

# Financial Results for the 3rd Quarter of Fiscal Year 2018

(April 1, 2018 – December 31, 2018)

**Healthy-Knee.com**

We support your joy of walking



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



**SEIKAGAKU CORPORATION**

(TSE:4548)

# Contents

## ■ 3Q Financial Results P3

- Net Sales P4-6
- Income P7
- Trend in R&D Expenses P8

## ■ Research and Development P9

- SI-6603 (Lumbar disc herniation) P10
- SI-613 (Osteoarthritis/Enthesopathy) P11
- SI-449 (Adhesion Barrier) P12
- Clinical Study Information P13

## ■ Basic Policy on Profit Distribution P14

## ■ Appendix 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 for 3rd Quarter of FY2018

(Millions of Yen)	3Q FY2018 Results	Year-on-Year		(Reference) FY2018 Full Year Forecasts	
		Change	% of Change	FY 2018 Forecasts	Degree of Progress
Net sales	21,586	-1,814	-7.8%	28,100	76.8%
Operating Income	1,351	-1,779	-56.8%	400	337.9%
Ordinary Income	2,953	-2,936	-49.9%	2,250	131.3%
Net Income	2,253	-2,097	-48.2%	1,700	132.6%
R&D Expenses (Ratio to net sales)	4,992 (23.1%)	-158 (+1.1pt)	-3.1%	7,050 (25.1%)	70.8%
Average Exchange Rate (1US\$)	¥111.15	-¥0.56		¥105.00	

	3Q FY2018 Results	3Q FY2017 Results	(Reference) FY2018 Forecasts
Net Income per Share	¥ 39.91	¥ 76.87	¥ 30.11

# Net sales by Business Segment (3Q of FY2018)

(Millions of Yen)	3Q FY2018 Results	Year-on-Year	% of Change
Net sales	21,586	-1,814	-7.8%
<b>Pharmaceuticals Business</b>	<b>16,713</b>	<b>-2,444</b>	<b>-12.8%</b>
<b>Domestic Pharmaceuticals</b>	<b>10,938</b>	<b>-1,942</b>	<b>-15.1%</b>
Overseas Pharmaceuticals	4,909	-674	-12.1%
Bulk Products	864	+172	+24.9%
LAL Business	4,873	+630	+14.8%
(Overseas sales)	8,968	-110	-1.2%

\*Foreign exchange impact on overall net sales:  
approx. -130 million yen

## Domestic Pharmaceuticals

### ➤ ARTZ (Joint function improving agent)

- Overall market contraction (-1.4% year on year)
- Deliveries to medical institutions up slightly accompanying introduction of a modified product (+0.3%)
- Seikagaku sales down sharply, reflecting the impact of NHI drug price reductions implemented in April 2018 (-14.3%)

### ➤ OPEGAN series (Ophthalmic surgery aid)

- Overall market expansion (+5.2% year on year)
- Deliveries to medical institutions up (+9.5%), surpassing market growth rate, on continued growth from SHELLGAN
- Seikagaku sales at prior-year level. Volume growth compensated for NHI drug price reductions (approx. -9%)

### ➤ HERNICORE

(treatment for lumbar disc herniation)

- Since the Aug. 2018 launch, actively providing information to medical institutions
- Seikagaku sales low in the launch year

### ➤ MucoUp

(Surgical aid for endoscopic mucosal resection)

- Seikagaku sales at the prior-year level

# Net sales by Business Segment (3Q of FY2018)

(Millions of Yen)	3Q FY2018 Results	Year-on-Year	% of Change
Net sales	21,586	-1,814	-7.8%
<b>Pharmaceuticals Business</b>	<b>16,713</b>	<b>-2,444</b>	<b>-12.8%</b>
Domestic Pharmaceuticals	10,938	-1,942	-15.1%
<b>Overseas Pharmaceuticals</b>	<b>4,909</b>	<b>-674</b>	<b>-12.1%</b>
Bulk Products	864	+172	+24.9%
LAL Business	4,873	+630	+14.8%
(Overseas sales)	8,968	-110	-1.2%

\*Foreign exchange impact on overall net sales:  
approx. -130 million yen

## Overseas Pharmaceuticals

\*Foreign exchange impact on Overseas Pharmaceuticals:  
approx. -40 million yen

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

- Market environment for hyaluronic acid injectable treatments increasingly difficult due to intensifying competition and tightening of reimbursement requirements by some insurance companies
- Local sales up approx. 5% on a volume basis due to sales partner sales promotion measures
- Seikagaku sales down due to the impact of lower local selling prices and slippage of shipments into 4Q

### ➤ ARTZ (Multiple injection)

#### ● SUPARTZ FX in the U.S.

- Intensification of competition and strong impact of tightening of reimbursement requirements by some insurance companies
- Local sales and Seikagaku sales down sharply

#### ● ARTZ in China

- Sales partner's successful sales expansion activities targeting both urban and surrounding areas
- Local sales and Seikagaku sales up

# Net sales by Business Segment (3Q of FY2018)

(Millions of Yen)	3Q FY2018 Results	Year-on-Year	% of Change
Net sales	21,586	-1,814	-7.8%
Pharmaceuticals Business	16,713	-2,444	-12.8%
Domestic Pharmaceuticals	10,938	-1,942	-15.1%
Overseas Pharmaceuticals	4,909	-674	-12.1%
Bulk Products	864	+172	+24.9%
LAL Business	4,873	+630	+14.8%
(Overseas sales)	8,968	-110	-1.2%

\*Foreign exchange impact on overall net sales: approx. -130 million yen

## Bulk Products

Sales of hyaluronic acid and chondroitin sulfate for pharmaceutical companies increased

\*Bulk Products : High-purity, high-quality hyaluronic acid and chondroitin sulfate for pharmaceuticals

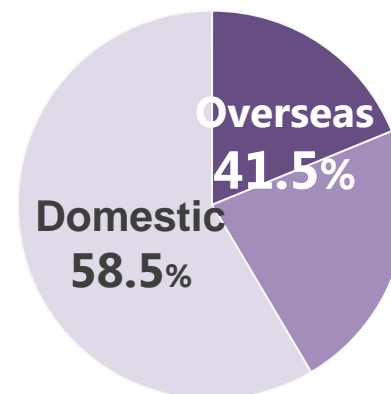
## LAL Business

\*Foreign exchange impact on LAL Business: approx. -90 million yen

Strong sales of endotoxin-detecting reagents and other products in Japan and overseas

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

## Overseas Sales Ratio



Year-on-Year:  
Up 2.7pt

# Income for 3Q of FY2018 (Year-on-Year)

(Millions of Yen)	3Q FY2018 Results	Year-on-Year	% of Change
Net sales	21,586	-1,814	-7.8%
Cost of Sales (Cost of Sales ratio)	9,970 (46.2%)	+207 (+4.5pt)	+2.1%
SGA expenses	10,264	-242	-2.3%
R&D Expenses (to Net sales ratio)	4,992 (23.1%)	-158 (+1.1pt)	-3.1%
Operating Income (to Net sales ratio)	1,351 (6.3%)	-1,779 (-7.1pt)	-56.8%
Ordinary Income	2,953	-2,936	-49.9%
Net Income	2,253	-2,097	-48.2%
Depreciation	2,169	-27	-1.2%

## Operating Income

### Cost of Sales Ratio (+4.5pt):

Increase due to the impact of NHI drug price reductions

### SGA Expenses (-242):

- Decrease due to expense cutting at Seikagaku, despite an increase at the overseas subsidiary accompanying reinforcing overseas sales activities in the LAL business
- Expected concentration of R&D expenses in 4Q

## Net Income

### Non-operating Income / Expenses (-1,156)

- Increase in gain on sale of investment securities (+577)
- Year-on-year decrease in royalty income (-1,491)

