions/Year-on-Year)

Joint-function improving agent <b>ARTZ</b>	1H FY2018 Results	FY2018 Forecasts			
	<ul> <li>Market contraction due in part to an increase in treatment options, such as the emergence of concomitant medications</li> <li>Only a slight decline in sales of ARTZ thanks to sales partner sales promotion measures</li> </ul>	<ul> <li>Introduction of a improformulation in October</li> <li>Aim for a further mark</li> <li>*ARTZ Dispo drug price rev</li> </ul>	r et share increase		
	ARTZ growth rate: -1.1% (Market growth rate: -2.5%) Market share: 59.2% (+0.9pt)	ARTZ growth rate +0.8% (forecast)	Market share <b>59.0%</b> (forecast)		
Ophthalmic surgical aids <b>OPEGAN</b>	1H FY2018 Results	FY2018 Fo	recasts		
(including SHELLGAN)	<ul> <li>Further market penetration for SHELLGAN due to vigorous sales promotion activities</li> <li>Market share expansion</li> <li>Publicize SHELLGAN's product fea Aim to capture share from compe- continuing targeted sales promotion</li> <li>*OPEGAN series price reduction rate:</li> </ul>				
	OPEGAN growth rate: +9.4% (Market growth rate: +3.9%) Market share: 43.9% (+2.2pt)	OPEGAN growth rate +7.2% (forecast)	Market share <b>44.5%</b> (forecast)		

## **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**

(As of November 2018)

#### Physicians to whom any of 1 to 3 below applies and who have experience in performing lumbar puncture

- **1.** Japanese Society for Spine Surgery and Related Research or Neurospinal Society of Japan accredited supervisory physician
- **2.** Physician under the direction of a Japanese Society for Spine Surgery and Related Research or Neurospinal Society of Japan accredited supervisory physician
- 3. Physician who has participated in a HERNICORE clinical trial

#### (As of November 2018) Facility requirements Facilities that meet all of the conditions below

- **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

We plan to review these requirements with the consent of PMDA\* approximately six months to one year after launching, following collection and careful examination of post-marketing safety information etc.

\*PMDA: Pharmaceuticals and Medical Devices Agency

#### SEIKAGAKU CORPORATION

## **Overseas Pharmaceuticals** (1H FY2018 Results Year-on-Year / value basis)

#### Overseas Pharmaceuticals Sales trend

(Millions of Yen)

#### <Breakdown>



**1H FY2018 Results** -**4.4%** (Foreign exchange impact -0.2%) Decrease on lower sales of SUPARTZ FX in the U.S., despite increases in Gel-One sales and exports of ARTZ to China **\*Foreign exchange impact: approx. -¥10million** 

## **Gel-One** (Single injection)

• Sales in the U.S.: Growth of approx. 3% (volume basis)

#### Seikagaku exports:

Increase accompanying a local sales increase

## **ARTZ** (Multiple injection)

#### • SUPARTZ FX in the U.S.

Local sales down sharply due to the strong impact of intensification of competition and suspension of reimbursement for HA\* injectable treatments by some insurance companies (approx. -11%, volume basis)

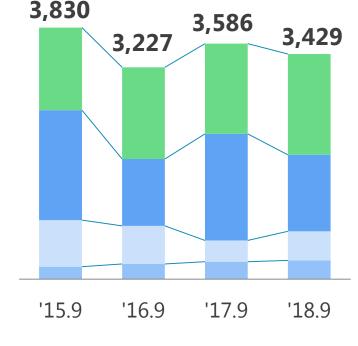
#### ARTZ in china

Increase due to successful strengthening of sales expansion activities targeting not only urban areas, but also surrounding areas

#### Seikagaku exports

Sharp decrease due to softening of sales of SUPARTZ FX in the U.S. and a decline in shipments from a high level in 1H FY2017, despite an increase in exports to China

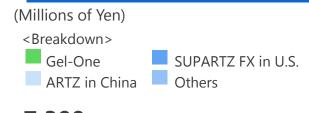
\*HA: Hyaluronic acid

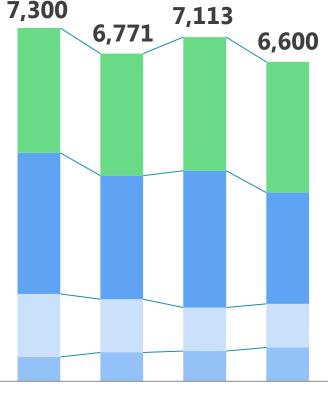




## **Overseas Pharmaceuticals** (FY2018 Forecast Year-on-Year / value basis)

#### **Overseas Pharmaceuticals Sales trend**





'18.3

'19.3 (forecast)

'17.3



**FY2018 Forecasts** -7.2%

Expected decrease due to the impact of suspension of reimbursement for HA\* injectable treatments by some insurance companies in the U.S.

## **Gel-One**(Single injection)

#### Sales in the U.S.:

Revision of projected growth rate from +7% to +3% (volume basis)

#### > Seikagaku exports:

Slight strengthening due to the positive impact of exchange rates due to yen depreciation exceeding the assumption at the beginning of the fiscal year

## **ARTZ** (Multiple injection)

#### SUPARTZ FX in the U.S.

Forecast revised downward (from -5% to -11%, volume basis) due to an uphill battle for local sales in an increasingly adverse market environment

#### ARTZ in China

Forecast of a continued increase, with sales in line with the assumption at the beginning of the fiscal year

#### Seikagaku exports

Exports weakening due to a decline in sales of SUPARTZ FX in the U.S. exceeding the assumption at the beginning of the fiscal year

\*HA: Hyaluronic acid

SEIKAGAKU CORPORATION

'16.3

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

#### LAL Business Sales trend

(Millions of Yen)

Full year
 <1H Breakdown>
 Overseas
 Domestic



## 1H FY2018 Results: +13.0% (Year-on-Year)

#### **Overseas**

\*Foreign exchange impact: approx. - ¥90million

Growth in sales of endotoxin-detecting reagents and glucan-detecting in-vitro diagnostic reagents (Products which are used for the diagnosis of fungal infections)

### Domestic

Increase in sales of endotoxin detection equipment

FY2018 Forecast: +1.2% (Year-on-Year)

#### **Overseas**

Continue the switch to direct selling in Europe from selling through distributors, and additional reinforcement of sales operations

