

*Exploring the Innovative Promise of Glycoscience*

# Financial Results for the Fiscal Year 2017

(April 1, 2017 – March 31, 2018)



<http://healthy-knee.com/>



**SEIKAGAKU CORPORATION**

(TSE:4548)

# Contents

<b>■ FY2017 Results</b>	<b>P3</b>	<b>■ Research and Development</b>	
● Net Sales / Income	P4-7	● Pipeline List	P16
<b>■ FY2018 Forecasts</b>	<b>P9</b>	● SI-6603 (Lumbar disc herniation)	P17-18
● Net Sales / Income	P9-10	● SI-613 (Osteoarthritis / Enthesopathy)	P19
● Trend in R&D Expenses	P11	● SI-614 (Dry eye)	P20
<b>■ Sales by Business Segment</b>		<b>■ Mid-term Management Plan</b>	<b>P21</b>
● Domestic Pharmaceuticals	P12	<b>■ Basic Policy on Profit Distribution</b>	<b>P22</b>
● Overseas Pharmaceuticals	P13-14	<b>■ Appendix</b>	<b>P23</b>
● LAL	P15		

## < 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 of Fiscal Year 2017

(Millions of Yen)	FY2017 Results	Year-on-Year		Comparison with Revised Forecasts	
		Change	% of Change	Change	% of Change
Net sales	<b>30,175</b>	<b>+586</b>	<b>+2.0%</b>	<b>+75</b>	<b>+0.3%</b>
Operating Income	<b>1,421</b>	<b>+139</b>	<b>+10.9%</b>	<b>+21</b>	<b>+1.6%</b>
Ordinary Income	<b>5,327</b>	<b>+2,850</b>	<b>+115.1%</b>	<b>+77</b>	<b>+1.5%</b>
Net Income	<b>3,922</b>	<b>+2,134</b>	<b>+119.4%</b>	<b>+122</b>	<b>+3.2%</b>
R&D Expenses (Ratio to net sales)	<b>8,408</b> <b>(27.9%)</b>	<b>+573</b> <b>(+1.4pt)</b>	<b>+7.3%</b>	<b>+58</b> <b>(+0.2pt)</b>	<b>+0.7%</b>
Average Exchange Rate (1US\$)	¥110.86円	+¥2.44			

	FY2017 Results	FY2017 Results	FY2017 Revised Forecasts
Net Income per Share	<b>¥ 69.30</b>	¥ 31.55	¥ 67.13
Dividend per Share	<b>¥ 26.00</b>	¥ 31.00*	¥ 26.00
Dividend Payout Ratio	<b>37.5%</b>	98.3%	38.7%
R O E	<b>5.4%</b>	2.5%	

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

# Net sales by Business Segment (FY2017)

(Millions of Yen)	FY2017 Results	Year-on-Year	% of Change
Net sales	30,175	+586	+2.0%
Pharmaceuticals	24,244	+92	+0.4%
Domestic Pharmaceuticals	16,125	-143	-0.9%
Overseas Pharmaceuticals	7,113	+341	+5.0%
Bulk Products	1,005	-106	-9.6%
LAL Business	5,931	+493	+9.1%
(Overseas sales)	12,051	+1,022	+9.3%

\*Foreign exchange impact on overall net sales:  
approx. +310 million yen

## Domestic Pharmaceuticals

### ➤ ARTZ (Joint-function improvement agent)

- Sales down due to restrained purchasing by medical institutions in connection with NHI drug price reductions implemented in April 2018



ARTZ :  
Joint-function improvement agent with hyaluronic acid as its active pharmaceutical ingredient

### ➤ OPEGAN series (Ophthalmic surgery aid)

- Strong sales of SHELLGAN maintained



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

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

- Sales at the prior-year level

# Net sales by Business Segment (FY2017)

(Millions of Yen)	FY2017 Results	Year-on-Year	% of Change
Net sales	30,175	+586	+2.0%
<b>Pharmaceuticals</b>	<b>24,244</b>	<b>+92</b>	<b>+0.4%</b>
Domestic Pharmaceuticals	16,125	-143	-0.9%
<b>Overseas Pharmaceuticals</b>	<b>7,113</b>	<b>+341</b>	<b>+5.0%</b>
Bulk Products	1,005	-106	-9.6%
LAL Business	5,931	+493	+9.1%
<b>(Overseas sales)</b>	<b>12,051</b>	<b>+1,022</b>	<b>+9.3%</b>

\*Foreign exchange impact on overall net sales:  
approx. +310 million yen

## Overseas Pharmaceuticals

\*Foreign exchange impact on Overseas Pharmaceuticals:  
approx. +310 million yen

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

- Sales up on higher local sales and the impact of yen depreciation



Gel-One:  
Single-injection joint function  
improving agent

### ➤ ARTZ (Multiple injection)

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

- Local sales down due to a preference for competing products requiring fewer injections
- Seikagaku sales up due to a sales partner's inventory buildup

#### ARTZ in China:

- Local sales up, with the government's price-curbing policy running its course
- Seikagaku sales down due to local inventory adjustments

# Net sales by Business Segment (FY2017)

(Millions of Yen)	FY2017 Results	Year-on-Year	% of Change
<b>Net sales</b>	<b>30,175</b>	<b>+586</b>	<b>+2.0%</b>
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Domestic Pharmaceuticals	16,125	-143	-0.9%
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<b>LAL Business</b>	<b>5,931</b>	<b>+493</b>	<b>+9.1%</b>
<b>(Overseas sales)</b>	<b>12,051</b>	<b>+1,022</b>	<b>+9.3%</b>

\*Foreign exchange impact on overall net sales:  
approx. +310 million yen

## Bulk Products

Overall sales down, reflecting fierce competition in the market for hyaluronic acid

\*Bulk Products :

High-purity, high-quality hyaluronic acid and chondroitin sulfate for pharmaceuticals

## LAL Business

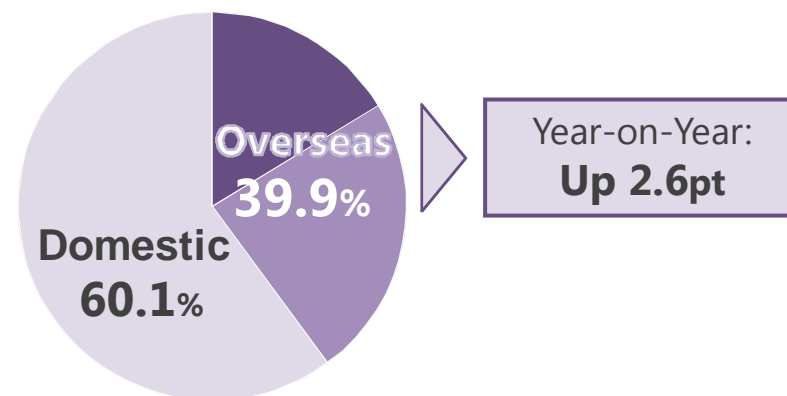
\*Foreign exchange impact on LAL Business: approx. +150 million yen

Overall sales up on strong overseas sales, despite lower sales to dialysis facilities in Japan

\*LAL Business :

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

## Overseas Sales Ratio



Year-on-Year:  
**Up 2.6pt**

# Income in FY2017 (Year-on-Year)

(Millions of Yen)	FY2017 Results	Year-on-Year	% of Change
Net sales	30,175	+586	+2.0%
Cost of Sales (Cost of Sales ratio)	13,008 (43.1%)	-239 (-1.7pt)	-1.8%
SGA expenses	15,745	+685	+4.6%
R&D Expenses (to Net sales ratio)	8,408 (27.9%)	+573 (+1.4pt)	+7.3%
Operating Income (to Net sales ratio)	1,421 (+4.7%)	+139 (+0.4pt)	+10.9%
Ordinary Income	5,327	+2,850	+115.1%
Net Income	3,922	+2,134	+119.4%
Depreciation	2,925	+5	+0.2%

## Operating Income

### Cost of Sales Ratio (-1.7pt):

Improvement in production efficiency in connection with introduction of a new syringe for ARTZ, among other factors

### SGA Expenses (+685):

Increase in R&D expenses due to progress with SI-613 clinical trials and development themes at the pre-clinical stage (+573)

## Net Income

### Non-operating Income / Expenses (+2,710):

Sharp increase in royalty income (+2,452)

\*Receipt of an upfront payment of 2.0 billion yen from Ono Pharmaceutical accompanying conclusion of an agreement related to SI-613 in Japan in September 2017 co-development and marketing collaboration in Japan

### Income Taxes (Tax Rate: 26.4%):

Decrease due to the impact of the Japan-U.S. profit contribution ratio (-1.4pt)

# Overview of Forecasts in FY2018

(Millions of Yen)	FY2018 Forecasts	FY2017 Results		
		Results	Change	% of Change
Net sales	28,100	30,175	-2,075	-6.9%
Operating Income	400	1,421	-1,021	-71.9%
Ordinary Income	2,250	5,327	-3,077	-57.8%
Net Income	1,700	3,922	-2,222	-56.7%
R&D Expenses (to Net sales ratio)	7,050 (25.1%)	8,408 (27.9%)	-1,358 (-2.8pt)	-16.2%
Average Exchange Rate (1US\$)	¥105.00	¥110.86	¥-5.86	
	FY2018 Forecasts	FY2017 Results	Exchange Rate Sensitivity (Impact of a change of ¥1 against the US\$)	
Net Income per share	¥30.03	¥69.30	Net sales	Approx. ¥110 million
Dividend per share	¥26.00	¥26.00	Operating income	Approx. ¥55 million
Dividend Payout ratio	86.6%	37.5%		



# Forecasts (Net sales) in FY2018

(Millions of Yen)	FY2018 Forecasts	Year-on-Year	
		Change	% of Change
Net sales	28,100	-2,075	-6.9%
Pharmaceuticals	22,100	-2,144	-8.8%
Domestic Pharmaceuticals	14,550	-1,575	-9.8%
Overseas Pharmaceuticals	6,600	-513	-7.2%
Bulk Products	950	-55	-5.5%
LAL Business	6,000	+68	+1.2%
(Overseas sales)	11,650	-401	-3.3%

\*Foreign exchange impact on overall net sales:  
approx. -660 million yen

## Net Sales

Forecast of lower sales due to NHI drug price 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

## Pharmaceuticals Business

### Domestic Pharmaceuticals:

- Sales decrease due to NHI drug price reductions (-13% in the second half), despite volume growth

### Overseas Pharmaceuticals:

- Higher shipments of Gel-One
- Forecast of lower sales of SUPARTZ FX in the U.S. and the impact of yen appreciation

### Bulk Products:

- Lower sales of hyaluronic acid

## LAL Business

Slight increase due to sales expansion at U.S. subsidiary ACC, despite the impact of yen appreciation

# Forecasts (Income) in FY2018

(Millions of Yen)	FY2018 Forecasts	Year-on-Year	
		Change	% of Change
Net sales	28,100	-2,075	-6.9%
Operating Income (to Net sales ratio)	400 (1.4%)	-1,021 (-3.3pt)	-71.9%
Ordinary Income	2,250	-3,077	-57.8%
Net Income	1,700	-2,222	-56.7%
Cost of Sales ratio	46.9%	+3.8pt	
R&D Expenses (to Net sales ratio)	7,050 (25.1%)	-1,358 (-2.8pt)	-16.2%
Depreciation	2,950	+24	+0.8%

## Income

Decrease in income due to decreases in sales and royalty income, despite lower R&D expenses