### Income Taxes (Tax Rate: 23.7%):

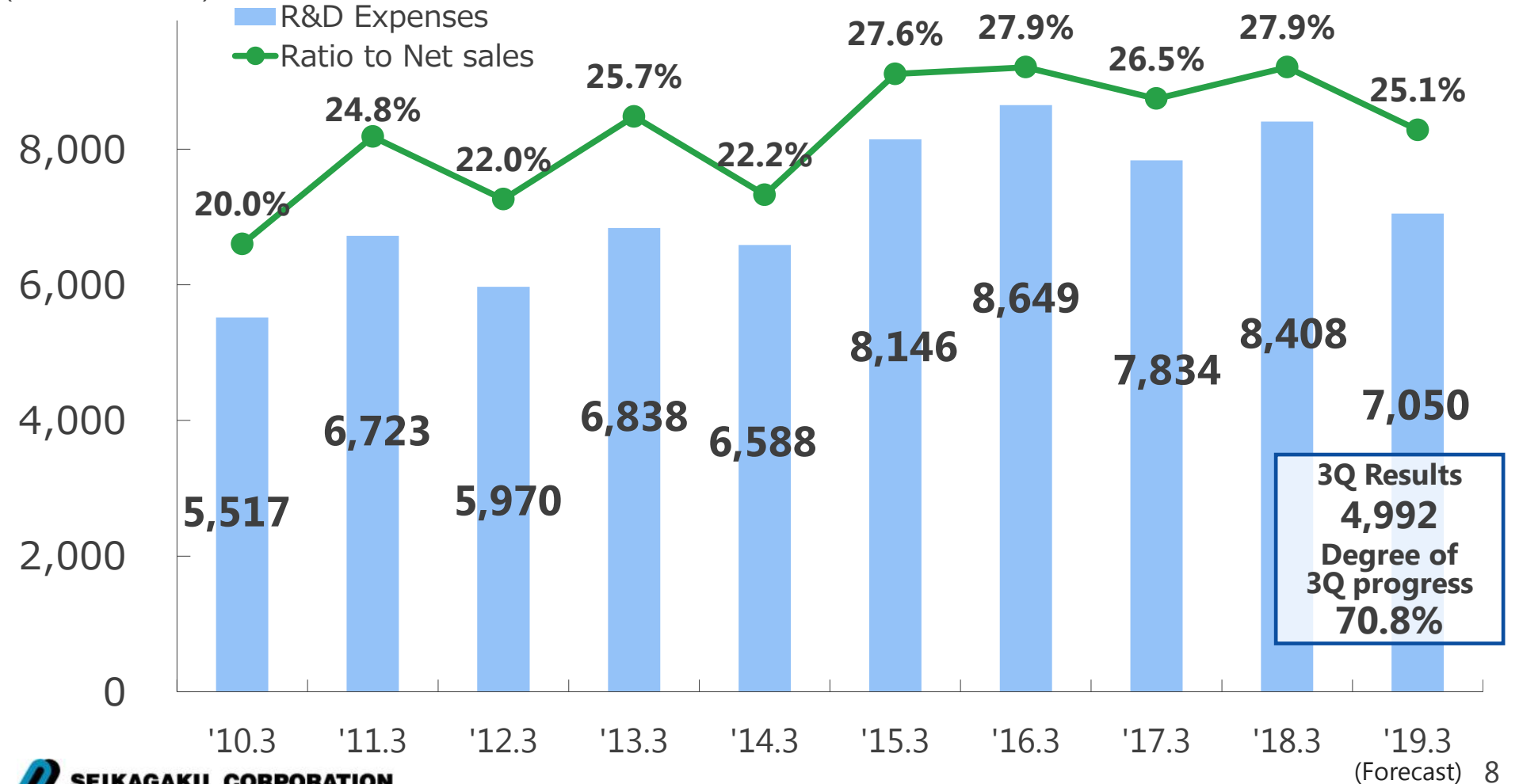
Impact of a tax decrease in the U.S. (-2.4pt)

# Trend in R&D Expenses

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

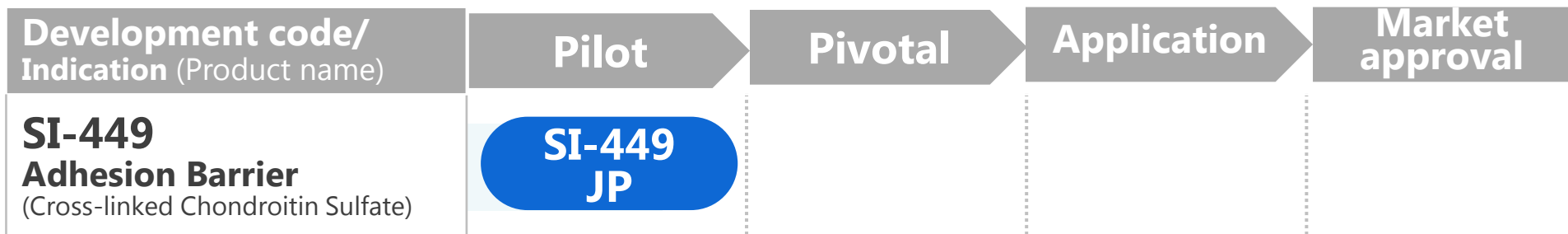
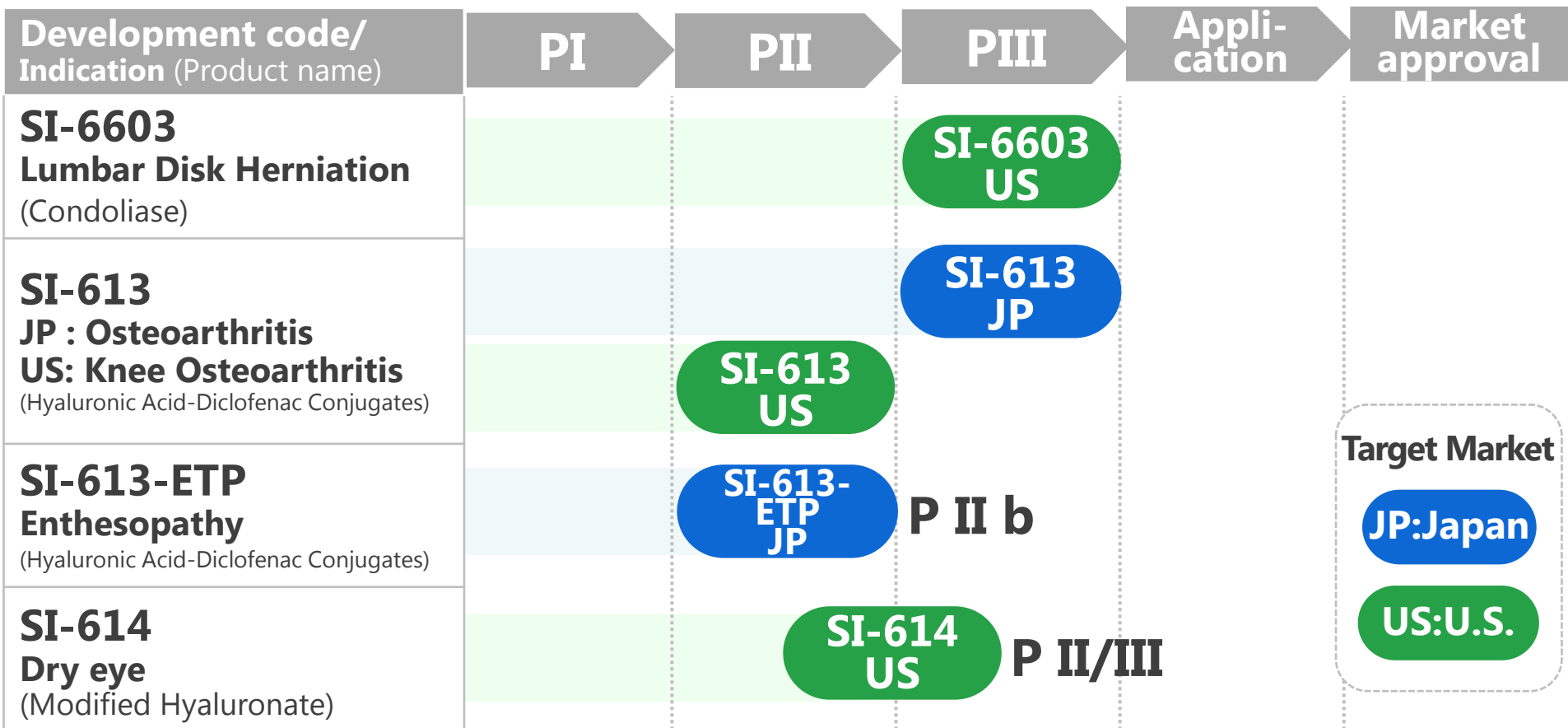
## Specializing in glycoscience and engaging in prioritized, efficient R&D

(Millions of Yen)