## Domestic

Forecast of sales at roughly the prior-year level

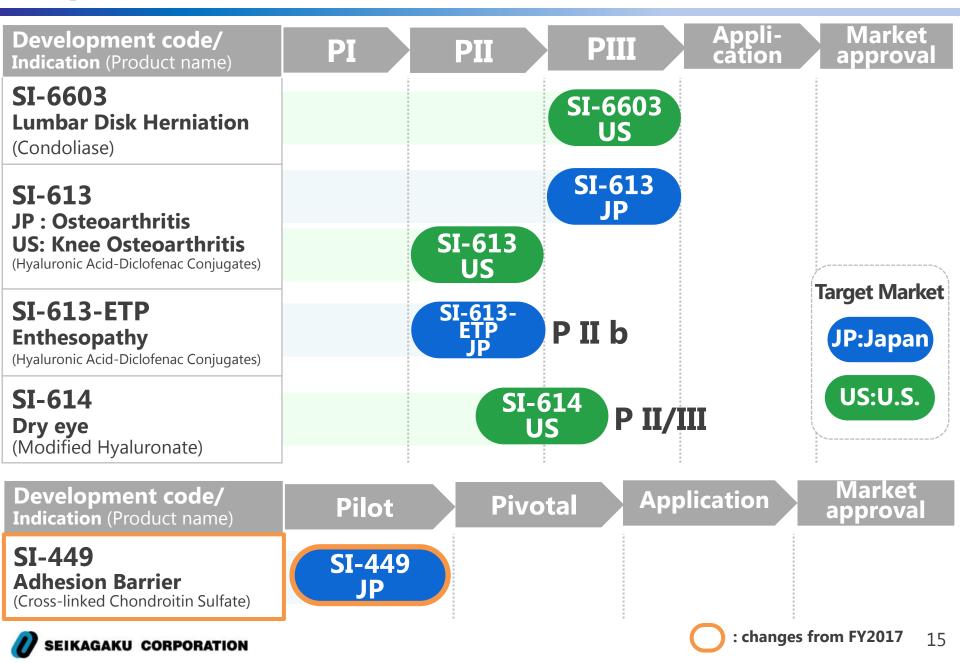
LAL Business :

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

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

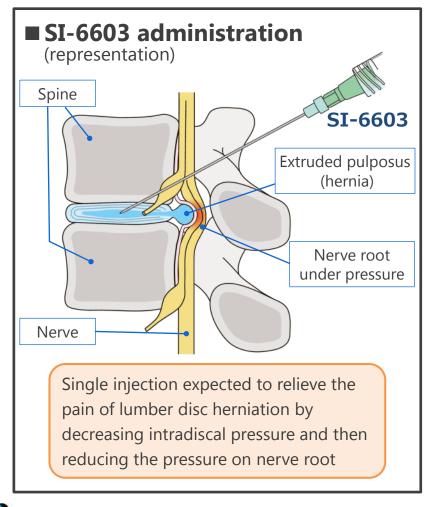


## **Pipeline List** (Research and Development themes)



## SI-6603 Outline (Treatment for Lumbar Disc Herniation)

## Initiated a Phase III additional study in the U.S. in Feb 2018 **Consider expansion to countries where approval data from** Japan can be used in NDA



- Development code: SI-6603 (Product name in Japan : HERNICORE)
- Generic name: Condoliase
- Indication: Lumbar disc herniation
- Method of use: Injection into lumbar disc (under X-ray observation)

### U.S. : P III

#### November 2017: Announcement of PIII (previous) study results

No statistically significant improvement in the primary endpoint found

#### February 2018: PIII additional study initiated

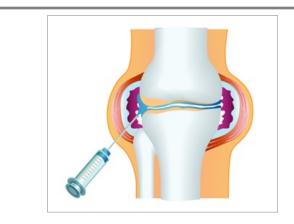
#### Increase the probability of success by making changes from the previous study

- Decrease the number of cases. (385  $\Box$ ) approx. 320 cases)
- Shorten the follow-up period. (2 years  $rac{1}{2}$  1 year)
- Introduce a more objective hernia evaluation and confirmation method at the pre-enrollment stage
- Change the local CRO (contract research organization)

16

# **SI-613 Outline** (Treatment of Osteoarthritis/Enthesopathy)

# Aiming at prompt and sustained relief of the pain and inflammation associated with osteoarthritis or Enthesopathy



- Substance: Hyaluronic Acid-Diclofenac Conjugates
- Formulation: Injection into the joint cavity or near the tendon or ligament enthesis

#### Japan: P III (Indication: Osteoarthritis) P IIb (Indication: Enthesopathy)

- February 2017: Phase III study initiated (3 studies conducted)
   Knee confirmatory study, study for four sites, long-term administration study
- September 2017: Definitive agreement on co-development and marketing collaboration in Japan concluded with Ono Pharmaceutical Co., Ltd.
- September 2017: Late-stage Phase II clinical trial for enthesopathy initiated

#### **U.S.**: **PII** (Indication: Knee osteoarthritis)

17

• June 2017: Phase II study initiated

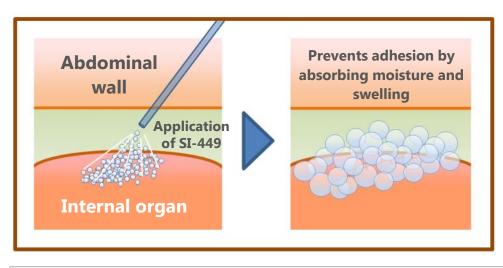
- Features
   Provision of prompt and sustained relief of the pain and inflammation associated with osteoarthritis and enthesopathy by combining hyaluronic acid with Diclofenac (Anti-Inflammatory Drug) using a proprietary technology, and designing the formulation for sustained release\* of the Diclofenac
  - Mitigation of NSAID (Non-Steroidial Anti-Inflammatory Drug) side effects reported in oral or topical administration

\* Sustained release: Gradual release of active ingredients to achieve a sustained therapeutic effect **KAGAKU CORPORATION** 



## SI-449 Outline (Adhesion Barrier / Medical Device)

## Powdered formulation for preventing or mitigating postoperative adhesions by forming a barrier between the surgical wound site and surrounding tissues



- Substance: Cross-linked chondroitin sulfate
- Description: Adhesion barrier
- Method of use: Intra-abdominal application (powdered formulation)

## Japan: Pilot study

#### May 2018: Pilot study initiated

Proceed with development with a view to global development

#### **Expected Features:**

- By absorbing moisture and swelling, SI-449 forms a barrier between the surgical wound site and the surrounding tissues and is expected to prevent or mitigates post-operative adhesions
- It consists of substances naturally present in the body, including the cross-linking agent, and is highly biocompatible
- Since SI-449 is a powdered formulation, it adheres well to uneven tissue surfaces and is thought to offer excellent utility in laparoscopic surgery, a common surgical procedure

# **Basic Policy on Profit Distribution**

# Aim to enhance shareholder returns and realize sustained growth by engaging in well-balanced business investment

## Shareholder Return Policy

- Aim for stable and continuous dividends from a medium to long term perspective
   Continue to pay an annual dividend of ¥26 per share
- Consider purchases of treasury stock, as appropriate, taking into account future business development and the total return ratio

Treasury stock purchases in June-July 2018 (200,000 shares / ¥302 million)

#### **Business Investment**

Business investment in R&D, production system development, and other areas

	FY2013	FY2014	FY2015	FY2016	FY2017	FY2018 (Forecast)
Net Income per share	¥83.55	¥64.27	¥45.39	¥31.55	¥69.30	¥30.11
Annual Total Dividend	¥26.00	¥26.00	¥26.00	<b>*</b> ¥31.00	¥26.00	¥26.00
<b>Dividend Payout Ratio</b>	31.1%	40.5%	57.3%	98.3%	37.5%	86.4%

\* including a 70th anniversary commemorative dividend of ¥5 per share



# **Toward the Next Mid-term Management Plan**

## Changes in the market environment

- Deteriorating profitability of existing products accompanying drug price system reform in Japan
- Intensification of competition for hyaluronic acid formulations and tightening of insurance reimbursement in the U.S