## Operating Income

### Cost of Sales Ratio (+3.8pt):

- Increase due to NHI drug price reductions and the impact of yen appreciation

### SGA Expenses (approx. -1,250):

- R&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 for SI-6603 in the U.S. and pre-clinical development themes recorded in FY2017
- Other SGA expense (approx. +100):  
HERNICORE post-marketing surveillance study expenses

## Net Income

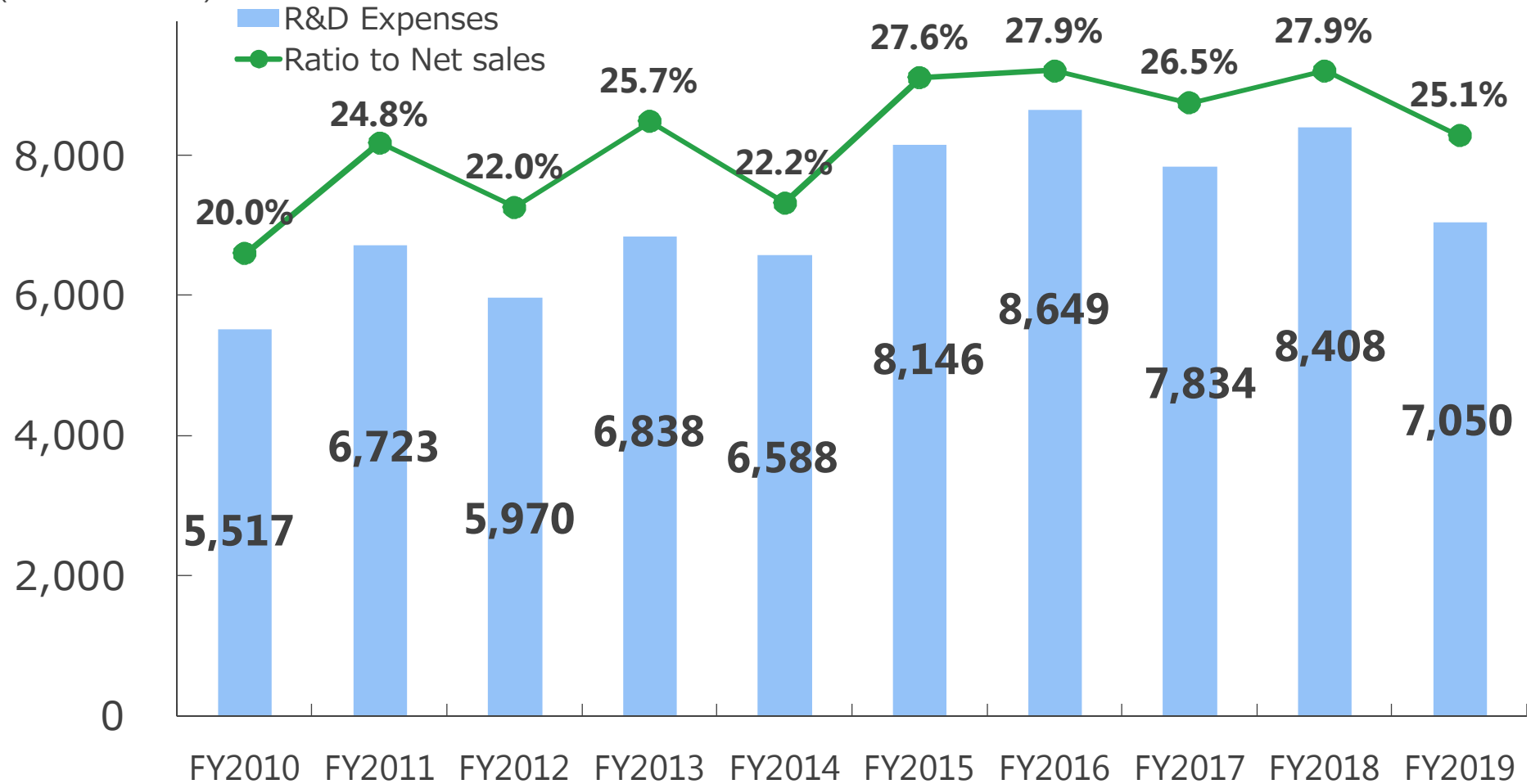
### Non-operating Income /Expenses (approx. -2,050):

- Forecast decrease in royalty income etc.

# Trend in R&D Expenses



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

(Millions of Yen)



# Domestic Pharmaceuticals

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

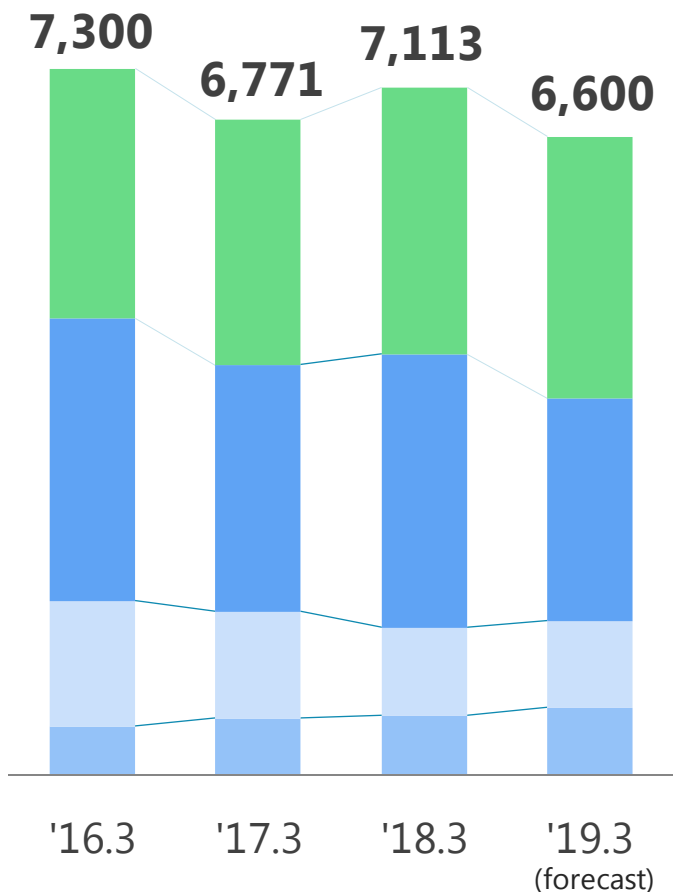
Joint-function improving agent <b>ARTZ</b>	FY2017 Results	FY2018 Forecasts			
	<ul style="list-style-type: none"> <li>● Impact of restrained purchasing by medical institutions in connection with drug price reductions implemented in April 2018</li> <li>● Decline following an increase in deliveries in FY2016 accompanying the introduction of a new syringe</li> </ul> <p>ARTZ growth rate:-2.2% (Market growth rate:-1.6%) Market share:58.2% (-0.3pt)</p>	<ul style="list-style-type: none"> <li>● Implement measures to increase product added value</li> <li>● Aim for growth to exceed market growth</li> </ul> <p>*ARTZ Dispo price reduction percentage: -14.3%</p> <table border="1" data-bbox="1285 635 2033 842"> <tr> <td data-bbox="1285 635 1704 842"> <ul style="list-style-type: none"> <li>● ARTZ growth rate <b>+0.8%</b> (forecast)</li> </ul> </td> <td data-bbox="1704 635 2033 842"> <ul style="list-style-type: none"> <li>● Market share <b>58.6%</b> (forecast)</li> </ul> </td> </tr> </table>		<ul style="list-style-type: none"> <li>● ARTZ growth rate <b>+0.8%</b> (forecast)</li> </ul>	<ul style="list-style-type: none"> <li>● Market share <b>58.6%</b> (forecast)</li> </ul>
<ul style="list-style-type: none"> <li>● ARTZ growth rate <b>+0.8%</b> (forecast)</li> </ul>	<ul style="list-style-type: none"> <li>● Market share <b>58.6%</b> (forecast)</li> </ul>				
Ophthalmic surgical aids <b>OPEGAN</b> (including SHELLGAN)	FY2017 Results	FY2018 Forecasts			
	<ul style="list-style-type: none"> <li>● Further market penetration for SHELLGAN due to vigorous sales promotion activities</li> <li>● Market share expansion</li> </ul> <p>OPEGAN growth rate:+18.6% (Market growth rate:+1.8%) Market share:42.4% (+6.0pt)</p>	<ul style="list-style-type: none"> <li>● Publicize SHELLGAN's product features</li> <li>● Aim to capture share from competitors by continuing targeted sales promotion activities</li> </ul> <p>*OPEGAN series price reduction percentage: Approx. -9%</p> <table border="1" data-bbox="1285 1246 2033 1450"> <tr> <td data-bbox="1285 1246 1704 1450"> <ul style="list-style-type: none"> <li>● OPEGAN growth rate <b>+6.0%</b> (forecast)</li> </ul> </td> <td data-bbox="1704 1246 2033 1450"> <ul style="list-style-type: none"> <li>● Market share <b>44.0%</b> (forecast)</li> </ul> </td> </tr> </table>		<ul style="list-style-type: none"> <li>● OPEGAN growth rate <b>+6.0%</b> (forecast)</li> </ul>	<ul style="list-style-type: none"> <li>● Market share <b>44.0%</b> (forecast)</li> </ul>
<ul style="list-style-type: none"> <li>● OPEGAN growth rate <b>+6.0%</b> (forecast)</li> </ul>	<ul style="list-style-type: none"> <li>● Market share <b>44.0%</b> (forecast)</li> </ul>				

# Overseas Pharmaceuticals (FY2017 Results Year-on-Year / value basis)

## Overseas Pharmaceuticals Sales trend

(Millions of Yen)

<Breakdown>



## FY2017 Results

**+5.0%**

(Foreign exchange impact +2.3%)

Sales increase due to higher shipments to the U.S. and the impact of yen depreciation, despite a decrease in exports to China

\*Foreign exchange impact: approx. +¥160 million

## Gel-One (Single injection)

- **Sales in the U.S.:** Growth of approx. 10% (volume basis)
- **Seikagaku exports:** Sales increase on volume growth and the impact of yen depreciation, despite a decline in local selling unit prices accompanying price adjustments for some major customers

## ARTZ (Multiple injection)

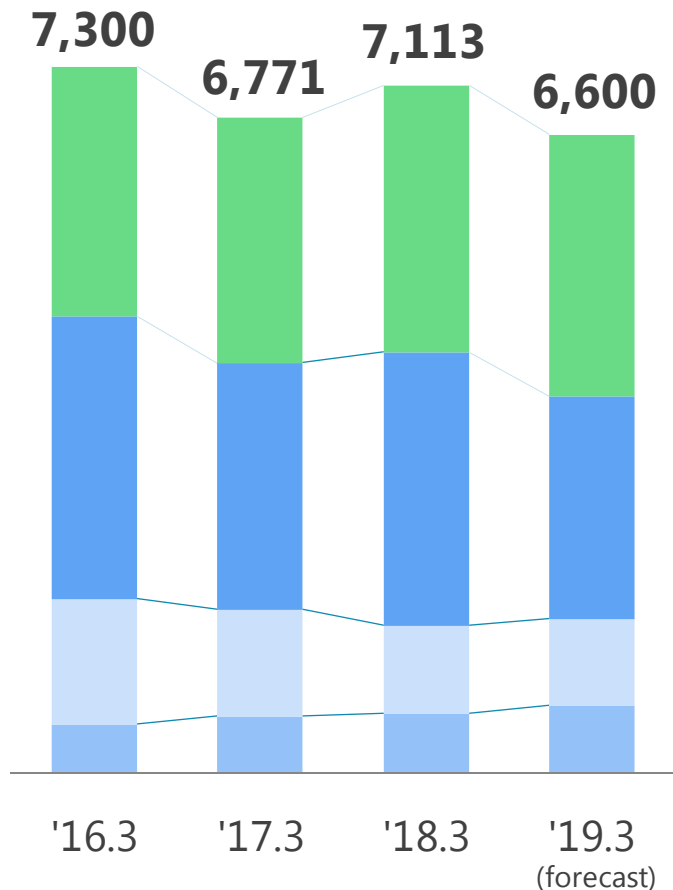
- **SUPARTZ FX in the U.S.**  
Local sales down due to preference for products requiring fewer injections
- **ARTZ in china**  
With the government's price-curbing policy running its course, a return to growth in local sales
- **Seikagaku exports**  
Exports to China down accompanying local inventory adjustments, but shipments of SUPARTZ FX to the U.S. up due to a distributor inventory buildup