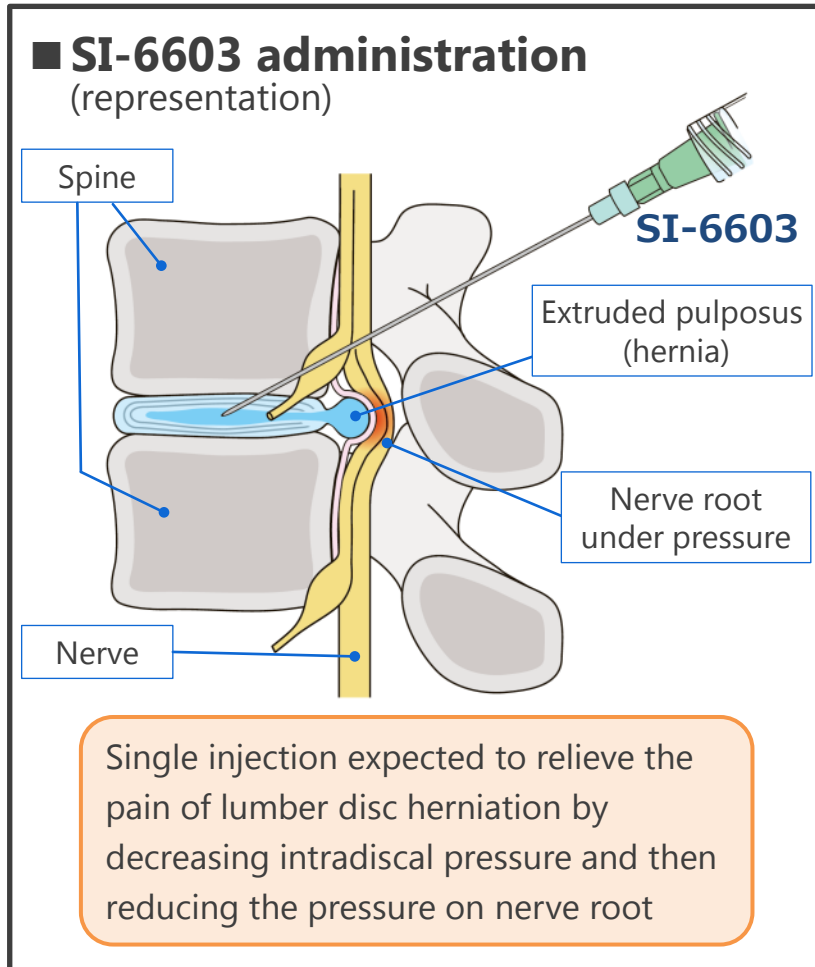


# Pipeline List (Research and Development themes)



# 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

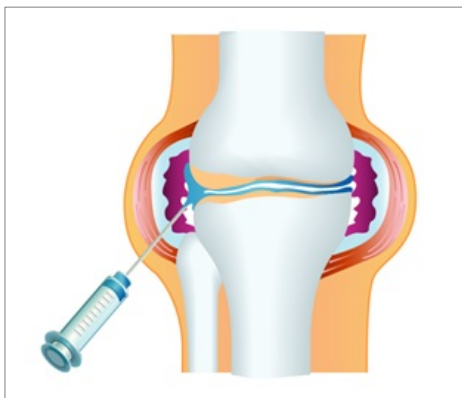
### February 2018: PIII additional study initiated

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

- Decrease the number of cases. (385 ⇨ 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/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. : P II (Indication: Knee osteoarthritis)

- June 2017: Phase II study initiated

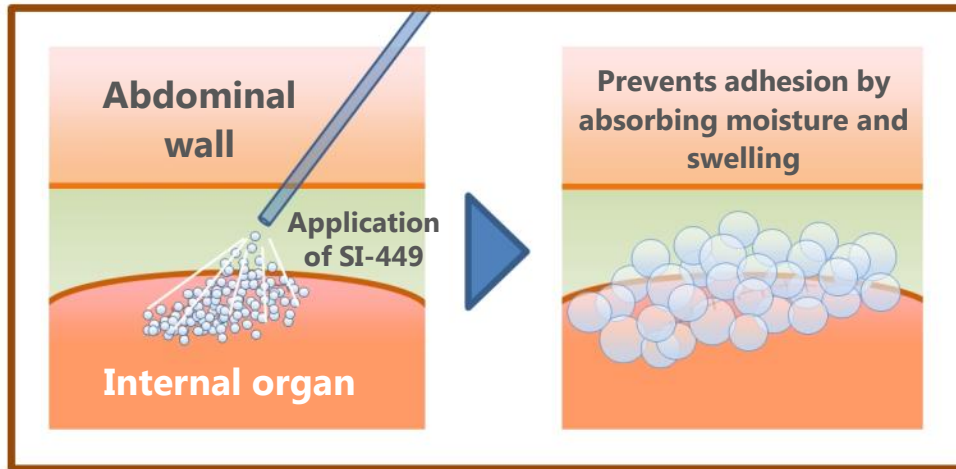
### Expected Features

- 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-449 Outline (Adhesion Barrier / Medical Device)

## Powdered formulation for preventing or mitigating post-operative 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 mitigate 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

# 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)
<b>SI-6603</b> Lumbar Disk Herniation	U.S.	Phase III additional study ( <a href="#">NCT03607838</a> )	320	May. 2018 – Nov. 2020	Leg pain (13 weeks)
<b>SI-613</b> Osteoarthritis	Japan	Phase III Knee confirmatory study ( <a href="#">JapicCTI-173537</a> )	440	Feb. 2017 – Jan. 2019	WOMAC(Knee pain) (12 weeks)
		Phase III study for four sites ( <a href="#">JapicCTI-173678</a> )	280	Aug. 2017 – Jun. 2019	Daily pain diary (12 weeks)
		Long-term administration study ( <a href="#">JapicCTI-183855</a> )	160	Feb. 2018 – Sep. 2019	Safety (52 weeks)
<b>SI-613-ETP</b> Enthesopathy	Japan	Late-stage Phase II clinical study ( <a href="#">JapicCTI-173758</a> )	240	Oct. 2017 – Oct. 2018	Pain in motion (4 weeks)
<b>SI-613</b> Knee Osteoarthritis	U.S.	Phase II clinical study ( <a href="#">NCT03209362</a> )	80	Oct. 2017 – Nov. 2018	WOMAC(Knee pain) (12 weeks)
<b>SI-614</b> Dry eye	U.S.	Phase II / III clinical study ( <a href="#">NCT02205840</a> )	240	Jul. 2014 – Nov. 2014	Corneal staining score, Symptom score (28 days)
<b>SI-449</b> Adhesion Barrier	Japan	Pilot study ( <a href="#">UMIN000033294</a> )	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) [http://www.clinicaltrials.jp/user/cteSearch\\_e.jsp](http://www.clinicaltrials.jp/user/cteSearch_e.jsp)
- University hospital Medical Information Network (UMIN) Center <http://www.umin.ac.jp/ctr/index.htm>
- ClinicalTrials.gov <https://clinicaltrials.gov/ct2/search>

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

# Basic Policy on Profit Distribution

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

## 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	¥31.00*	¥26.00	¥26.00
Dividend Payout Ratio	31.1%	40.5%	57.3%	98.3%	37.5%	86.4%

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

# Appendix

A decorative graphic consisting of several overlapping, wavy blue lines that sweep across the middle of the page from left to right.

# Overview of Forecasts in FY2018

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

(Millions of Yen)	FY2018 Forecasts	FY2017 Results			(Reference) Degree of 3Q progress
		Results	Change	% of Change	
Net sales	28,100	30,175	-2,075	-6.9%	76.8%
Operating Income	400	1,421	-1,021	-71.9%	337.9%
Ordinary Income	2,250	5,327	-3,077	-57.8%	131.3%
Net Income	1,700	3,922	-2,222	-56.7%	132.6%
R&D Expenses (to Net sales ratio)	7,050 (25.1%)	8,408 (27.9%)	-1,358 (-2.8pt)	-16.2%	70.8%
Average Exchange Rate (1US\$)	¥105.00	¥110.86	¥-5.86		

	FY2018 Forecasts	FY2017 Results
Net Income per share	¥30.11	¥69.30
Dividend per share	¥26.00	¥26.00
Dividend Payout ratio	86.4%	37.5%

Exchange Rate Sensitivity (Impact of a change of ¥1 against the US\$)	
Net sales	Approx. ¥110 million
Operating income	Approx. ¥55 million



# Forecasts (Net sales) in FY2018

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

(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

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

(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.