## Earnings structure improvement

- Clear identification of high-priority research and development themes
- Rigorous cost-cutting, including product cost reduction

# Business development in preparation for a new growth trajectory

- Cultivation of growth drivers (HERNICORE, SI-613 in Japan, SI-6603 in the U.S.)
- Expansion of existing products into other countries

## Consideration of capital policy





# Forecasts (Net sales) in FY2018

approx. -660 million yen

SEIKAGAKU CORPORATION

	* There is no change in forecast announced on May 11, 2018.									
	FY2018	Year-o		Net Sales						
(Millions of Ye	n) Forecasts	Change	% of Change	Forecast of lower sales due to NHI drug price						
Net sales	28,100	-2,075	-6.9%	reductions of domestic pharmaceuticals and the impact of yen appreciation						
				*Forecast of a small amount of sales in Japan for HERNICORE in its launch year						
Pharmaceutica	als 22,100	-2,144	-8.8%	Pharmaceuticals Business						
Domestic Pharmaceutica	als 14,550	-1,575	<b>-9.8</b> %	Domestic Pharmaceuticals:						
Overseas	6,600	-513	-7.2%	<ul> <li>Sales decrease due to NHI drug price reductions (-13% in the second half), despite volume growth</li> </ul>						
Pharmaceutica				<b>Overseas Pharmaceuticals:</b>						
Bulk Products	950	-55	-5.5%	<ul> <li>Higher shipments of Gel-One</li> <li>Forecast of lower sales of SUPARTZ FX in the U.S. and the impact of yen appreciation</li> </ul>						
LAL Business	6,000	+68	+1.2%	<ul> <li>Bulk Products:</li> <li>Lower sales of hyaluronic acid</li> </ul>						
(Overseas sale	s) <b>11,650</b>	-401	-3.3%	LAL Business						
*Foreign excha	*Foreign exchange impact on overall net sales: approx 660 million you									

appreciation

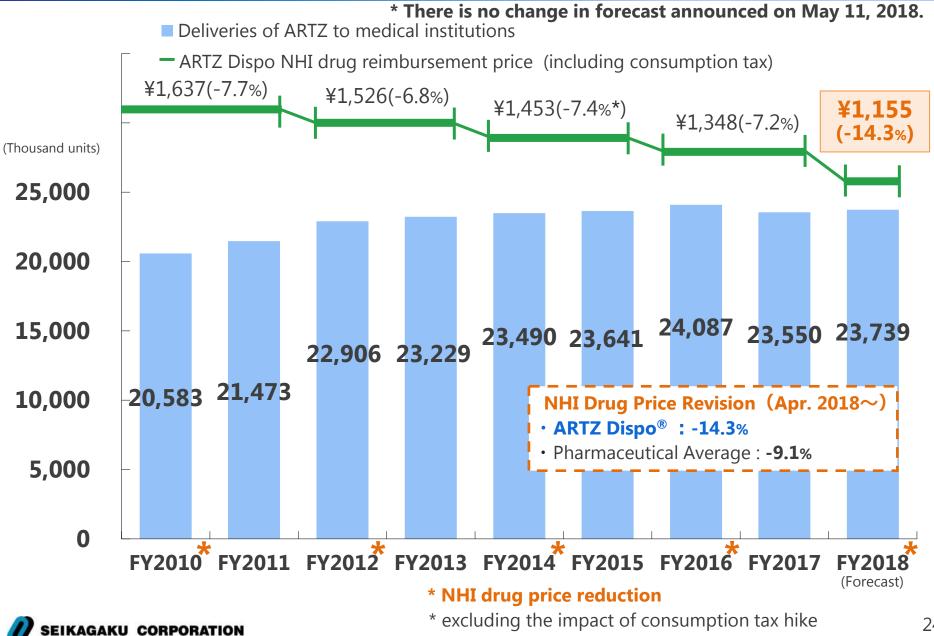
22

# Forecasts (Income) in FY2018

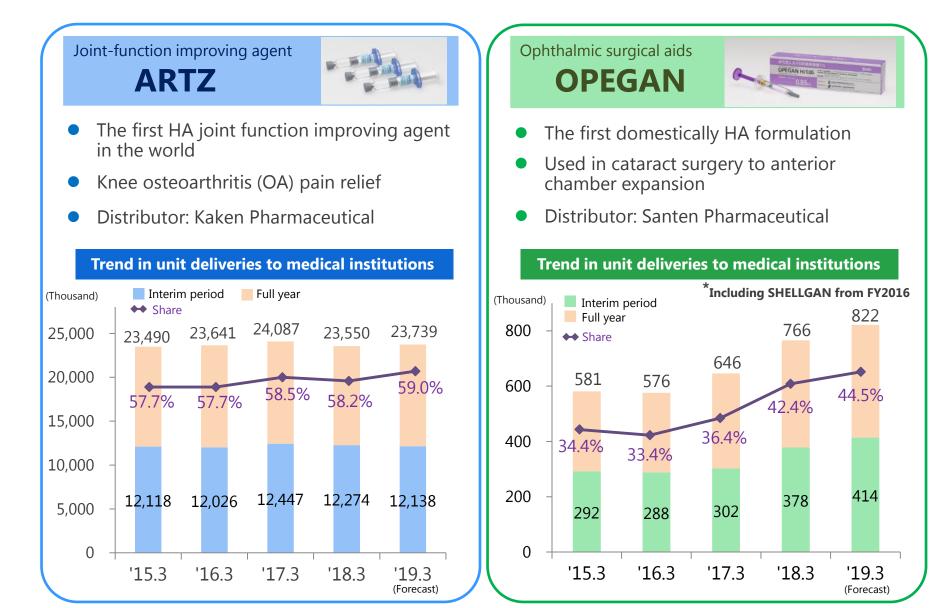
SEIKAGAKU CORPORATION

* There is no change in forecast announced on May 11, 2018.									
	FY2018	Year-o	n-Year	Income					
(Millions of Yen)	Forecasts	Change	% of Change						
Net sales	28,100	-2,075 -6.9%		Decrease in income due to decreases in sales and royalty income, despite lower R&D expenses					
	_0,_00	_/ • / •		Operating Income					
Operating	400	-1,021	-71.9%	operating meene					
Income	(1.4%)	(-3.3pt)	1 2.0 /0	Cost of Sales Ratio (+3.8pt):					
(to Net sales ratio)	()	(		<ul> <li>Increase due to NHI drug price reductions</li> </ul>					
Ordinary	2,250	-3,077 -57.8%		and the impact of yen appreciation					
Income	2,250	-3,077	-37.0%	SGA Expenses (approx1,250):					
Net Income	1,700	-2,222	- <b>56.7</b> %	<ul> <li>R&amp;D expenses (-1,358): Decrease due to the backlash, among other things, for the non-recurrence of substantial expenses associated with the open label trial</li> </ul>					
				expenses associated with the open-label trial for SI-6603 in the U.S. and pre-clinical					
Cost of Sales	10.00			development themes recorded in FY2017					
ratio	46.9%	+3.8pt		<ul> <li>Other SGA expense(approx. +100): HERNICORE post-marketing surveillance</li> </ul>					
R&D Expenses	7,050	-1,358	-16.2%	study expenses					
(to Net sales ratio)	(25.1%)	(-2.8pt)	/	Net Income					
Depreciation	2,950	+24	+0.8%	Non-operating Income /Expenses (approx2,050):					
SEIKAGAKU CORPORATION				<ul> <li>Forecast decrease in royalty income etc.</li> </ul>					