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

## Overseas Pharmaceuticals Sales trend

(Millions of Yen)

<Breakdown>



## FY2018 Forecasts

**-7.2%**

(Foreign exchange impact -4.4%)

Sales decrease due to suspension of compensation for hyaluronic acid injectables by some U.S. insurance companies and the impact of yen appreciation

**\*Foreign exchange impact: approx. - ¥310 million**

## Gel-One (Single injection)

- **Sales in the U.S.:** Forecast of growth of approx. 7% (volume basis)
- **Seikagaku exports:** Slight decrease in sales due a decline in local selling unit prices and the impact of yen appreciation, despite projected volume growth commensurate with growth in local sales

## ARTZ (Multiple injection)

- **SUPARTZ FX in the U.S.**  
Decrease in local sales in a fierce market environment for 5-injection products
- **ARTZ in China**  
Expected increase from strengthening of sales activities targeting not only to urban areas, but also surrounding areas
- **Seikagaku exports**  
Decrease in shipments of SUPARTZ FX for the U.S. due to yen appreciation, decrease in local sales, and a decline from a high level of shipments in FY2017  
Shipments to China at the prior-year level due to local inventory adjustments

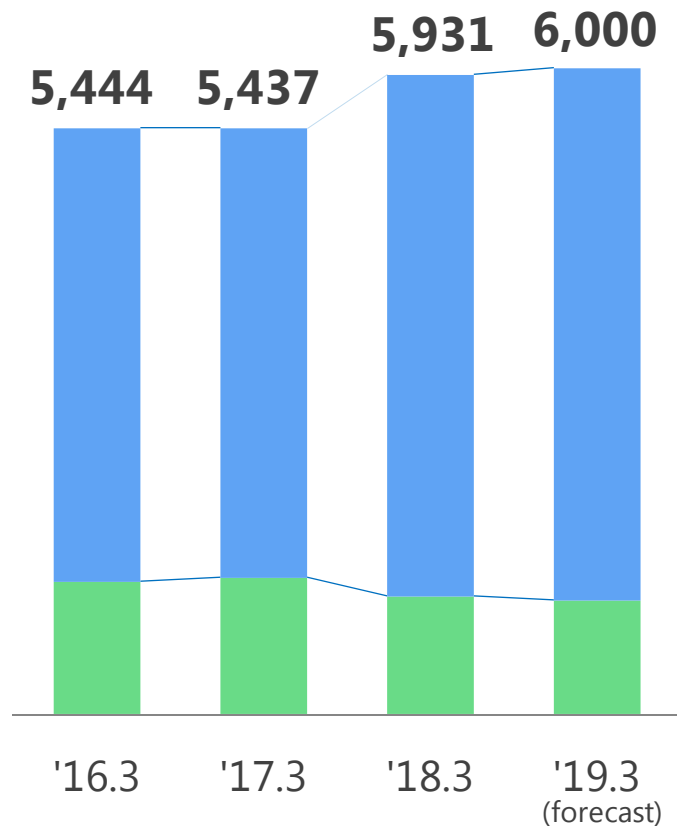
# Sales of LAL Business (value basis/year-on-year)

## LAL Business Sales trend

(Millions of Yen)

<Breakdown>

■ Overseas ■ Domestic



## FY2017 Results: +9.1% (Year-on-Year)

### Overseas

\*Foreign exchange impact: approx. -¥150million

Sales increase due to higher sales of products such as endotoxin detection reagents used in quality control and the impact of yen depreciation

### Domestic

Decrease in sales to dialysis facilities in connection with a change in water quality control standards

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

### Overseas

\*Foreign exchange impact: approx. -¥350million

Only a slight increase due to the impact of yen appreciation, despite a forecast of a local sales increase to result from capturing of share from competitors

### Domestic

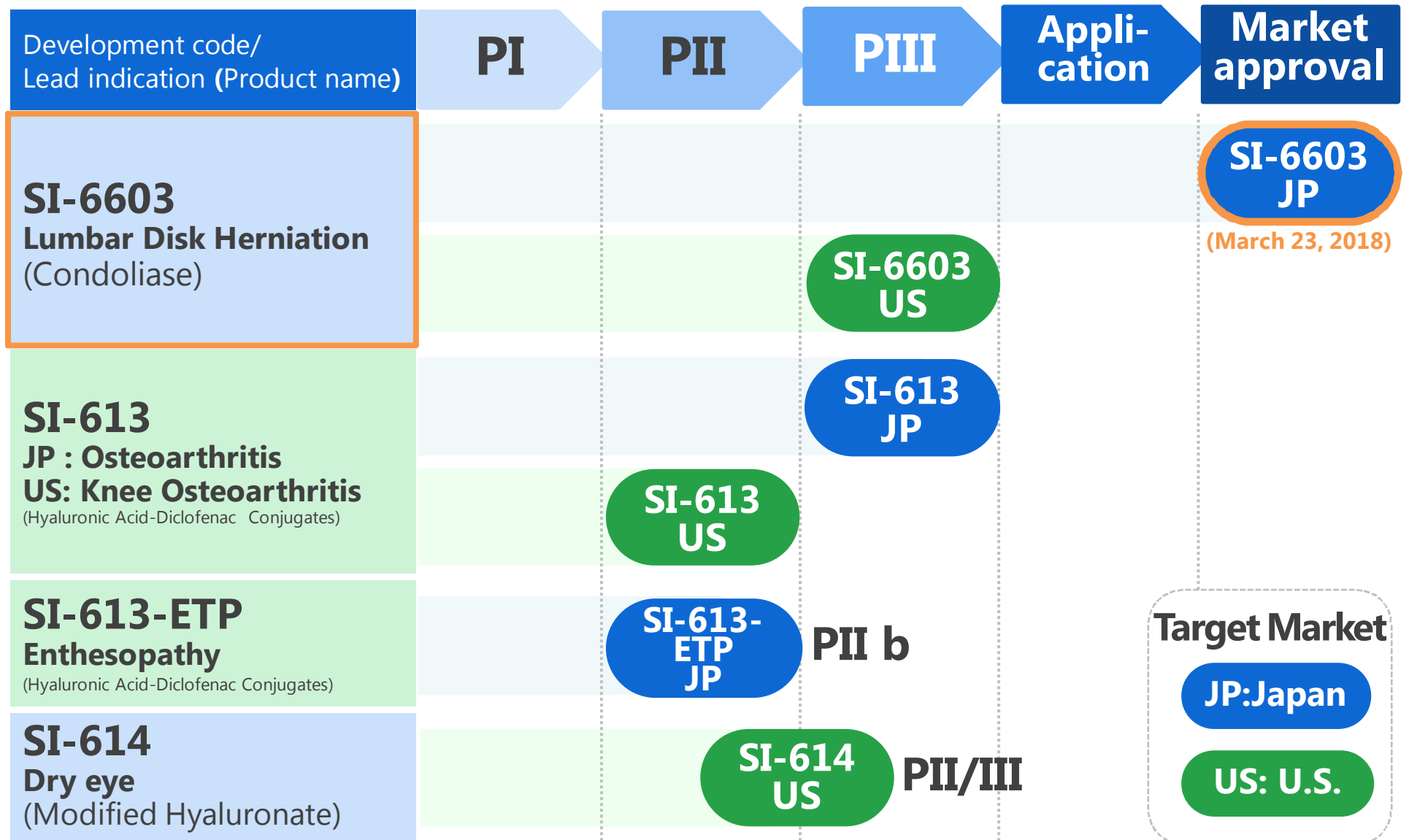
Continued decrease in sales to dialysis facilities

### 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)





# HERNICORE (SI-6603, a treatment for lumbar disc herniation) Product Outline

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

腰椎椎間板ヘルニア治療剤

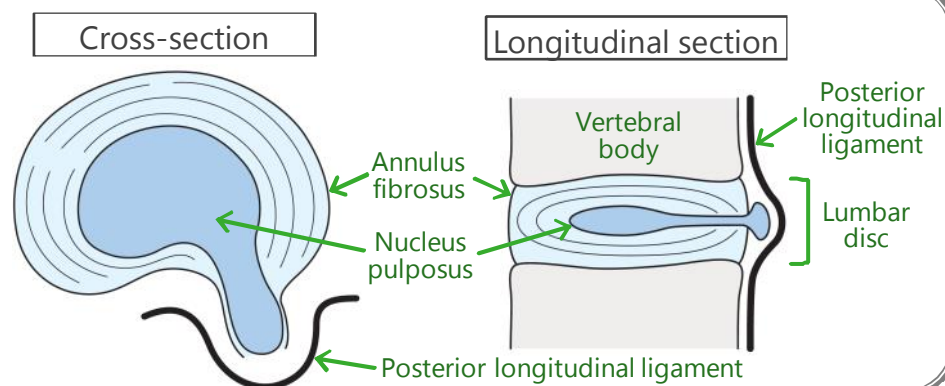
**ヘルニコア<sup>®</sup>** 椎間板注用1.25単位

HERNICORE<sup>®</sup> 1.25units for Intradiscal inj.  
注射用コンドリナーゼ

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.		