# Domestic Pharmaceuticals

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

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

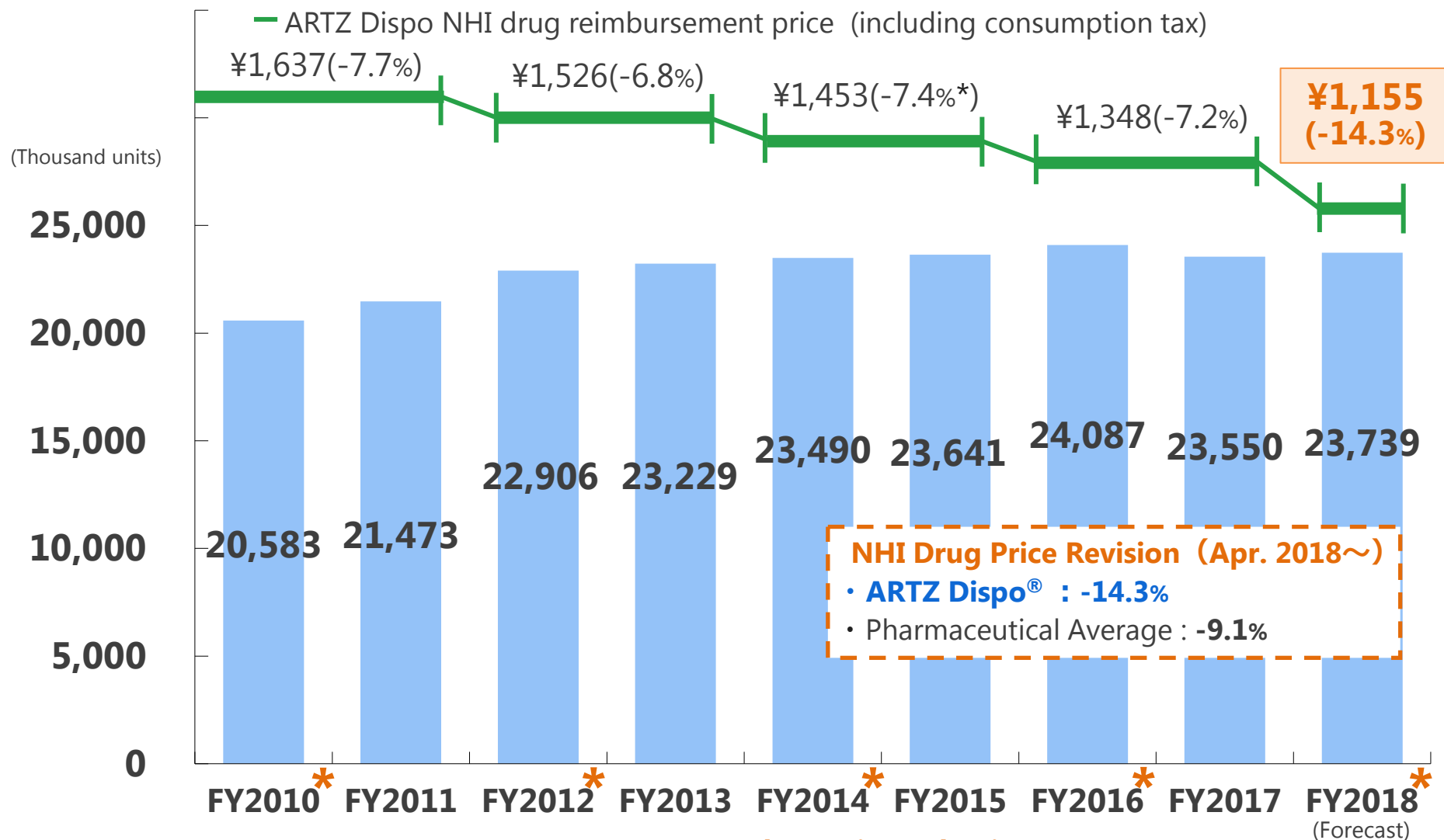
Joint-function improving agent <b>ARTZ</b>	<b>1H FY2018 Results</b>	<b>FY2018 Forecasts</b>	
	<ul style="list-style-type: none"> <li>● Market contraction due in part to an increase in treatment options, such as the emergence of concomitant medications</li> <li>● Only a slight decline in sales of ARTZ thanks to sales partner sales promotion measures</li> </ul>	<ul style="list-style-type: none"> <li>● Introduction of a improved syringe formulation in October</li> <li>● Aim for a further market share increase</li> </ul> <p>*ARTZ Dispo drug price revision rate: -14.3%</p>	
	ARTZ growth rate: -1.1% (Market growth rate: -2.5%) Market share: 59.2% (+0.9pt)	ARTZ growth rate <b>+0.8%</b> (forecast)	Market share <b>59.0%</b> (forecast)
Ophthalmic surgical aids <b>OPEGAN</b> (including SHELLGAN)	<b>1H FY2018 Results</b>	<b>FY2018 Forecasts</b>	
	<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>	<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 rate: Approx. -9%</p>	
	OPEGAN growth rate: +9.4% (Market growth rate: +3.9%) Market share: 43.9% (+2.2pt)	OPEGAN growth rate <b>+7.2%</b> (forecast)	Market share <b>44.5%</b> (forecast)

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

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

■ Deliveries of ARTZ to medical institutions

— ARTZ Dispo NHI drug reimbursement price (including consumption tax)



\* NHI drug price reduction

\* excluding the impact of consumption tax hike

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

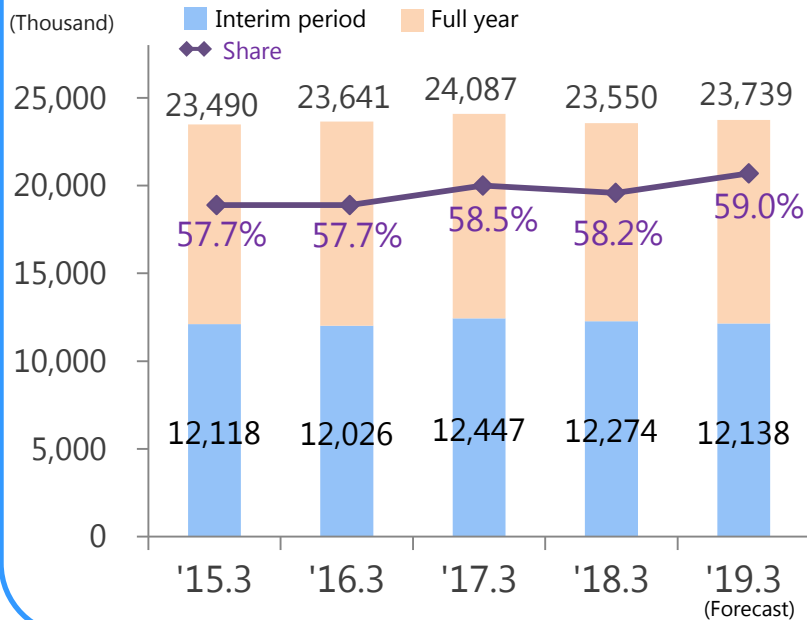
Joint-function improving agent

## 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



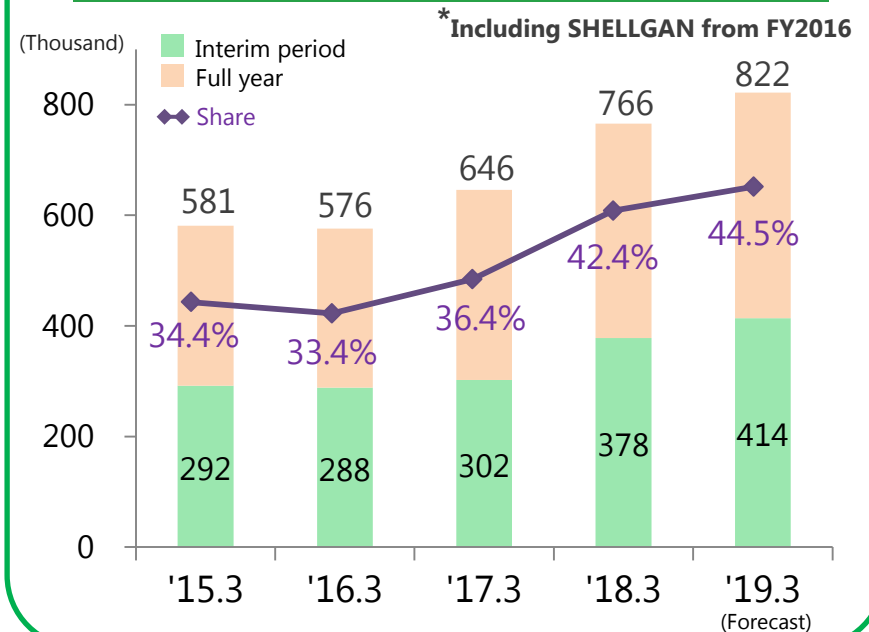
Ophthalmic surgical aids

## 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

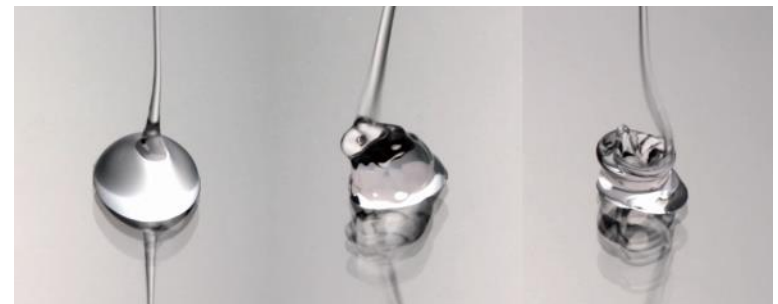


## Product SHELLGAN Outline

- 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

# 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

Product name	HERNICORE® 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

腰椎椎間板ヘルニア治療剤

薬価基準収載



**ヘルニコア®** 椎間板注用1.25単位

HERNICORE® 1.25units for Intradiscal inj.  
注射用コンドリアーゼ

処方箋医薬品 (注意—医師等の処方箋により使用すること)