# Trend in NHI Reimbursement Price and Trend in Deliveries of ARTZ to Domestic Medical Institutions



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



## **Ophthalmic Surgical Aid SHELLGAN** (Launched July 2016)

## 眼科手術補助剤 シェルガン<sup>®</sup>0.5 眼粘弾剤

精製ヒアルロン酸ナトリウム/コンドロイチン硫酸エステルナトリウム



## Product SHELLGAN Outline

- Suited to a surgical procedure that has become more pervasive in recent years
- Can be stored at room temperature
  - A product feature unavailable from competitors
- Strengthening of the OPEGAN series product line
  - Seven-product line up provides a wider range of options appropriate to symptoms and physician needs



The OPEGAN series, used mainly in cataract surgery



The OPEGAN series viscoelasticity comparison



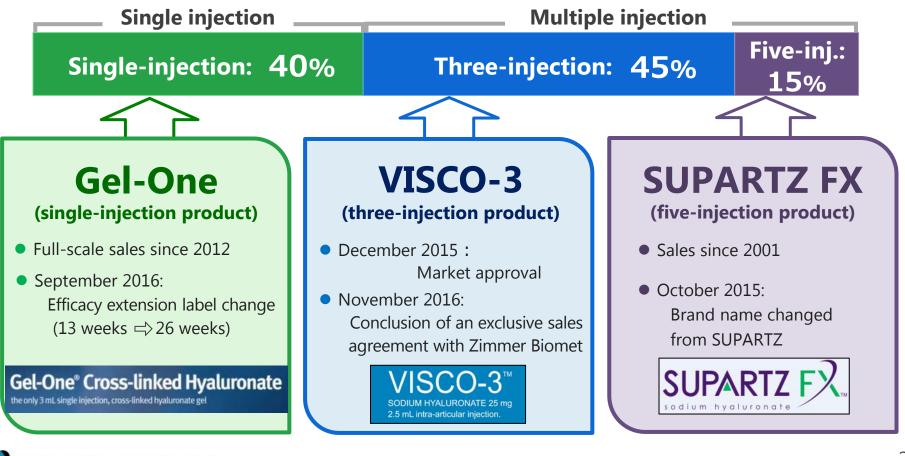
Market Situation of Hyaluronic Acid Products in the U.S.

# Market size of US\$1,070 mil. in 2017

The market can be segmented according to the number of injections.

#### **U.S.** market share by number of injections

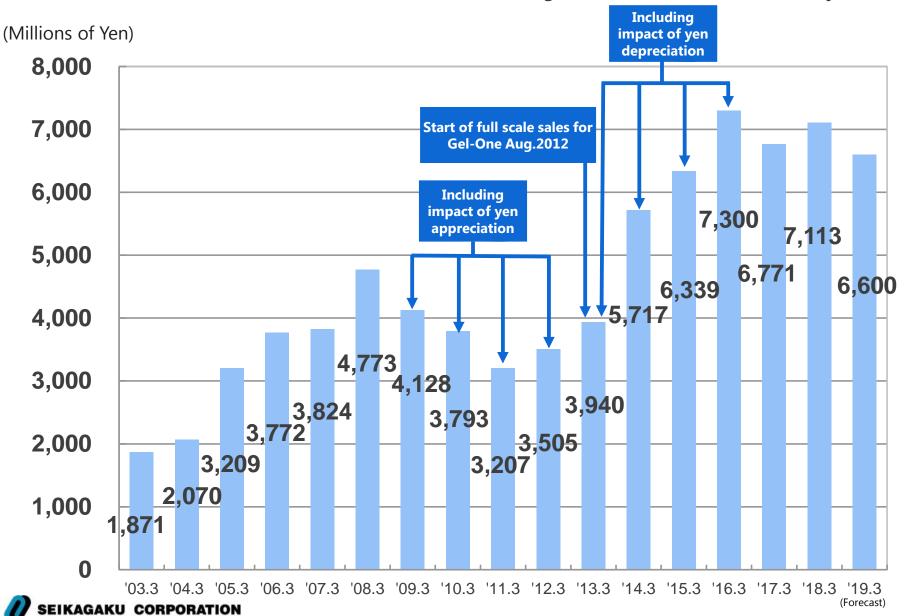
(value basis, 2017 figures, including competitors. Seikagaku estimates)



## **Trend in Overseas Sales of Hyaluronic Acid Products**

\* There is no change in forecast announced on May 11, 2018.

28



# **The LAL Business**

#### What is the LAL business?

The manufacturing and sale of reagents used in the quality control of pharmaceuticals and in water quality Control in dialysis at hospitals

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

\*Endotoxins are substances derived from bacteria. Since they cause fever even in minute amounts, testing for endotoxin contamination in pharmaceuticals is compulsory

#### Size of the global market: Approx. ¥25.0 billion

(Seikagaku estimate, including associated equipment)

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

- U.S. subsidiary of Seikagaku Corporation (established in 1974, acquired by Seikagaku in 1997)
- Developed the world's first endotoxin detection reagent and obtained FDA approval in 1977
- A sales network spanning 80 countries
- Solid business performance in recent years

#### SEIKAGAKU CORPORATION



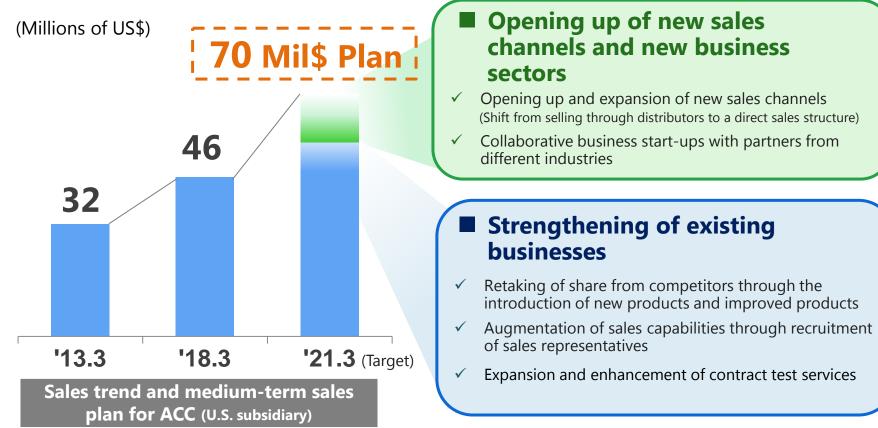
Endotoxin detection reagents (for quality control of pharmaceuticals and medical devices)