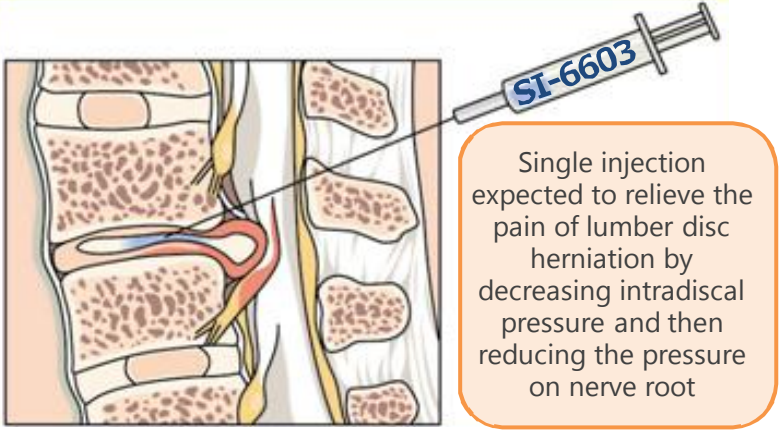
### ※Herniation by prolapse of the posterior longitudinal ligament (subligamentous extrusion)

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



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

Obtained new drug application approval in Japan in Mar 2018 in Japan  
Initiated a Phase III study and additional study in the U.S. in Feb 2018



Single injection expected to relieve the pain of lumbar disc herniation by decreasing intradiscal pressure and then reducing the pressure on nerve root

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

## Japan : Market Approval

**January 2014: NDA filed**

**March 2018: Obtained approval**

Launch timing announcement planned after listing in the NHI drug price list

## U.S. : PIII

**November 2017: Announcement of PIII**

(previous) study results

No statistically significant improvement in the primary endpoint found

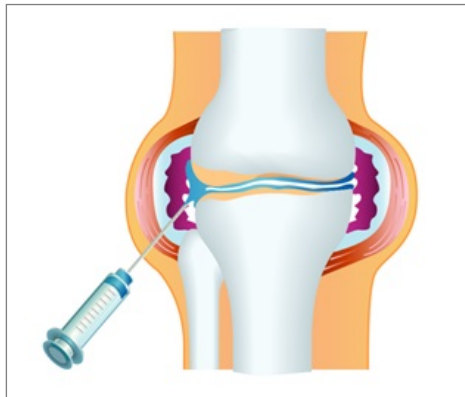
**February 2018: PIII additional study initiated**

› **Increase the probability of success by making changes from the previous study.**

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

# SI-613 Outline (Treatment of Osteoarthritis)

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



- 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)

- June 2017: Phase II study initiated

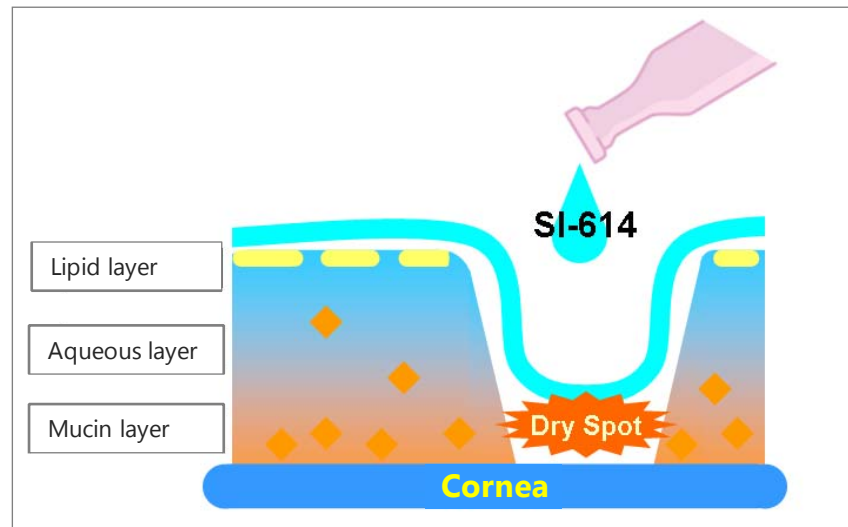
#### Expected Features

- 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-Steroidal Anti-Inflammatory Drug) side effects reported in oral or topical administration

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

# 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)
- Indication : Dry eye
- Formulation : Ophthalmic solution

**U.S. : P II/III**

- January 2015: Phase II/III clinical trials completed
- Proceed with consideration of a PIII trial and sales partner search

## 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 efficacy are available in the U.S. currently. SI-614 will provide a new alternative to the treatment of dry eye through its promising mode of action.

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

(Unit : hundred million)

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

《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 ¥110 ⇔ ¥105)

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

# 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

## 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	¥30.03
Annual Total Dividend	¥26.00	¥26.00	¥26.00	¥31.00 <sup>※1</sup>	¥26.00 <sup>※2</sup>	¥26.00
Dividend Payout Ratio	31.1%	40.5%	57.3%	98.3%	37.5%	86.6%

※1:including a 70th anniversary commemorative dividend of ¥5 per share

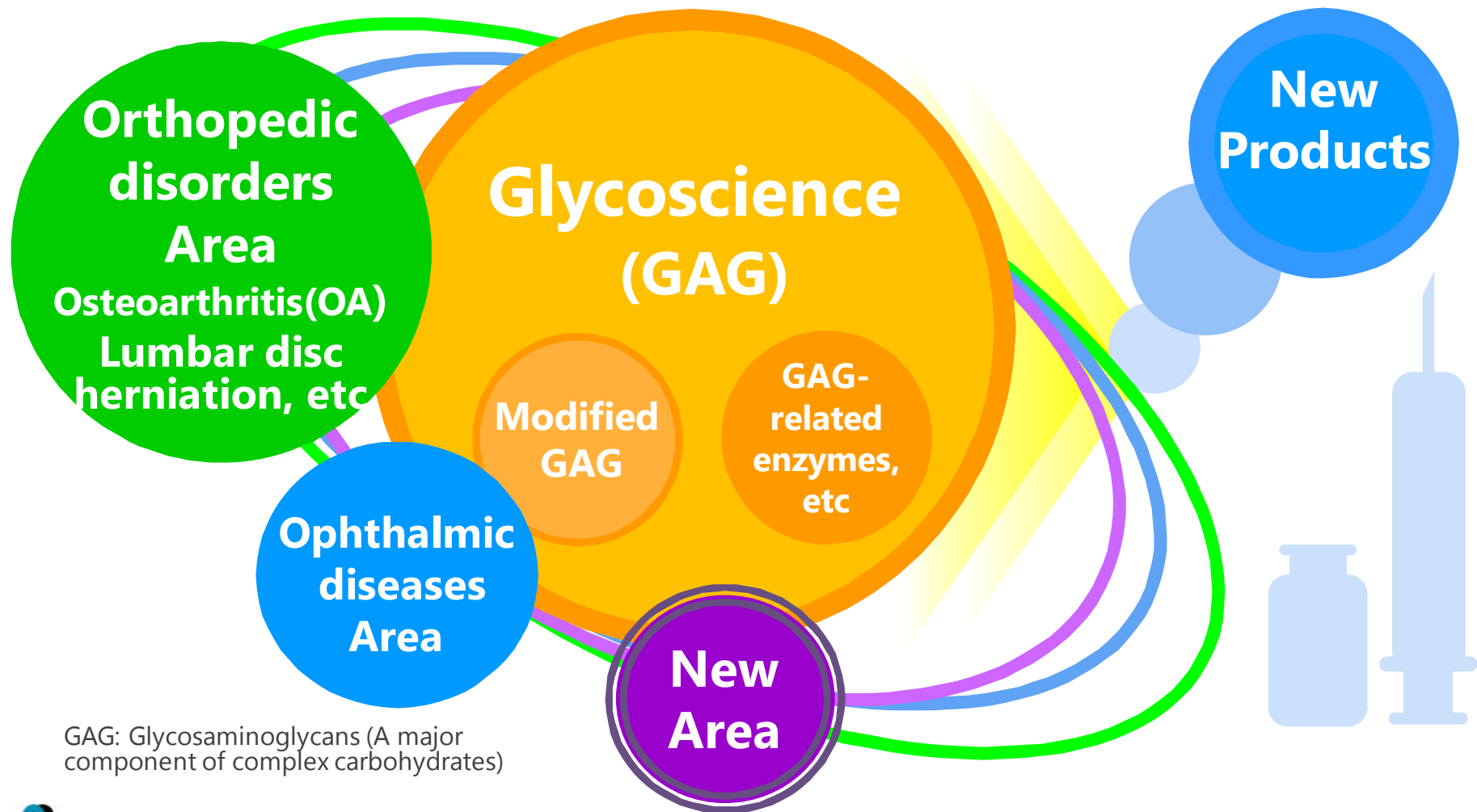
※2:A year-end dividend of ¥13 per share is scheduled to be decided at the Ordinary General Meeting of Shareholders to be held in June 2018.