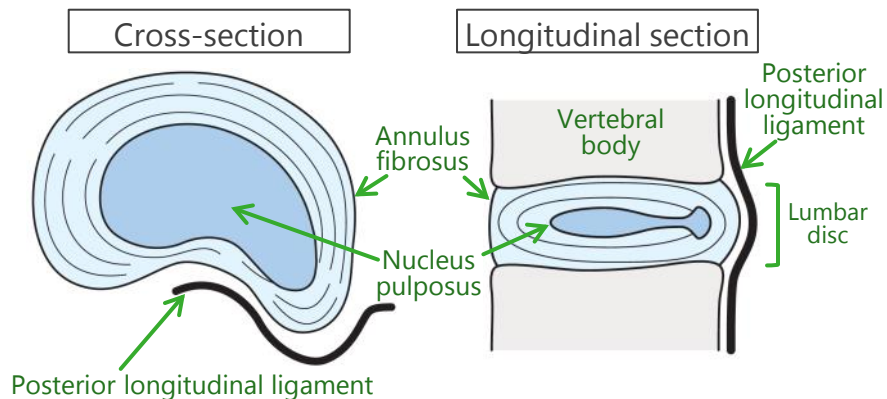
<Photograph of the HERNICORE>



# Four types of lumbar disc herniation

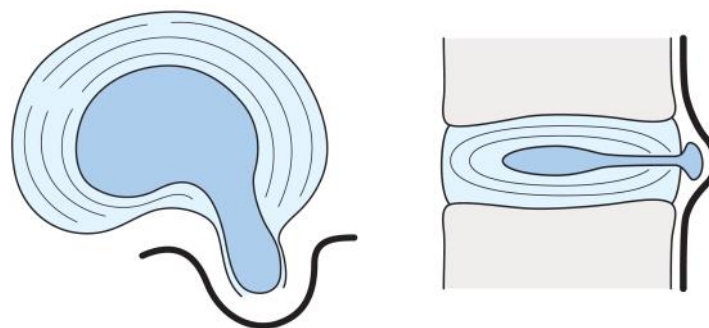
## 1. Protrusion

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



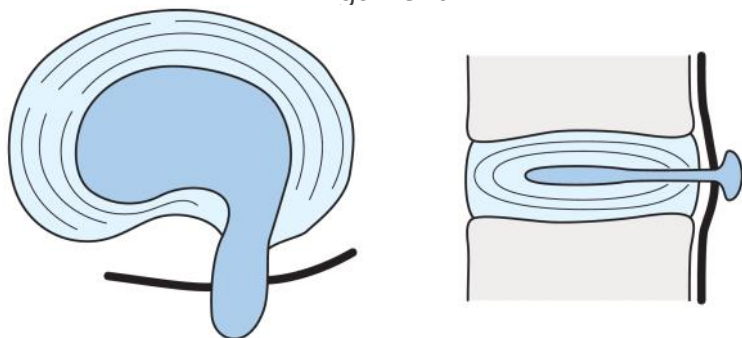
## 2. Subligamentous extrusion

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



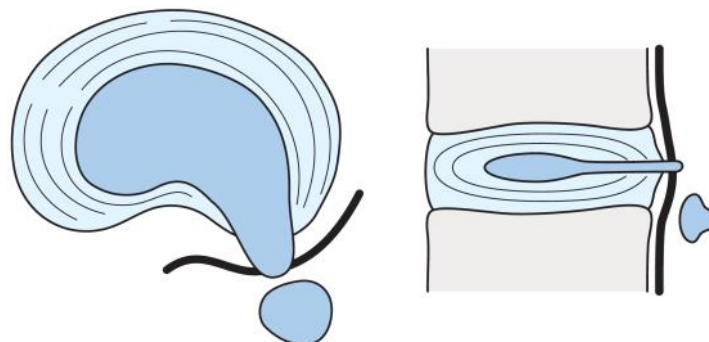
## 3. Transligamentous extrusion

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

(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

### Facility requirements Facilities that meet all of the conditions below

(As of November 2018)

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.**

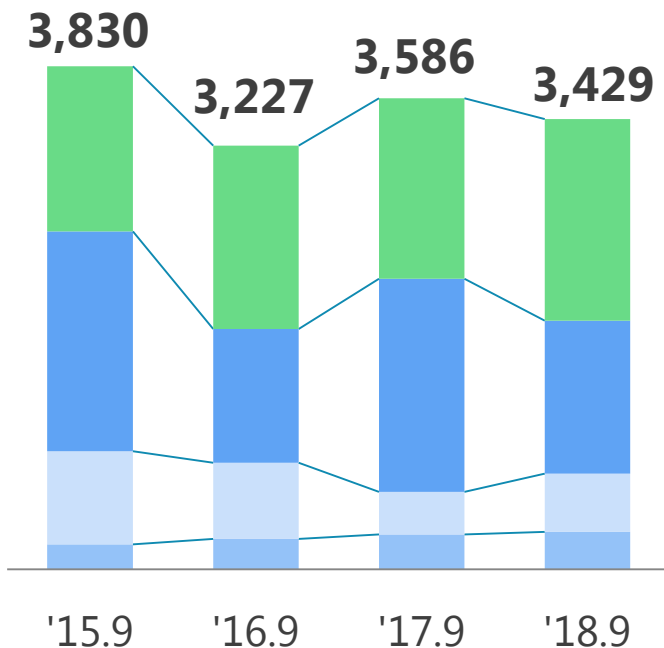
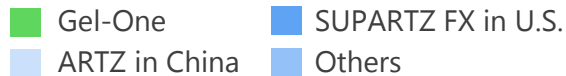
\*PMDA: Pharmaceuticals and Medical Devices Agency

# 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)

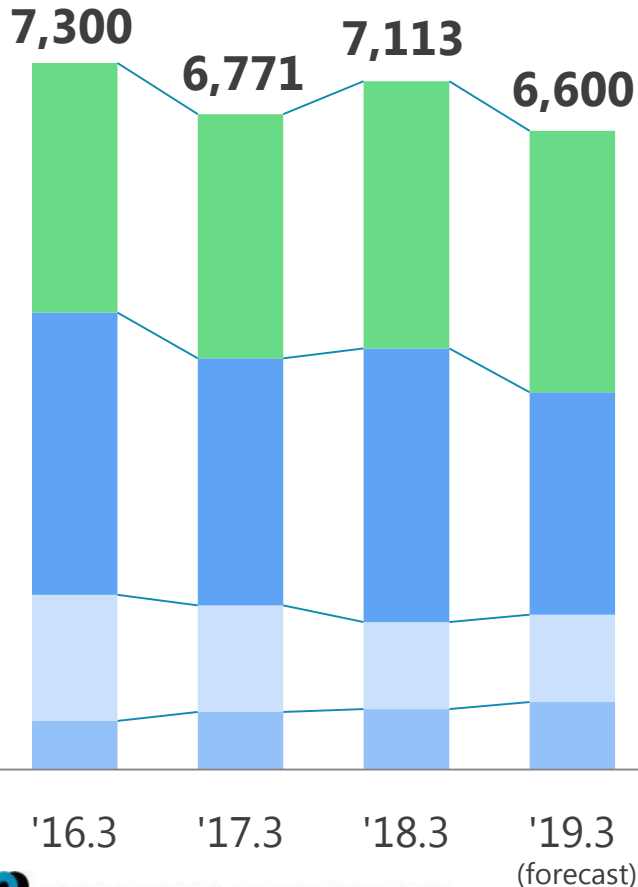
\* There is no change in forecast announced on May 11, 2018.

## Overseas Pharmaceuticals Sales trend

(Millions of Yen)