# Growth Strategy for ACC (U.S. Subsidiary)



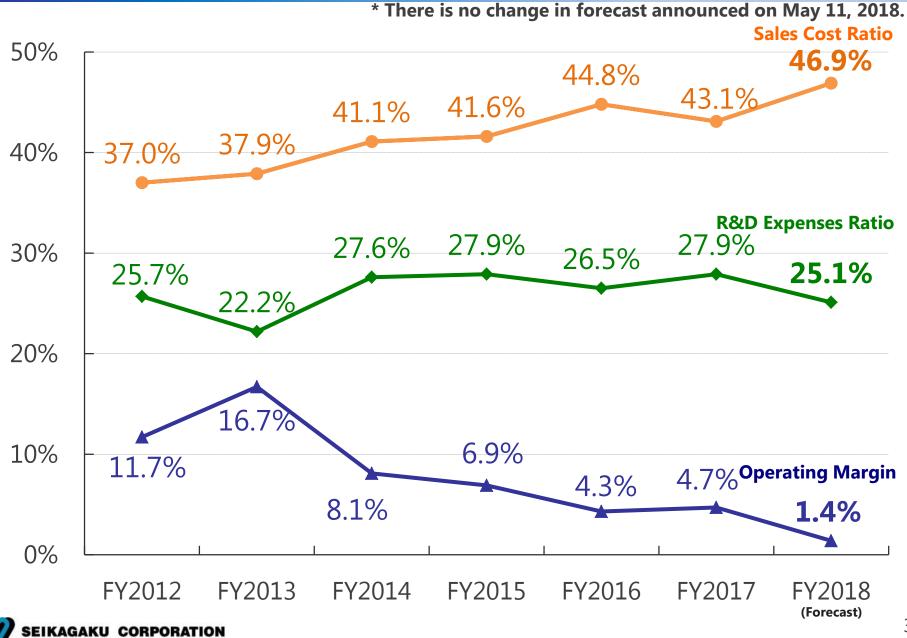
## Acceleration of sales channel expansion at ACC, the core of the LAL Business



LAL Business: The manufacturing and sales of endotoxin detection reagents and other products used in the quality control of pharmaceuticals and medical devices ACC: Associates of Cape Cod, Inc. (U.S. subsidiary)



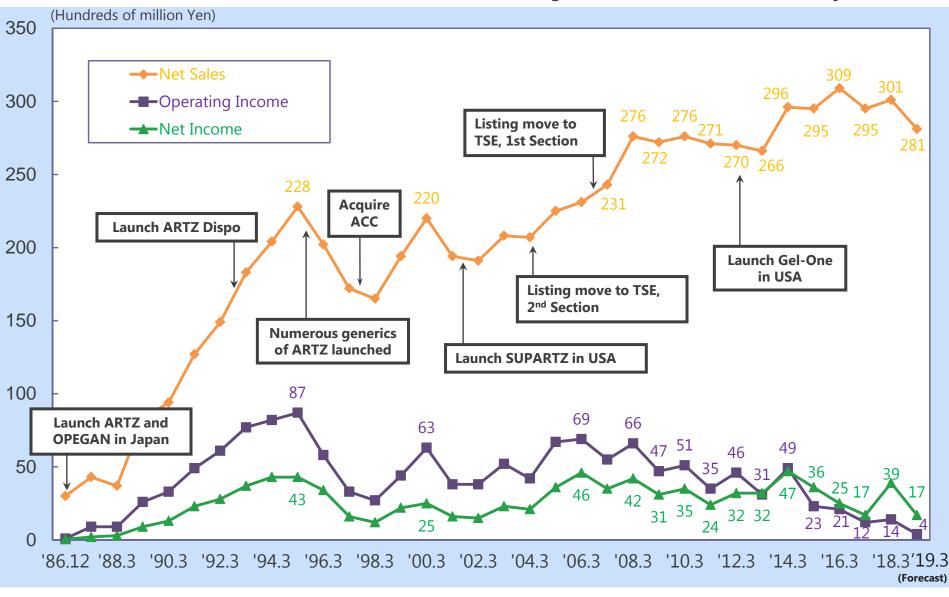
# **Trend in Financial Index**



## **Business Progress & Highlights**

SEIKAGAKU CORPORATION

\* There is no change in forecast announced on May 11, 2018.



\*Consolidated results from '99.3

# **Trend in Capital Investments**

\* There is no change in forecast announced on May 11, 2018.

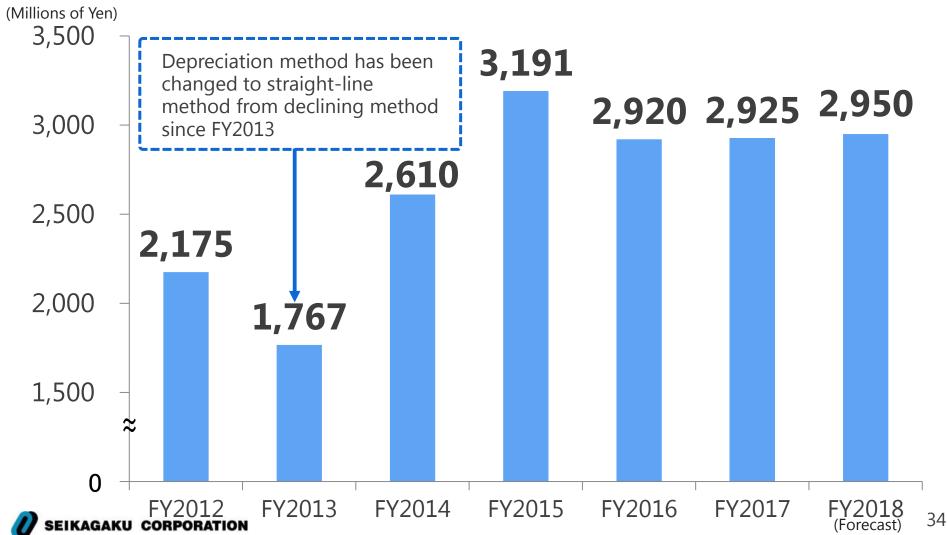
Facilities	Amounts (¥ bill.)	FY2011	FY2012	FY2013	FY2014	FY2015	FY2016	FY2017	<b>FY2018</b> (Forecast)
SI-6603 Bulk Production Facilities	1.1				Start 4.10				
No. 5 Production Building (for ARTZ Dispo)	9.6	Start '12.3				peration '15.1	)		
Hyaluronic Acid Bulk Production Facilities	3.1	Start '12.1			Operatio '14.2	n			
Production Facilities for Gel-One	3.0	Start '11.12			eration 13.10				
Chondroitin Sulfate Bulk Production Facilities	1.2		Opera '12.						
<b>Amounts</b> (Millions of Yen)		5,718	9,164	7,222	2,095	1,975	1,173	1,591	2,000

SEIKAGAKU CORPORATION

# **Trend in Depreciation**

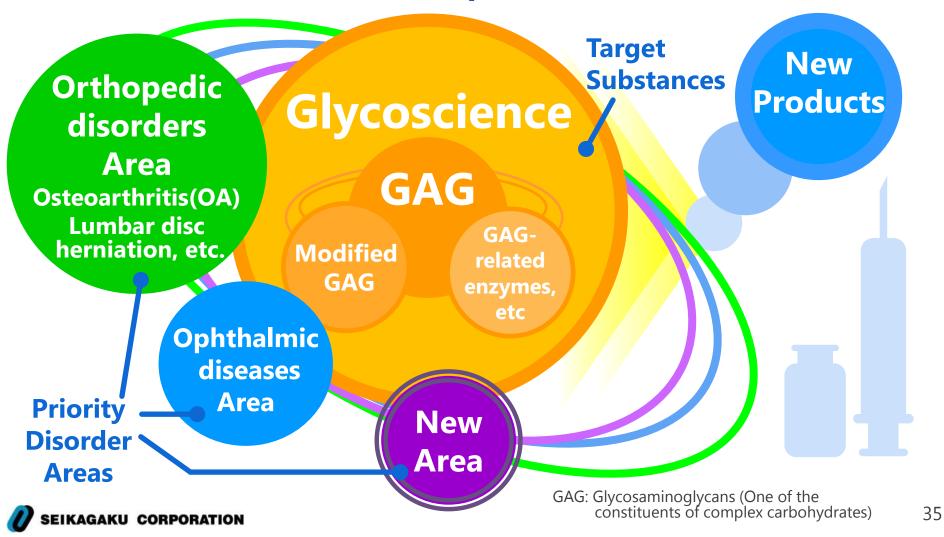
\* There is no change in forecast announced on May 11, 2018.