# Appendix



# 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**

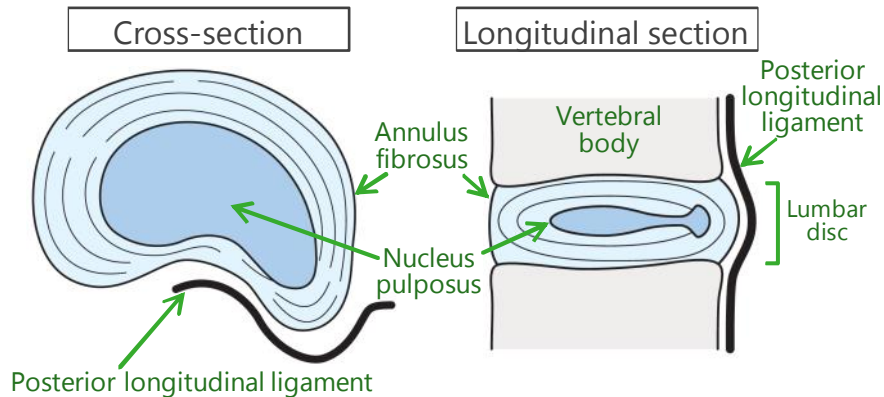




# Four types of lumbar disc herniation

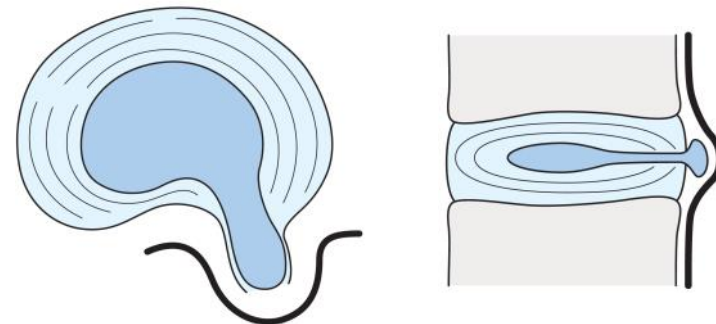
## 1. Protrusion

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



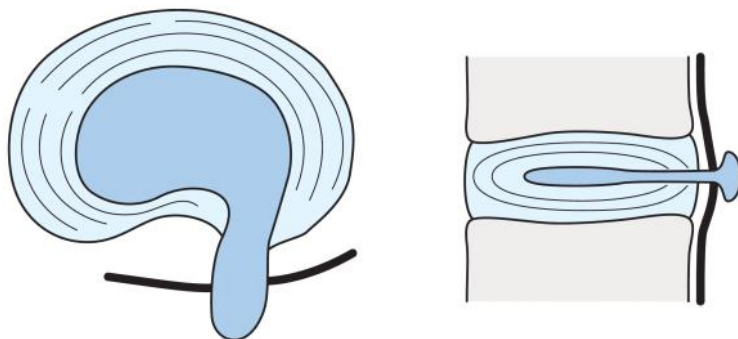
## 2. Subligamentous extrusion

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



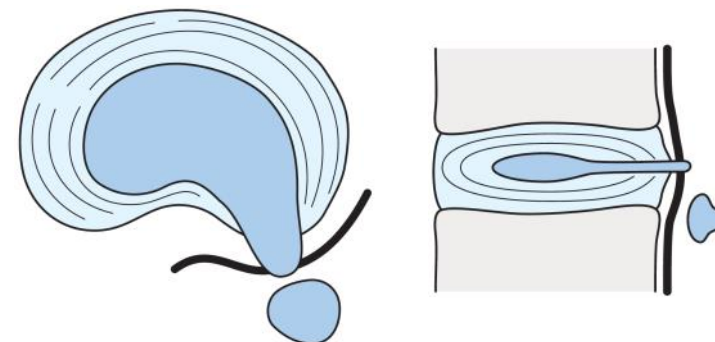
## 3. Transligamentous extrusion

The hernia perforates the posterior longitudinal ligament



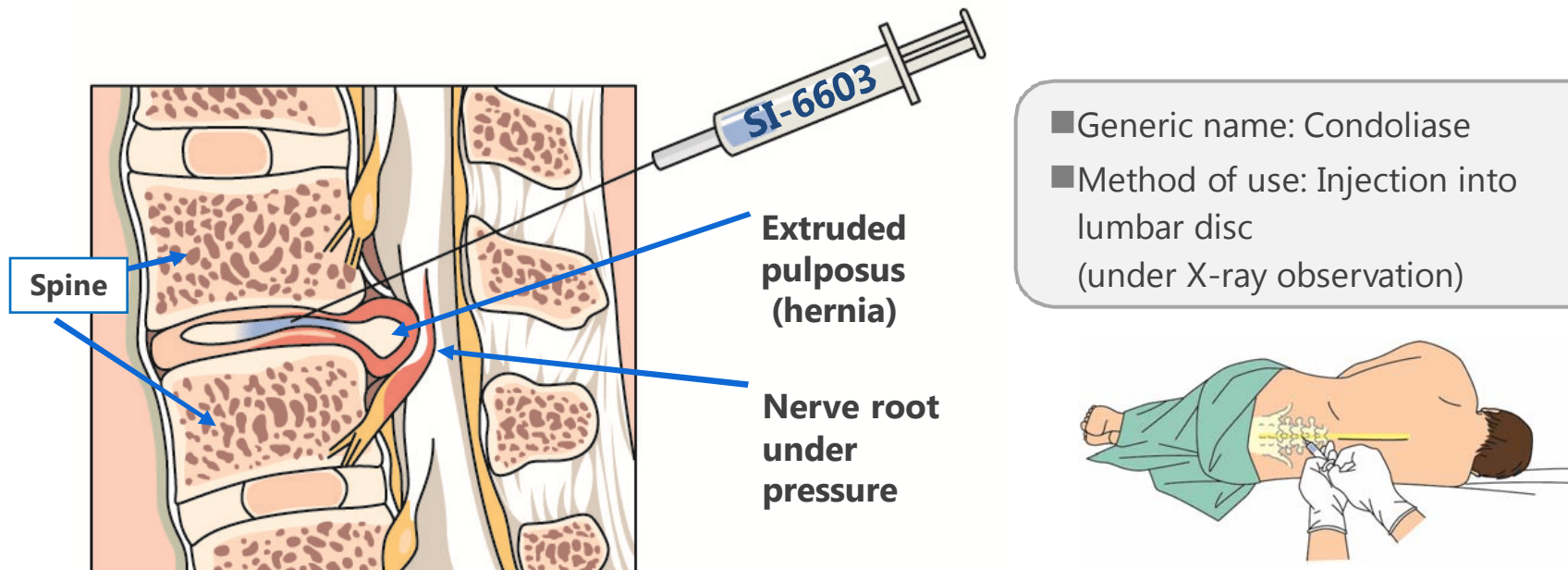
## 4. Sequestration

The hernia migrates outside the dura mater



# 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 (A major component of complex carbohydrates)

# 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

## 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 ~ Mar. 2017

\*VAS : Visual Analogue Scale

\*FPI : First Patient-in, LPO : Last Patient-out

# 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**

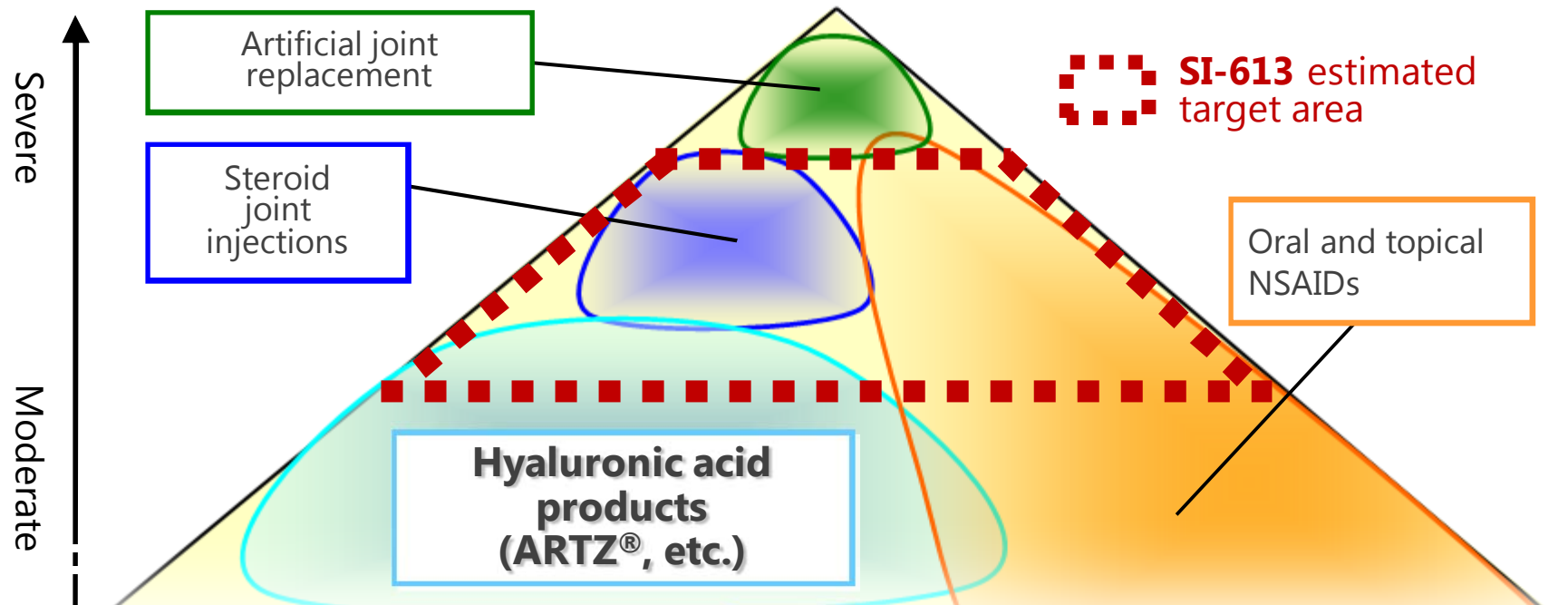
## Improvement at alleviation of leg pain (Subjective indicator)

- 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



**Target market size in Japan**  
\*Including applications outside the knee

Oral NSAIDs	¥88 billion
Topical NSAIDs	¥157 billion
HA injections	¥48 billion
Steroid injections	¥12 billion

# 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

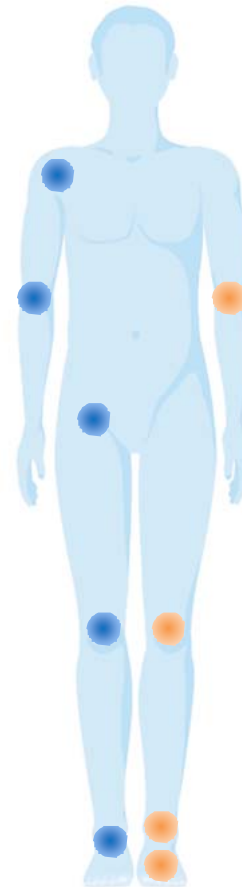
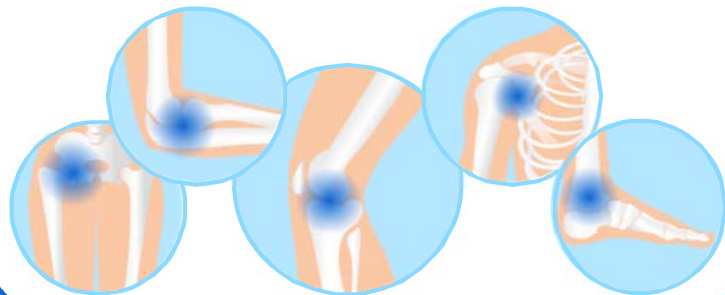
A disease in which joint tissue deteriorates due to abrasion of the articular cartilage, leading to inflammation and pain