<Breakdown>

■ Gel-One      ■ SUPARTZ FX in U.S.  
■ ARTZ in China      ■ Others



**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

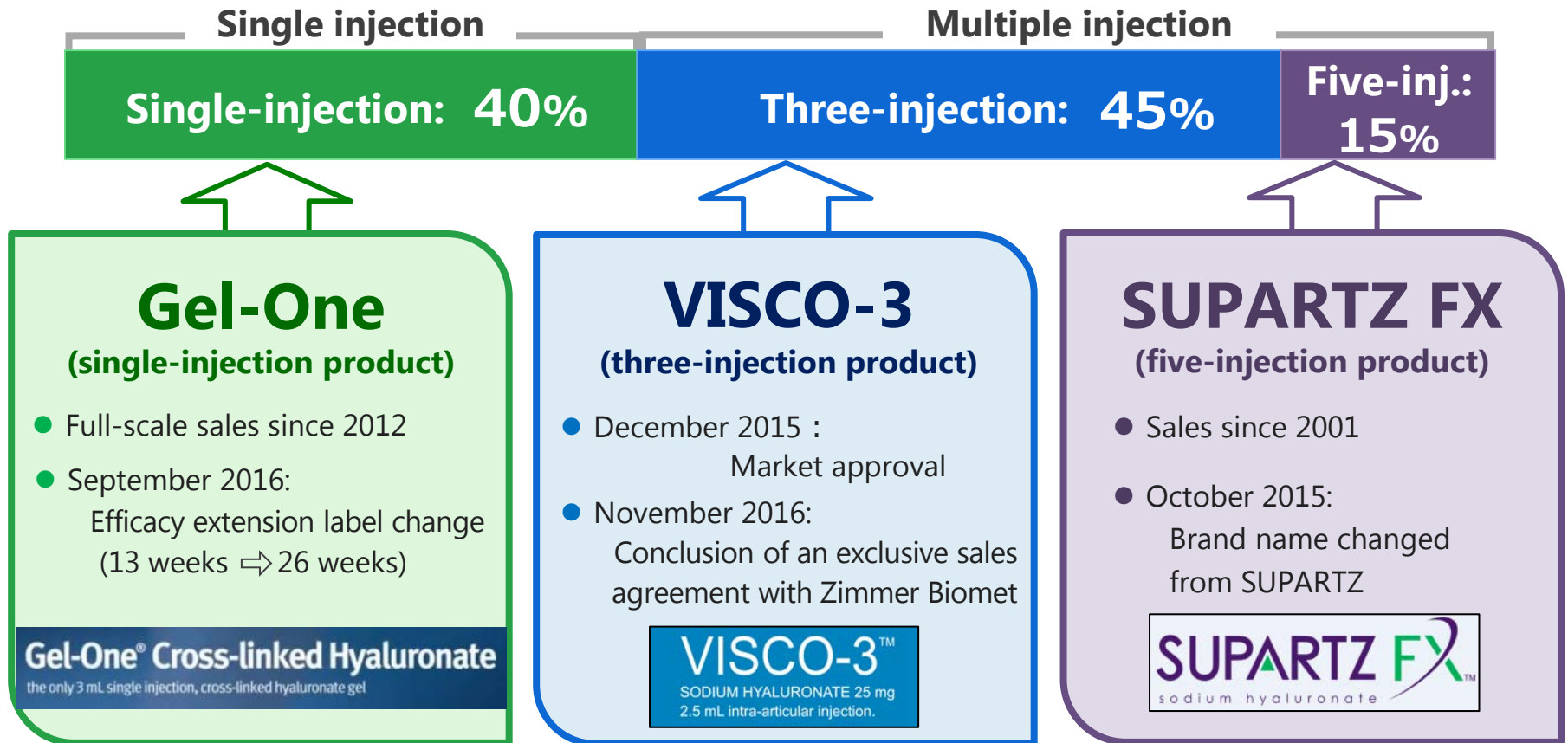
# Market Situation of Hyaluronic Acid Products in the U.S.

## 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

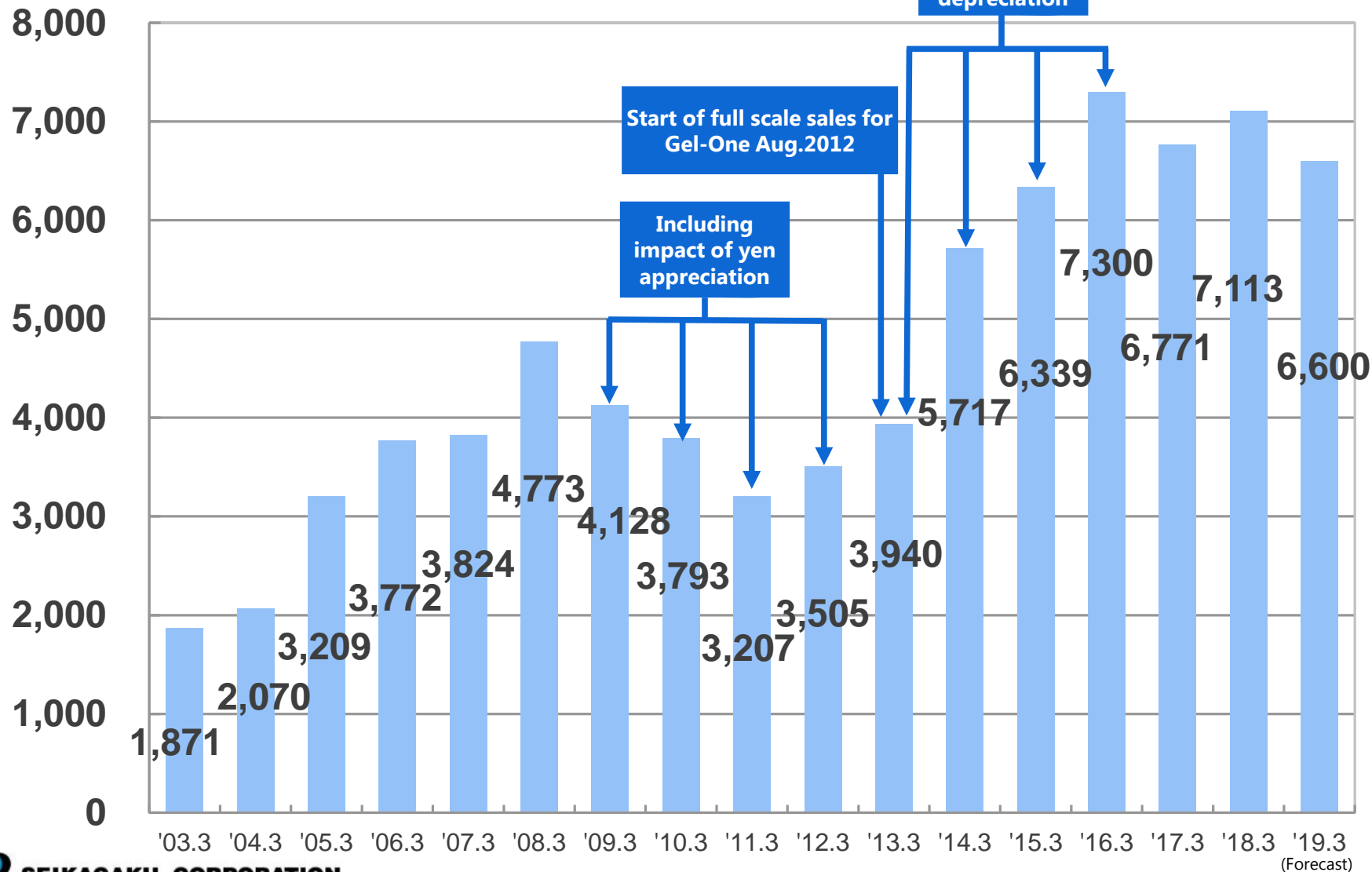
(value basis, 2017 figures, including competitors. Seikagaku estimates)



# Trend in Overseas Sales of Hyaluronic Acid Products

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

(Millions of Yen)



# 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



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



Exterior of the ACC offices

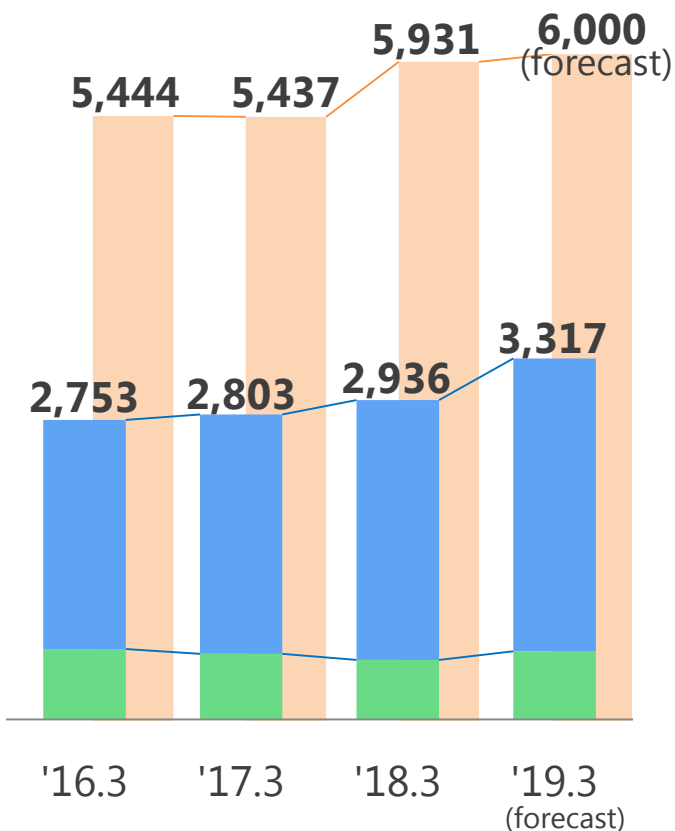
PYROCHROME®

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

## LAL Business Sales trend

(Millions of Yen)