# Depreciation peaked out at FY2015 and anticipate the level of ¥3,000 million from now on



# **Basic Policy on Research and Development**

Aiming for the early, continuous introduction of new products that meet high treatment needs, focusing on glycoscience as an area of specialization



## The first therapeutic agent for lumbar disc herniation in Japan To aim for a phased rollout with promoting appropriate use

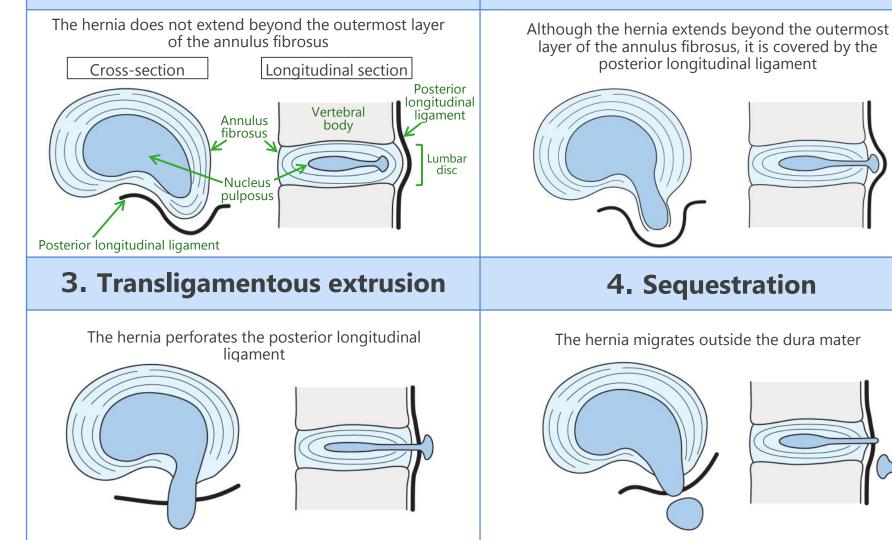
Product name	HERNICORE <sup>®</sup> 1.25 Units for Intradiscal Injection	Generic name	Condoliase
Efficacy and effects	Lumbar disc herniation by prolapse of the posterior longitudinal ligament for which sufficient improvement cannot be obtained through conservative treatment		
Usage and dosage	For adults, 1.25 units of condoliase are administered by a single injection in the intervertebral disc that is the source of the symptoms.		
NHI drug price	81,676 yen (1 bottle containing 1.25 units)	Launch date	August 1, 2018



<Photograph of the HERNICORE>

# Four types of lumbar disc herniation

### **1. Protrusion**

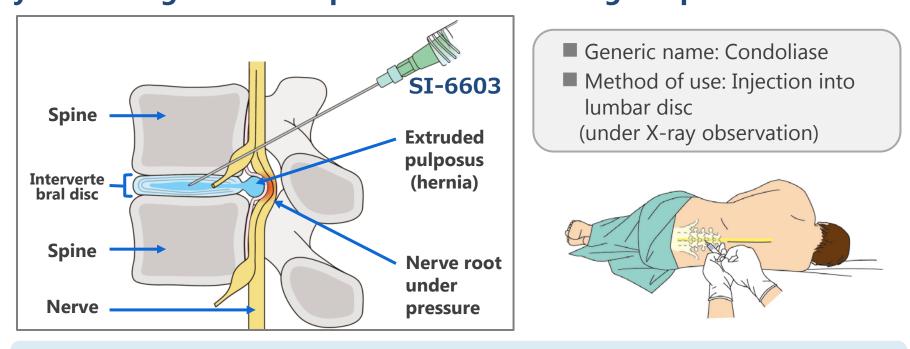


#### 2. Subligamentous extrusion

EIKAGAKU CORPORATION

## Outline of SI-6603 (Treatment for Lumbar Disc Herniation)

Single injection is to relieve pain by specifically degrading GAGs, the main components of the nucleus pulposus by decreasing intradiscal pressure and reducing the pressure on nerves



#### **Expected Features:**

- Single injection expected to relieve the pain of lumbar disc herniation
- Not required general anesthesia and less invasive to the patient than surgical treatment
- Expected to contribute to quality of life of the patient as new treatment option

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

#### SEIKAGAKU CORPORATION

### **Outline of SI-6603 Phase III Clinical Trial in the U.S.**

### **Conducted following 2 clinical trials as phase III in the U.S.**

### **Double Blind Study**

(A Multicenter, Randomized, Double-blind, Controlled, Comparative Study)

#### • Objective:

to evaluate efficacy and safety

- Primary end point: improvement of leg pain at 13 weeks after administration \*VAS; change from baseline
- Number of patients: 385

(Planned number: 360)

- Follow-up period (after administration):
  - •Efficacy : 13 weeks
  - •Safety: 104 weeks (2 years)
- **FPI~LPO:** Oct. 2013 ~ Aug. 2017

\*VAS : Visual Analogue Scale \*FPI : First Patient-in, LPO : Last Patient-out

### **Open Label Study** (Un-blind study)

#### • Objective:

to evaluate safety and efficacy (Primary objective was safety)

#### Primary end point: safety of administration

at 26 weeks after administration

- Number of patients: 1,011 (Planned number: 1,000)
- Follow-up period (after administration): 26 weeks
- FPI~LPO:

Apr. 2015  $\sim$  Mar. 2017



### **Outline of Result for SI-6603 Phase III Clinical Trial in the U.S.**

### Significant improvement in the primary endpoint was demonstrated in Phase III study of Japan but it was not made in Phase III study in the U.S.