### 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)

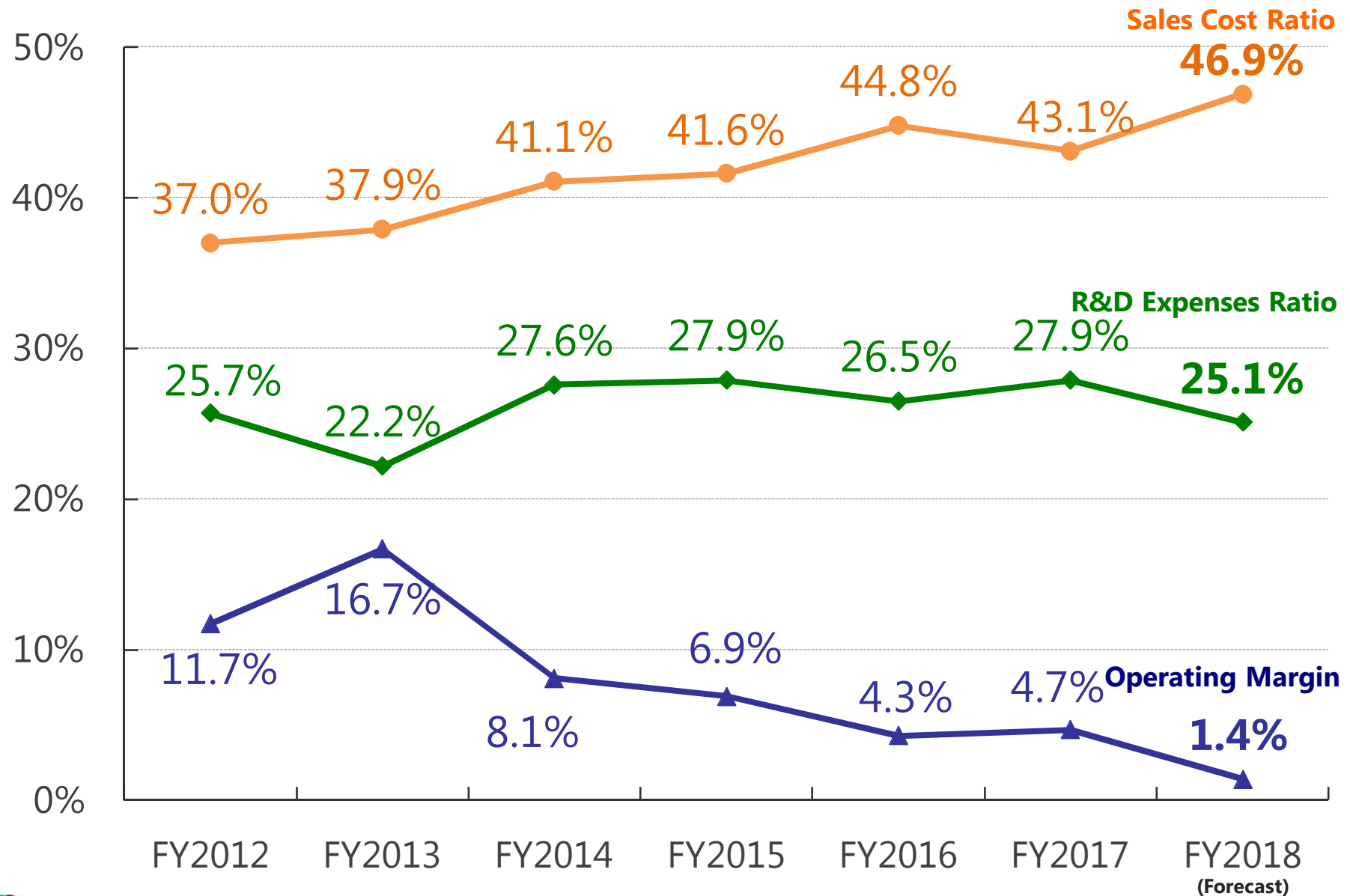


# Contract Status by R&D Theme

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

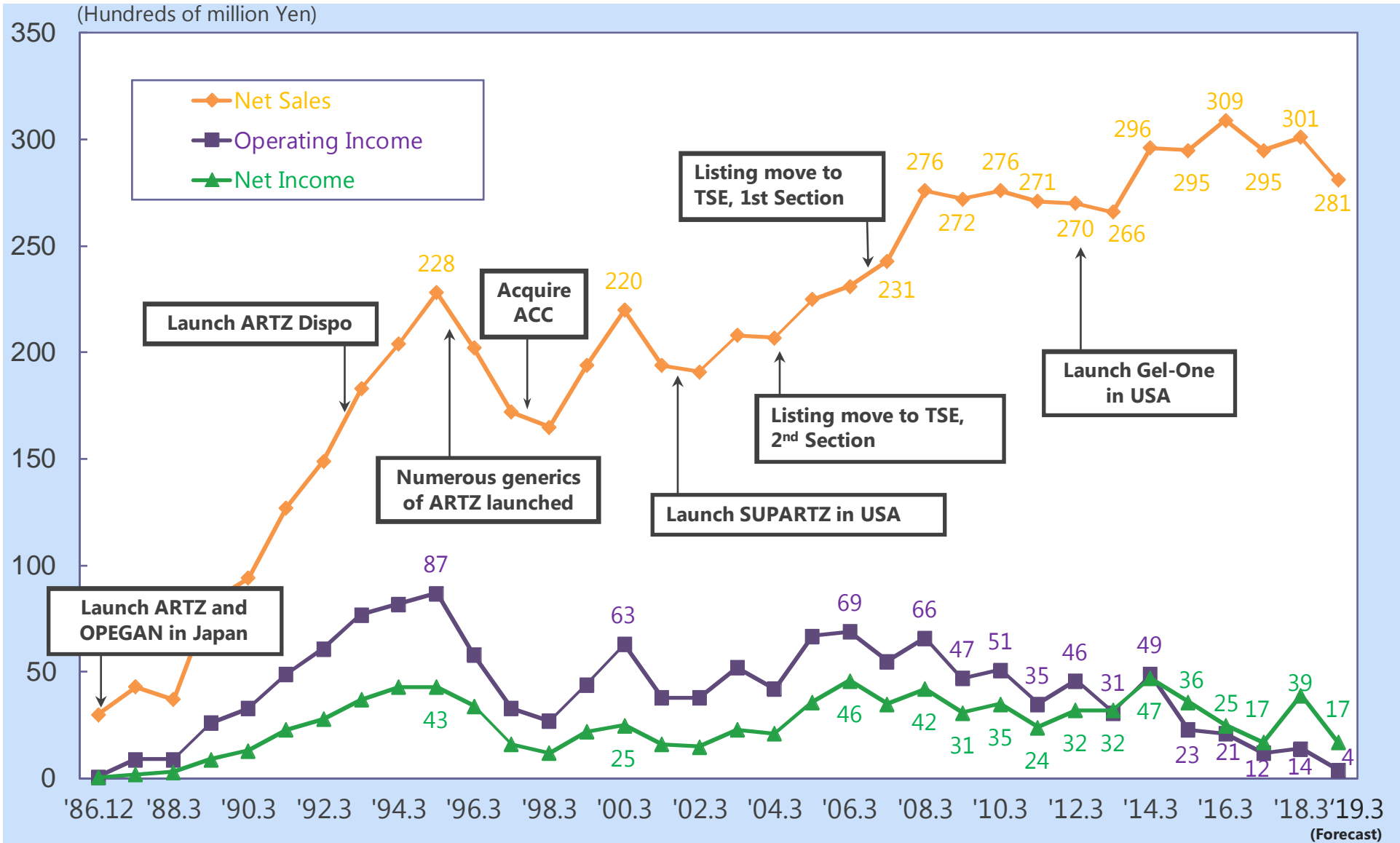
Development Code Indication	Development Location	Sales Partner	Total Amount of Milestone Royalties ( of which, in upfront payment )
SI-6603 Lumbar Disk Herniation	Japan	Kaken Pharmaceutical Co., Ltd.	Non-disclosure
	U.S.	Ferring Pharmaceuticals (Switzerland)	Max. US \$95 million (US \$5 million)
SI-613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

# Trend in Financial Index





# Business Progress & Highlights

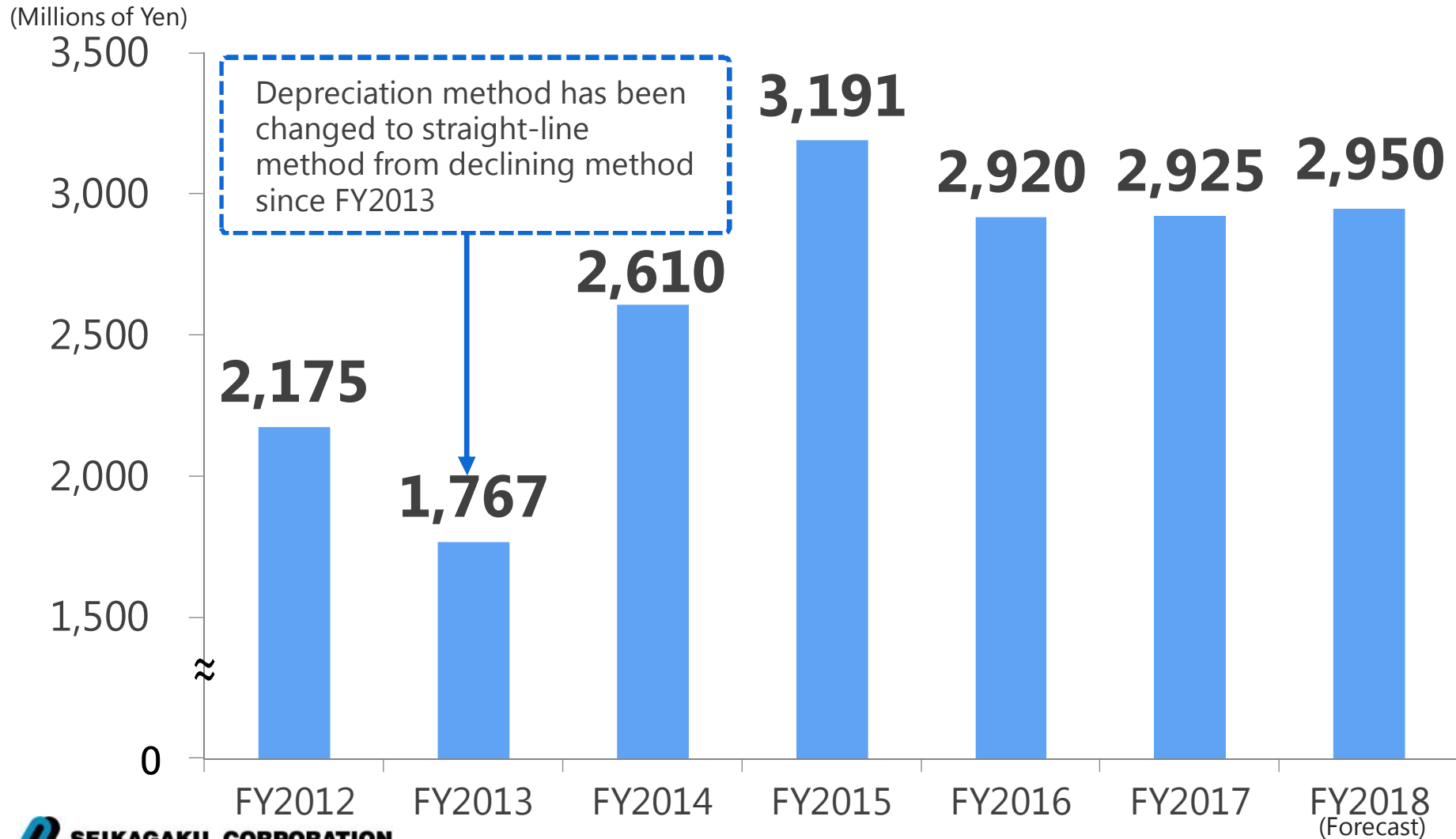


# Trend in Capital Investments

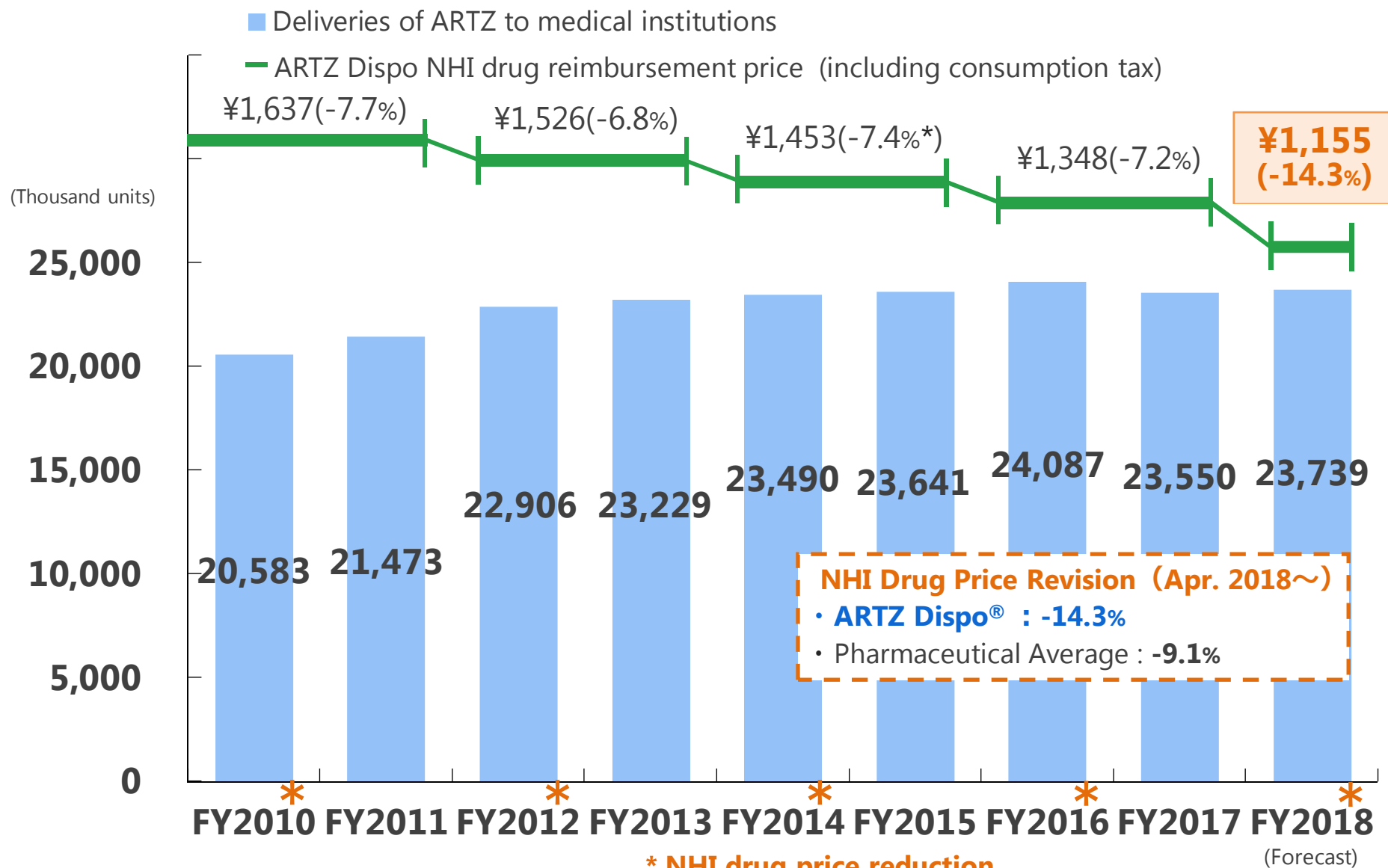
Facilities	Amounts (¥ bill.)	FY2011	FY2012	FY2013	FY2014	FY2015	FY2016	FY2017	FY2018 (Forecast)
SI-6603 Bulk Production Facilities	1.1				Start '14.10				
No. 5 Production Building (for ARTZ Dispo)	9.6	Start '12.3				Operation '15.1			
Hyaluronic Acid Bulk Production Facilities	3.1	Start '12.1			Operation '14.2				
Production Facilities for Gel-One	3.0	Start '11.12			Operation '13.10				
Chondroitin Sulfate Bulk Production Facilities	1.2		Operation '12.7						
<b>Amounts (Millions of Yen)</b>		<b>5,718</b>	<b>9,164</b>	<b>7,222</b>	<b>2,095</b>	<b>1,975</b>	<b>1,173</b>	<b>1,591</b>	<b>2,000</b>