■ Full year  
■ Overseas ■ Domestic  
 <1H Breakdown>



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

## 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).

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

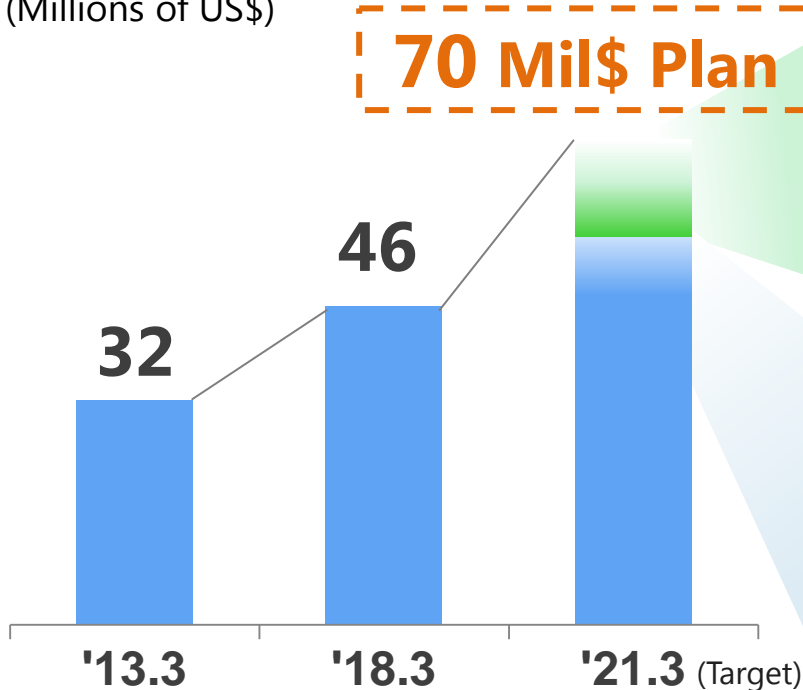


ASSOCIATES OF  
**CAPE COD**  
INCORPORATED

Specialists in Endotoxin and Glucan Detection

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

(Millions of US\$)



Sales trend and medium-term sales  
plan for ACC (U.S. subsidiary)

## ■ 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)



# Trend in Capital Investments

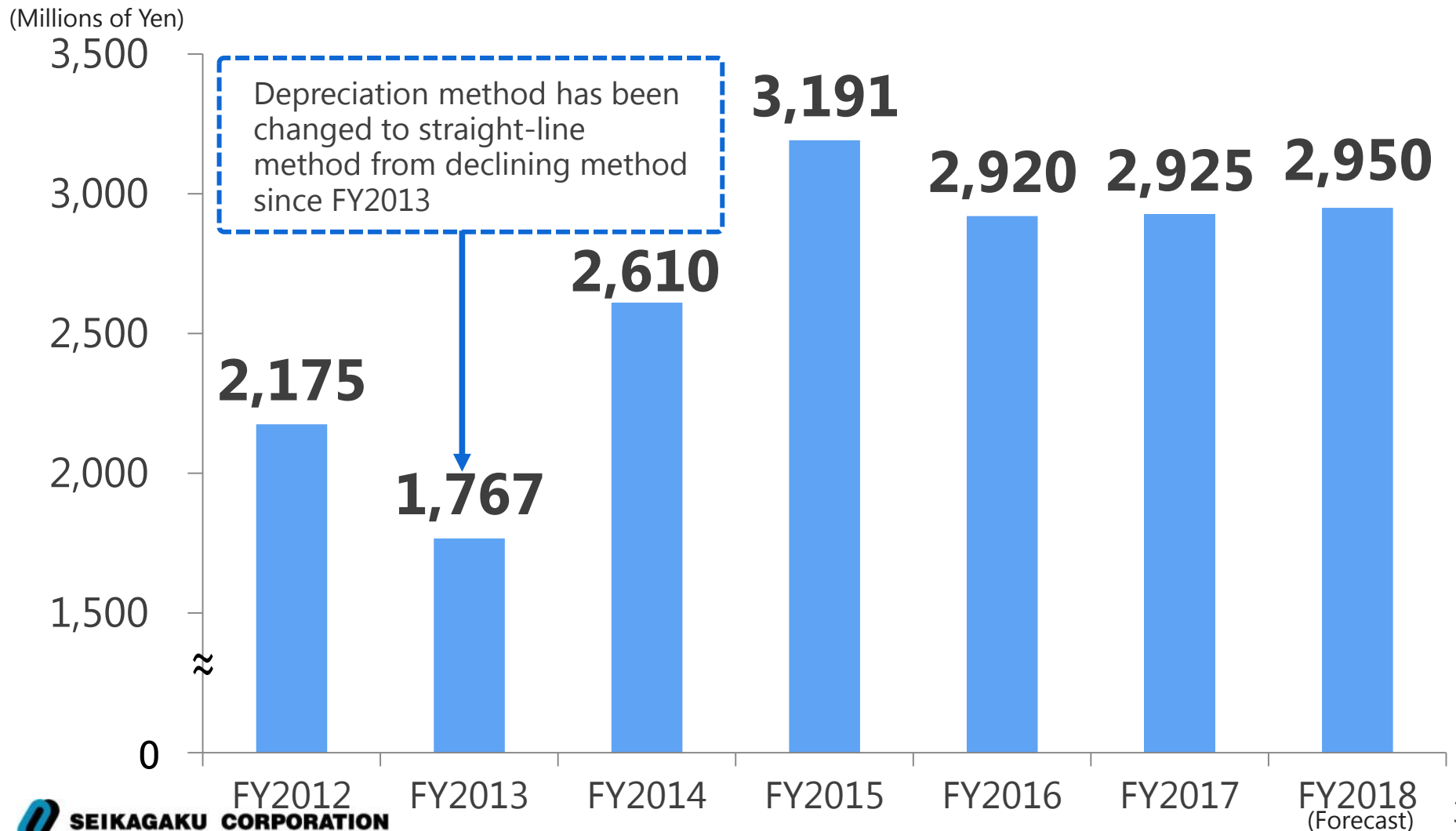
\* There is no change in forecast announced on May 11, 2018.

Facilities	Amounts (¥ bill.)	FY2011	FY2012	FY2013	FY2014	FY2015	FY2016	FY2017	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

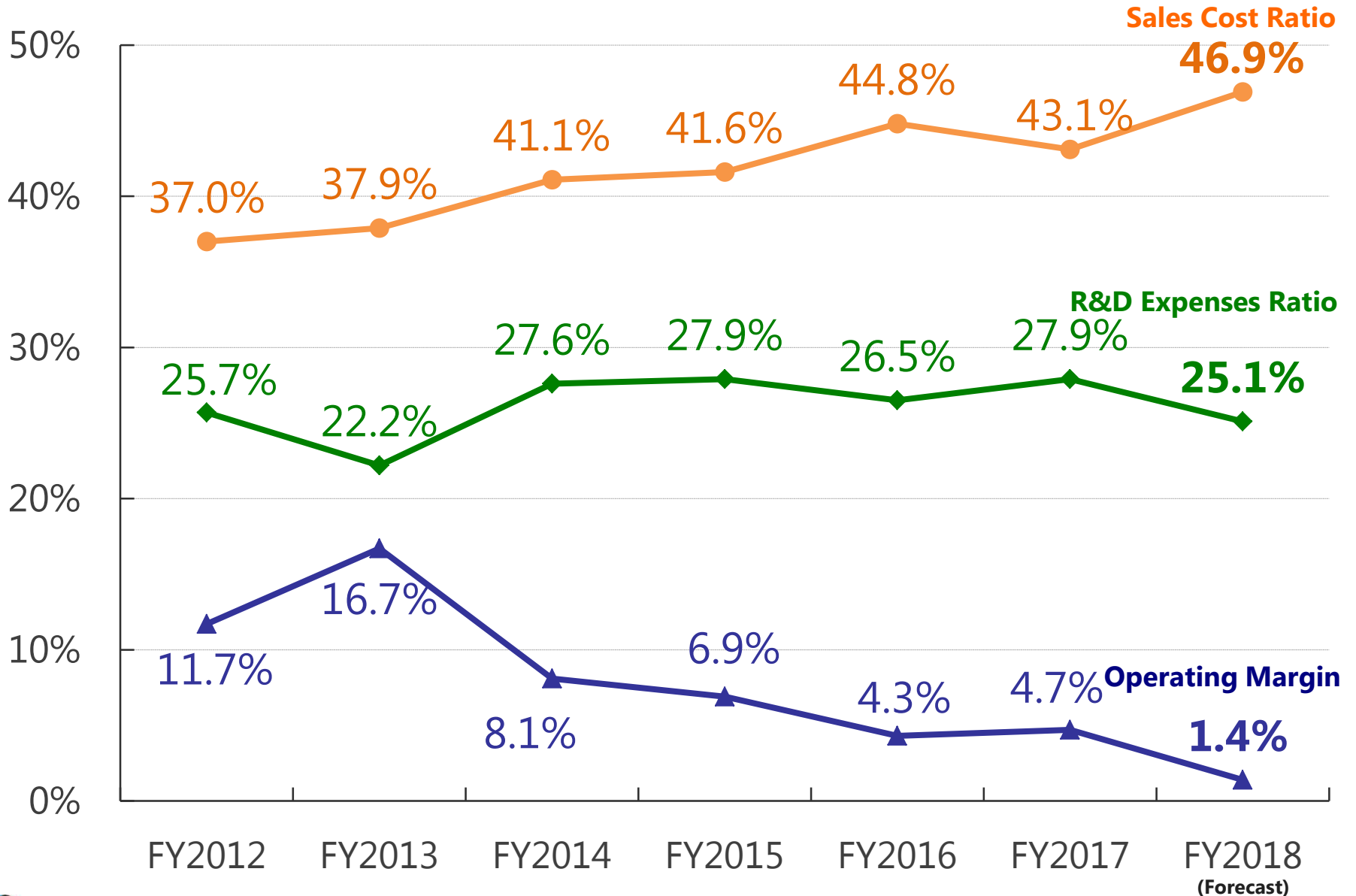
\* There is no change in forecast announced on May 11, 2018.