#### **Pharmacological effect (Objective indicator)**

Statistically significant decrease in the intervertebral disc and herniation volume assessed with MRI: **Confirmed pharmacological effect of SI-6603** 

#### **Evaluation of safety**

No major concern such as adverse reactions was observed: Confirmed safety of SI-6603

#### Improvement at alleviation of leg pain (Subjective indicator)

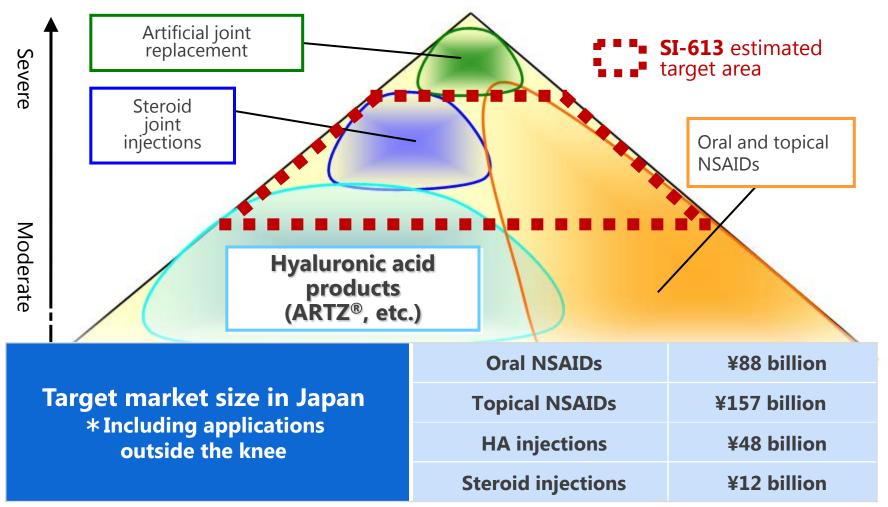
- Statistically significant improvement of leg pain at 13 weeks by VAS was not demonstrated
- 1 There is a guideline for diagnostic and pathology of lumbar disc herniation in Japan, however there is no widely used guideline in the U.S. Therefore, there is possibility that some patients out of Japanese guideline were included in the clinical trial in the U.S.

**②**There is possibility that some factors such as complications biased assessment of leg pain

Increasing the certainty of success for the additional study by reflecting the knowledge and perception obtained from result of the study

## **SI-613 Estimated Target Patients**

Estimated patients with pain and being treated with oral or topical NSAIDs or intra-articular steroid injection





\*Numbers in this slide are estimated by Seikagaku, as of March 31, 2017 41

### Initiatives to maximize the product value of SI-613

Promote in co-development with Ono Pharmaceutical, the product that can be administered to greater numbers of patients

### **Osteoarthritis: PIII**

A disease in which joint tissue deteriorates due to abrasion of the articular cartilage, leading to inflammation and pain

#### **Conduct of three clinical trials**

- Confirmatory study (knee joint)
- Study for four sites (hip, ankle, elbow, shoulder)
- Long-term administration study (knee joint)

# Number of patients examined per year : Approx. 8.7 million

(Seikagaku estimate for five main sites: knee, hip, ankle, elbow, shoulder in Japan)



### **Enthesopathy: PII b**

An inflammatory disease that occurs as a result of excessive load on sites of attachment of ligaments and tendons to other bone or muscle, such as the knee, elbow, heel

#### **Typical examples**

- Lateral epicondylitis (tennis elbow)
- Plantar fasciitis
- Patellar tendinitis (jumper's knee)
- Achilles tendonitis, etc.

#### Number of patients receiving drug therapy per year: Approx. 0.9 million

(Seikagaku estimate for the above four

diseases in Japan)



### SI-614 Outline (Treatment of Dry Eye)

### Aimed at improvement of symptoms of dry eye by protecting the ocular surface and promoting corneal epithelial wound healing

Substance : SI-614(Modified Hyaluronate)

Formulation : Ophthalmic solution

January 2015: Phase II/III clinicaltrials

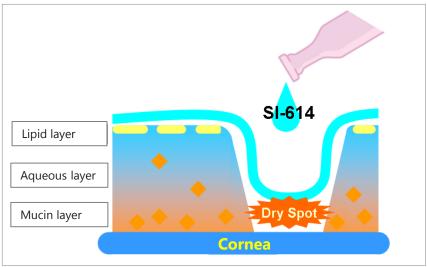
partner has been decided

Plan to conduct a PIII trial after a sales

Indication : Dry eye

U.S. : P II/III

completed



#### **Expected Features :**

- SI-614 is a modified hyaluronate produced by Seikagaku's proprietary technology
- It is expected to improve symptoms of dry eye by protecting the ocular surface and promoting corneal epithelial wound healing in dry eye patients
- Although dry eye is a multifactorial disease, only drugs with relatively strong is available in the U.S. currently. SI-614 will provide a new alternative to the treatment of dry eye through the promising mode of action

#### EIKAGAKU CORPORATION

# **Clinical Study Information**

Development code/ Indication	Develop- ment Location		Target Enroll- ment	Estimated Period	Primary End Point (Primary Follow-up period)
<b>SI-6603</b> Lumbar Disk Herniation	U.S.	Phase III additional study ( <u>NCT03607838</u> )	320	May. 2018 – Nov. 2020	Leg pain (13 weeks)
<b>SI-613</b> Osteoarthritis	Japan	Phase III Knee confirmatory study ( <u>JapicCTI-173537</u> )	440	Feb. 2017 – Jan. 2019	WOMAC(Knee pain) (12 weeks)
		Phase III study for four sites (JapicCTI-173678)	280	Aug. 2017 – Jun. 2019	Daily pain diary (12 weeks)
		Long-term administration study (JapicCTI-183855)	160	Feb. 2018 – Sep. 2019	Safety (52 weeks)
<b>SI-613-ETP</b> Enthesopathy	Japan	Late-stage Phase II clinical study ( <u>JapicCTI-173758</u> )	240	Oct. 2017 – Oct. 2018	Pain in motion (4 weeks)
<b>SI-613</b> Knee Osteoarthritis	U.S.	Phase II clinical study ( <u>NCT03209362</u> )	80	Oct. 2017 – Nov. 2018	WOMAC(Knee pain) (12 weeks)
<b>SI-614</b> Dry eye	U.S.	Phase II / III clinical study ( <u>NCT02205840</u> )	240	Jul. 2014 – Nov. 2014	Corneal staining score, Symptom score (28 days)
<b>SI-449</b> Adhesion Barrier	Japan	Pilot study ( <u>UMIN000033294</u> )	20	Jul. 2018 –	Safety, Manageability (–)

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) <u>http://www.clinicaltrials.jp/user/cteSearch\_e.jsp</u>

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 <u>https://clinicaltrials.gov/ct2/search</u>



Note: Actual enrollments or trial periods may differ from targets and plans due to various factors.