# Trend in Depreciation

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



# 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

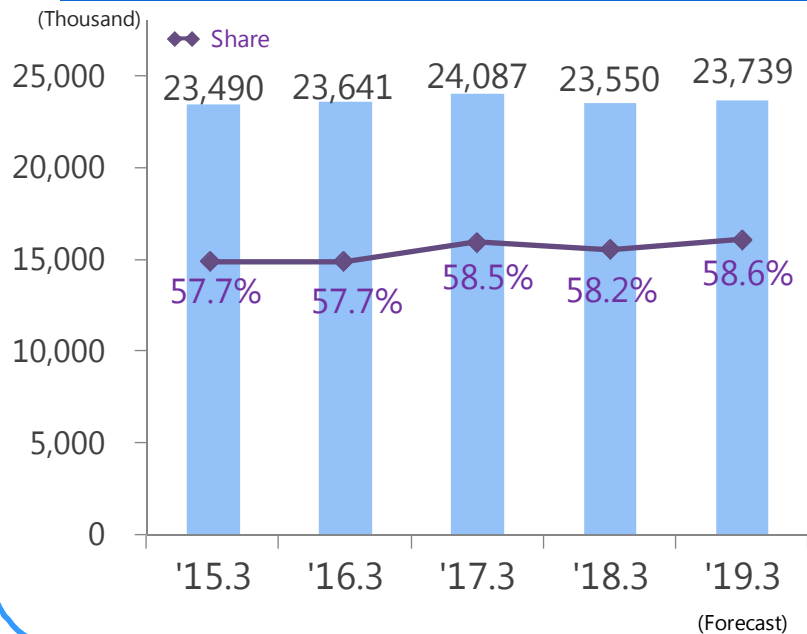
Joint-function improving agent

## 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



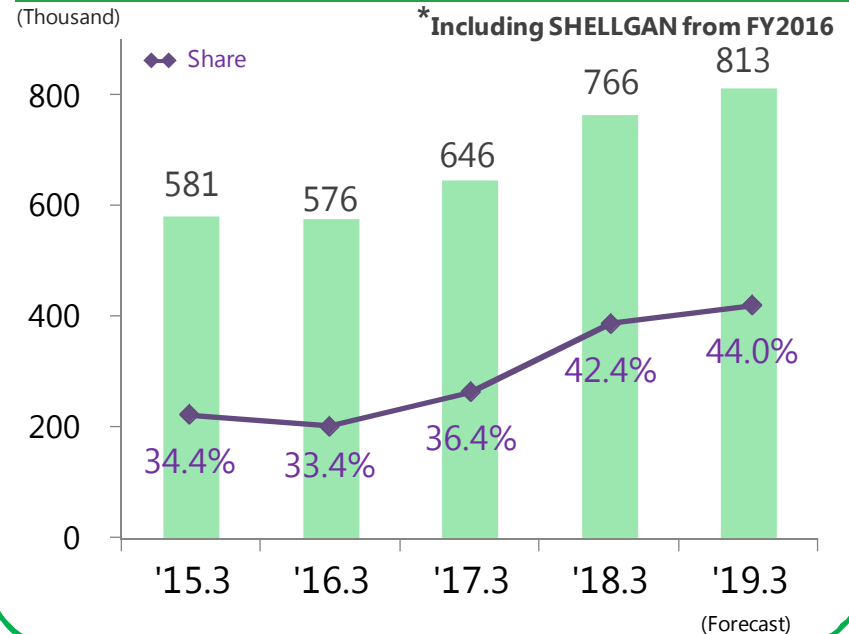
Ophthalmic surgical aids

## OPEGAN



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

### Trend in unit deliveries to medical institutions



# Ophthalmic Surgical Aid SHELLGAN (Launched July 2016)

眼科手術補助剤

薬価基準収載

## シェルガン® 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



OPEGAN OPEGAN Hi SHELLGAN

The OPEGAN series viscoelasticity comparison

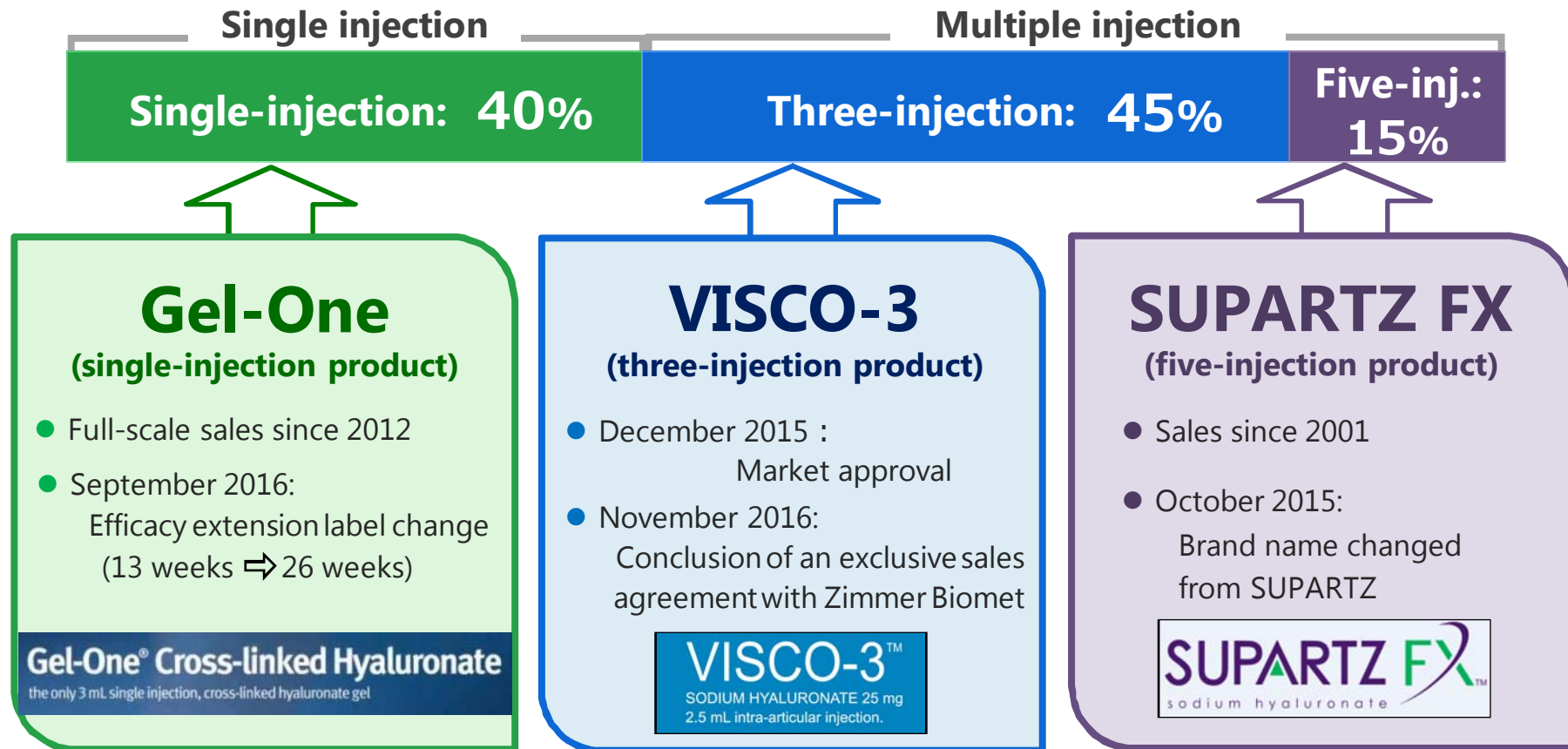
# Market Situation of Hyaluronic Acid Products in the U.S.

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

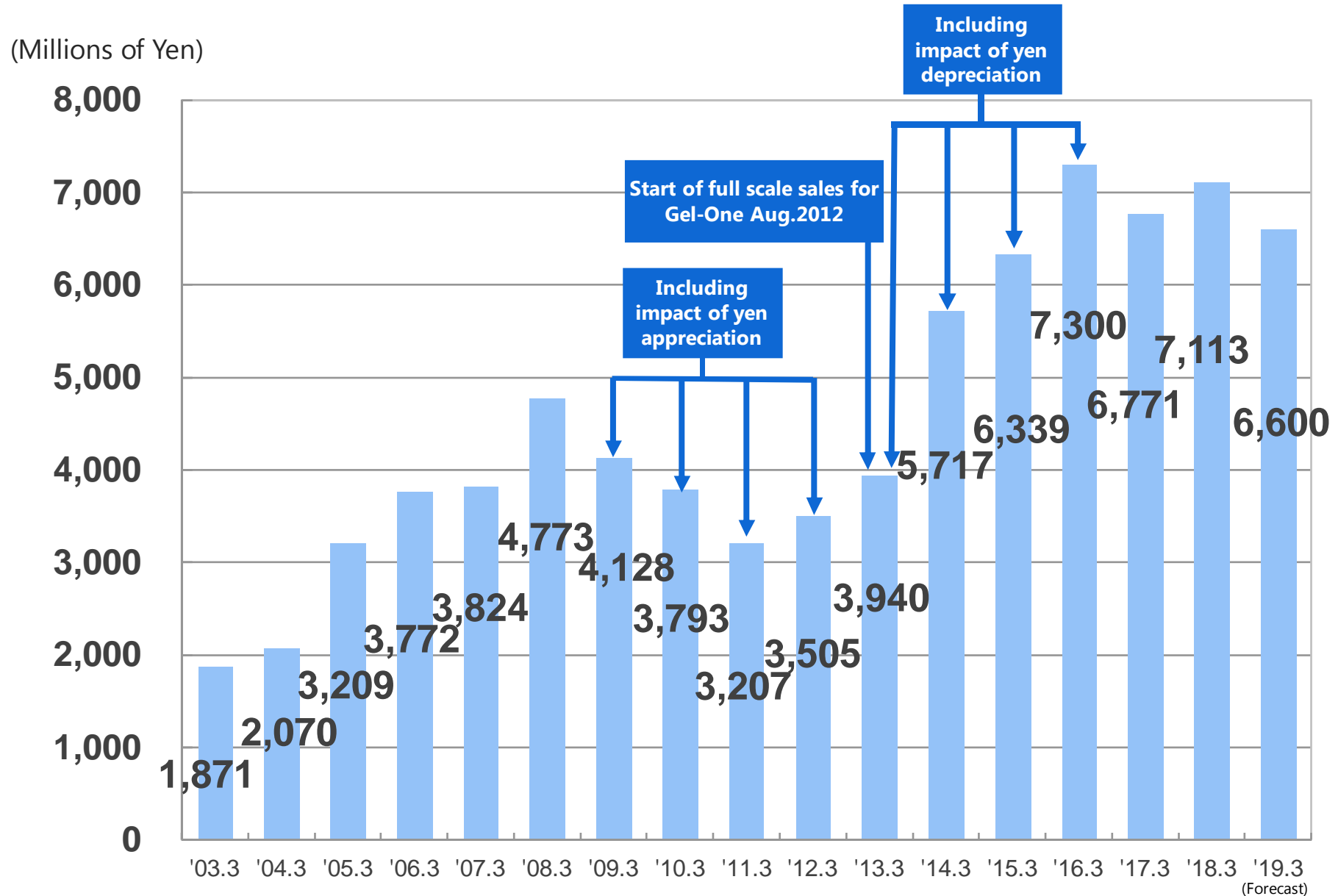
The market can be segmented according to the number of injections.