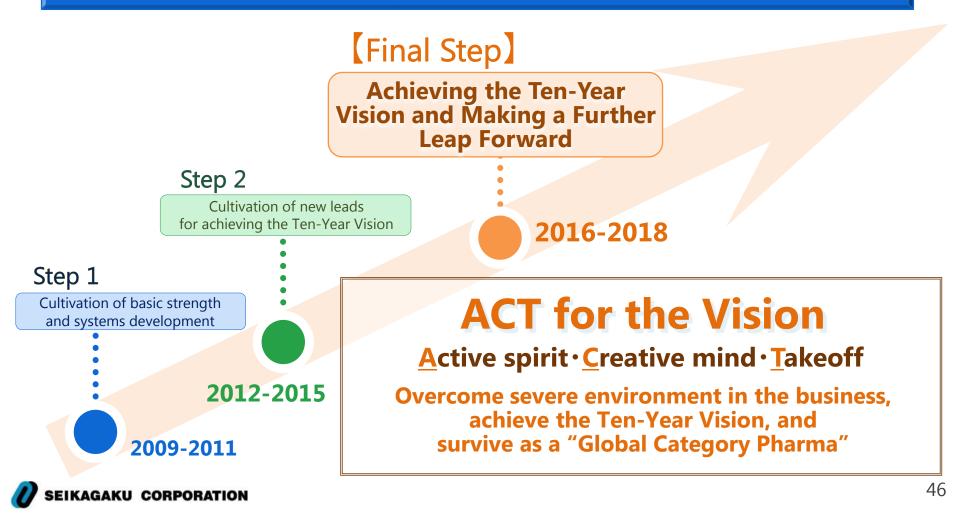
# **Contract Status by R&D Theme**

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

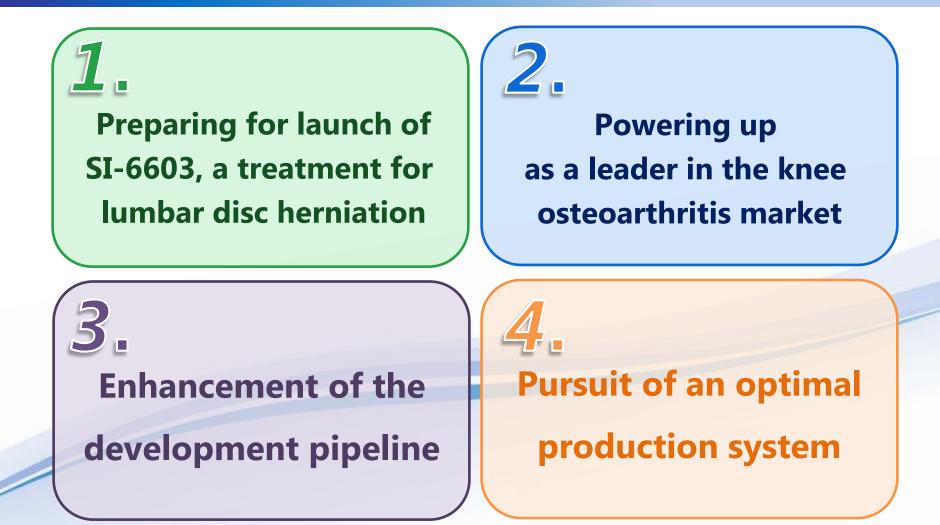
Development Code Indication	Develop- ment Location	Sales Partner	Total Amount of Milestone Royalties ( of which, in upfront payment )
<b>SI-6603</b> Lumbar Disk Herniation	U.S.	Ferring Pharmaceuticals (Switzerland)	Max. US \$95 million (US \$5 million)
<b>SI-613</b> Japan: Osteoarthritis	Japan	Ono Pharmaceutical Co., Ltd.	Max. ¥10.0 billion (¥2.0 billion)
U.S. : Knee Osteoarthritis	U.S.	Searching	_
<b>SI-613-ETP</b> Enthesopathy	Japan	Ono Pharmaceutical Co., Ltd.	*included in the above
SI-614 Dry eye U.S. Searching			
<b>SI-449</b> Adhesion Barrier	Japan	_	_

### Mid-term Management Plan (FY2016 to FY2018)

### **Ten-Year Vision"Global Category Pharma"** Focus research and development on glycoscience Establishes global Competitiveness



### Mid-term Management Plan: Four High-Priority Strategies



Achieving the Ten-Year Vision and Making a Further Leap Forward

### Mid-term Management Plan: Numerical Targets (announced in May 2016)

		(Unit : hundred million)
FY2018	<b>Target</b> (announced in May 2016)	<b>Forecasts</b> (announced in May 2018)
Net sales	320	281
Operating income	25	4
Ordinary income	45	22.5

《The main Factors of expected Shortfall》

- Market penetration lag of Gel-One in U.S.
- Delayed launch of SI-6603(HERNICORE) in Japan and the U.S.
- Effect for NHI drug price reduction of long term listed drug by drastic reform of NHI structure
- Impact of foreign exchange (assumption  $\pm 110 \Rightarrow \pm 105$ )

Expected shortfall for numerical target, despite some progress on R&D pipeline

#### **Topics for Advancing to the Next Stage** (Schematic Representation of Growth)

New Products: SI-6603 leads to growth	*Announced in
Existing overseas products:	
Share expansion for Gel-One in the U.S.	
LAL Business:	
Further growth from new product development and strengthening of sales	
Existing domestic products:	
Gradual decrease due to the impact of price revisions	<b>SI-6603</b>

#### **XAnnounced in May 2016**



# **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

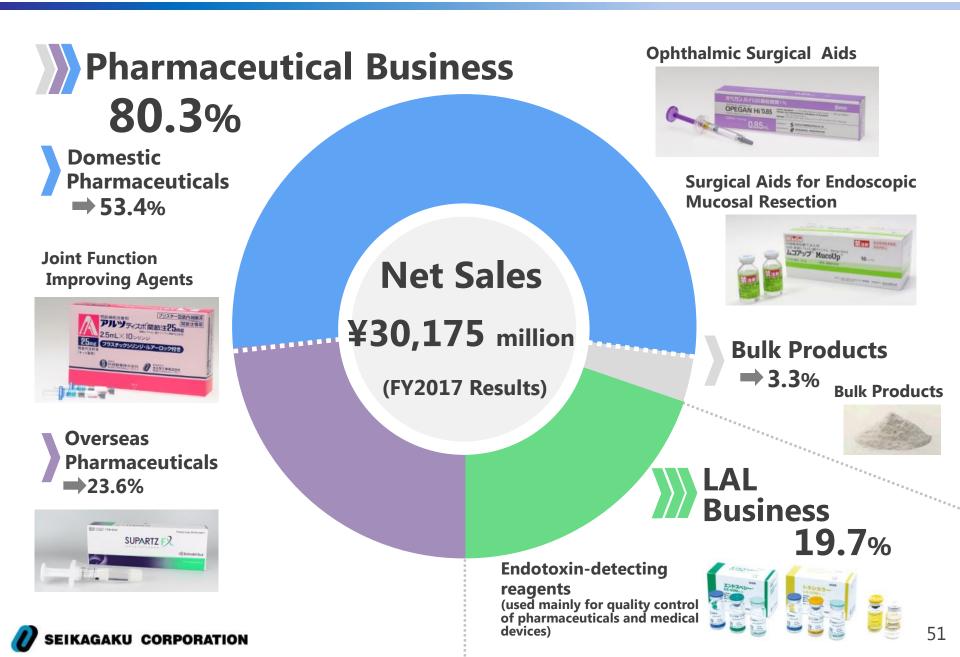
### State-of-the-art technology related to GAG

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

### <u>Unique business model</u>

- Concentration on R&D and manufacturing
- R&D staff comprising one-third of our total employees
- Allocation of 25% to 30% of net sales to R&D investment

# **Our Business Segment**



# Main Hyaluronic Acid (HA) Products

**ARTZ<sup>®</sup>** Knee osteoarthritis (OA) pain relief 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> Knee OA pain relief by a single injection

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



#### **Exploring the Innovative Promise of Glycoscience**

#### Cautionary Notes

This material contains forward-looking statements regarding future management strategies or performance forecasts. These descriptions 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 descriptions due to various factors.

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



Copyrights(C)2018 SEIKAGAKU CORPORATION. All rights reserved.