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

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



# Trend in Overseas Sales of Hyaluronic Acid Products





# 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)



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

## 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



PYROCHROME®



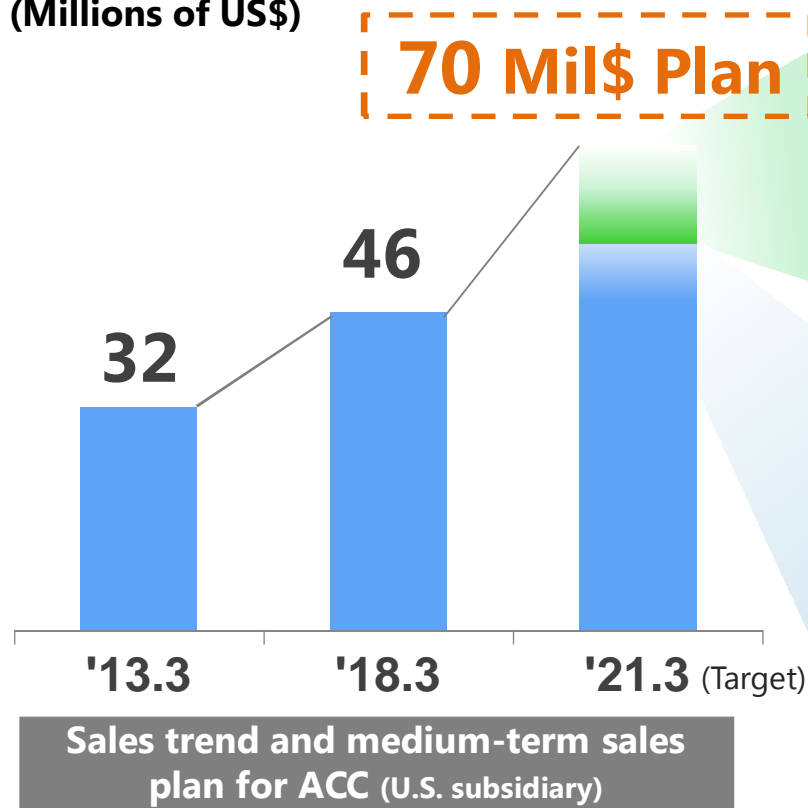
Exterior of the ACC offices

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



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

(Millions of US\$)



## ■ Opening up of new sales channels and new business sectors

- ✓ Opening up and expansion of new sales channels (Shift from selling through distributors to a direct sales structure)
- ✓ Collaborative business start-ups with partners from different industries

## ■ Strengthening of existing businesses

- ✓ Retaking of share from competitors through the introduction of new products and improved products
- ✓ Augmentation of sales capabilities through recruitment of sales representatives
- ✓ Expansion and enhancement of contract test services

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)

# 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**

**1.**

**Preparing for launch of SI-6603, a treatment for lumbar disc herniation**

**2.**

**Powering up as a leader in the knee osteoarthritis market**

**3.**

**Enhancement of the development pipeline**

**4.**

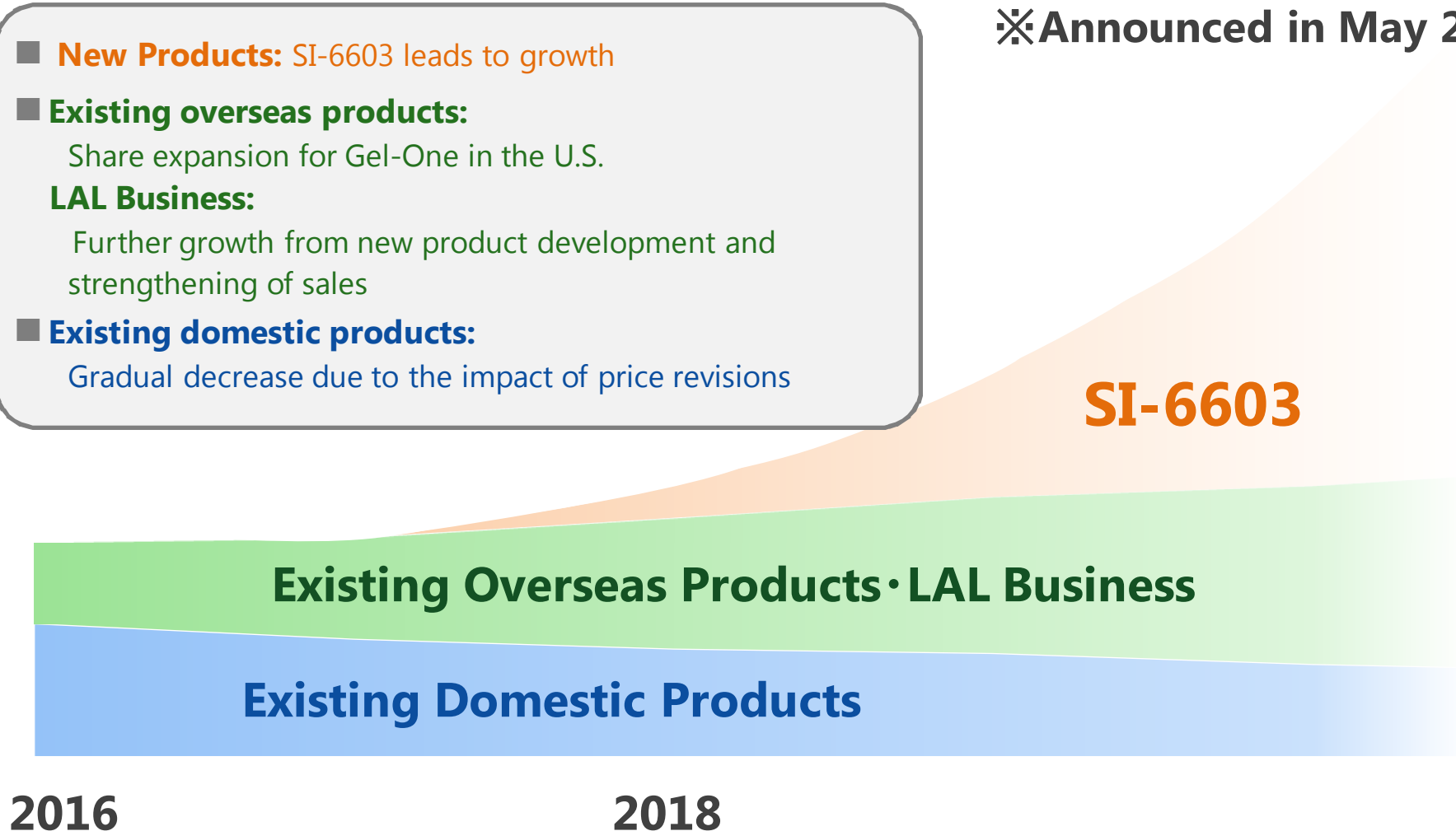
**Pursuit of an optimal production system**

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

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

※Announced in May 2016

- **New Products:** SI-6603 leads to growth
- **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



Existing Overseas Products · LAL Business

Existing Domestic Products

SI-6603

2016

2018

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

# Special Profile

1

## 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

## Unique business model

- 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

3

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

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

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

# Our Business Segment

## Pharmaceutical Business

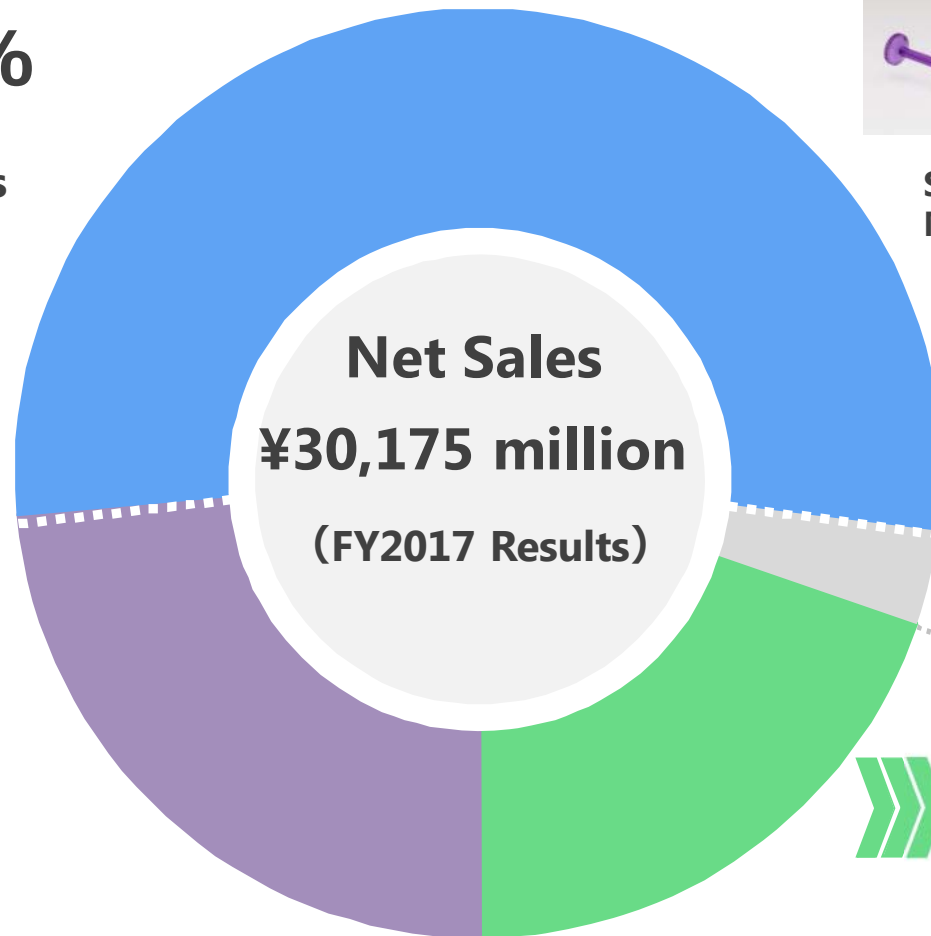
80.3%

Domestic  
Pharmaceuticals  
→ 53.4%

Joint Function  
Improving Agents



Overseas  
Pharmaceuticals  
→ 23.6%



Ophthalmic Surgical Aids



Surgical Aids for Endoscopic  
Mucosal Resection



Bulk Products  
→ 3.3%



LAL  
Business  
19.7%

Endotoxin-detecting  
reagents  
(used mainly for quality control  
of pharmaceuticals and medical  
devices)



# 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.



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