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



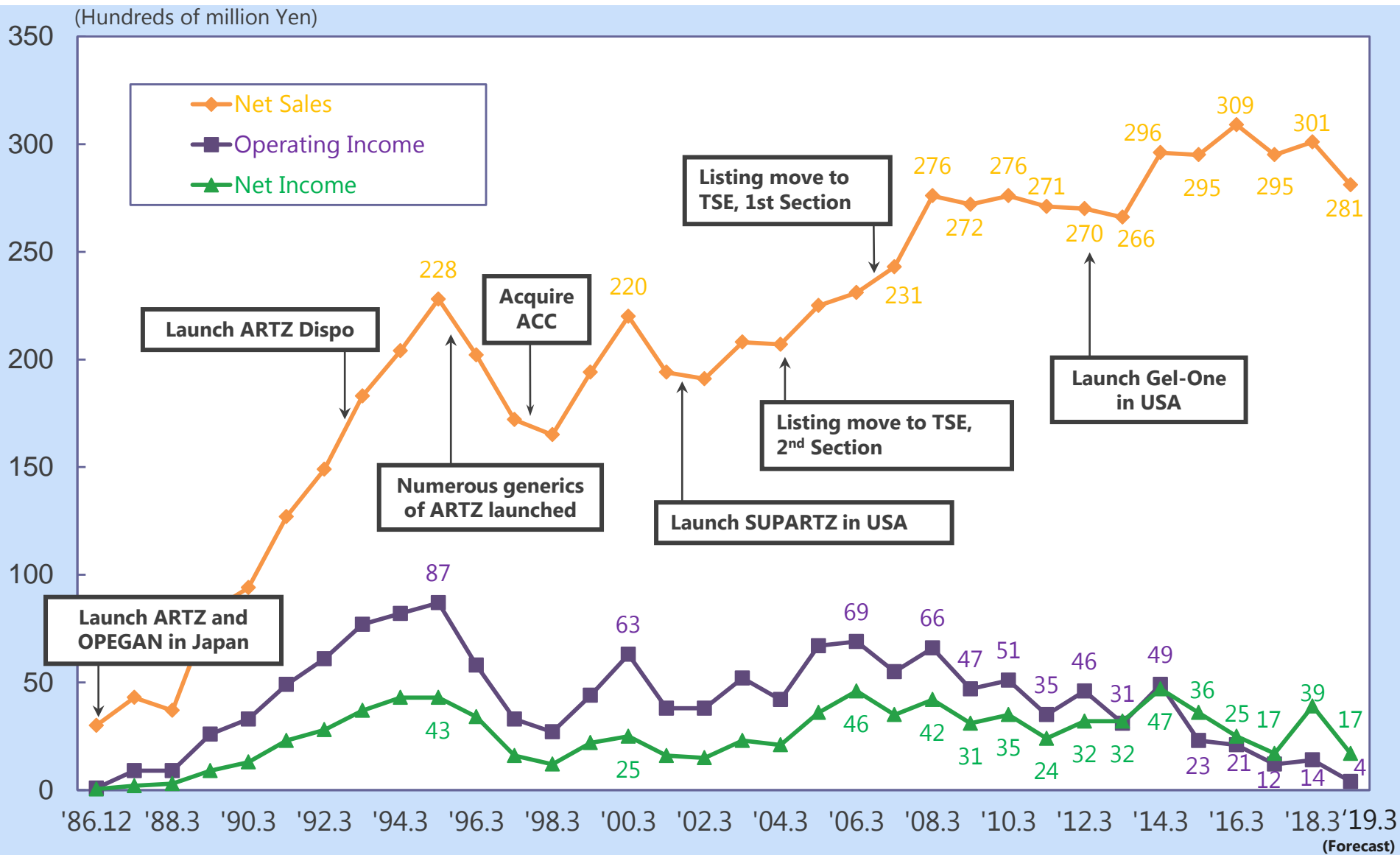
# Trend in Financial Index

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



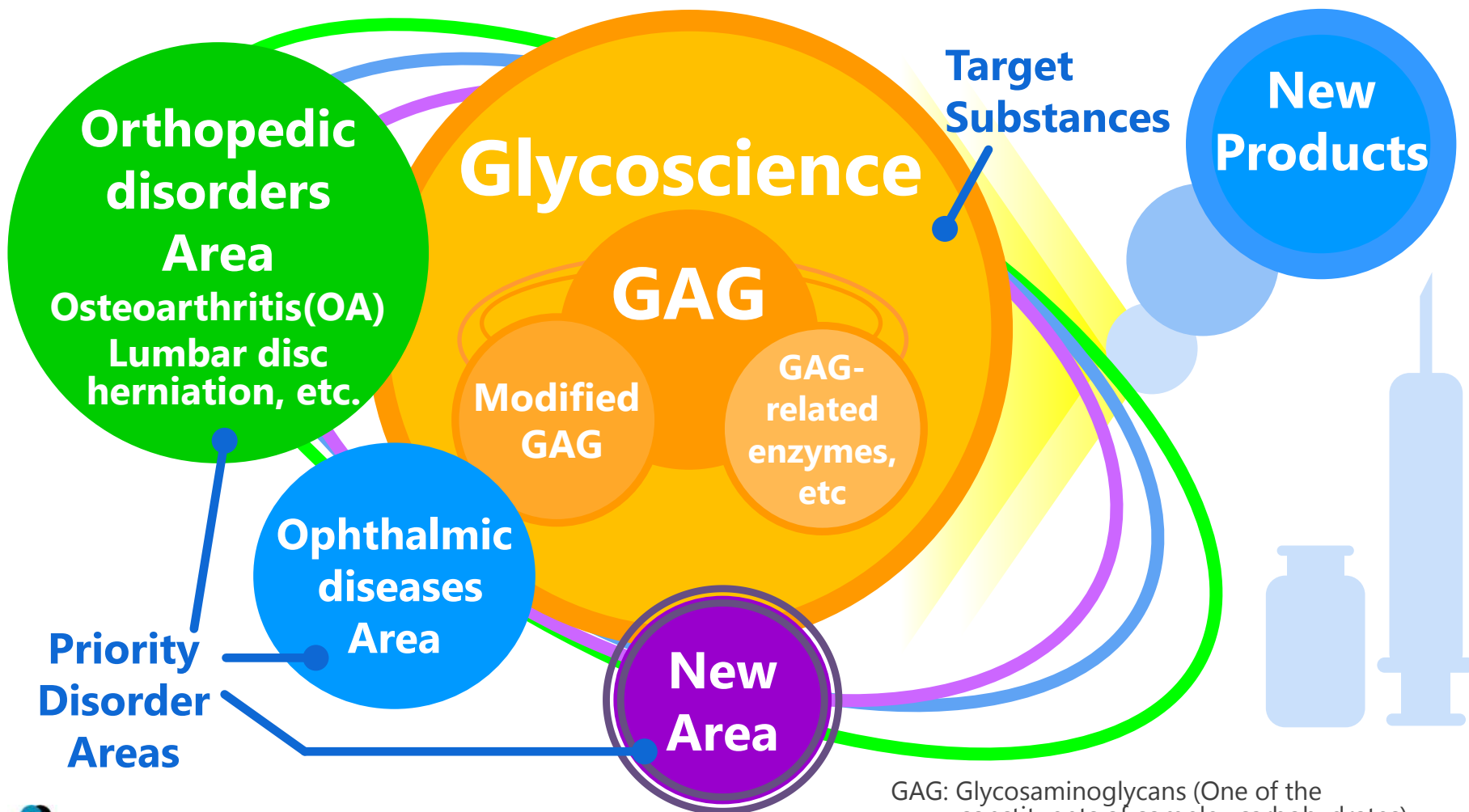
# Business Progress & Highlights

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



# Basic Policy on Research and Development

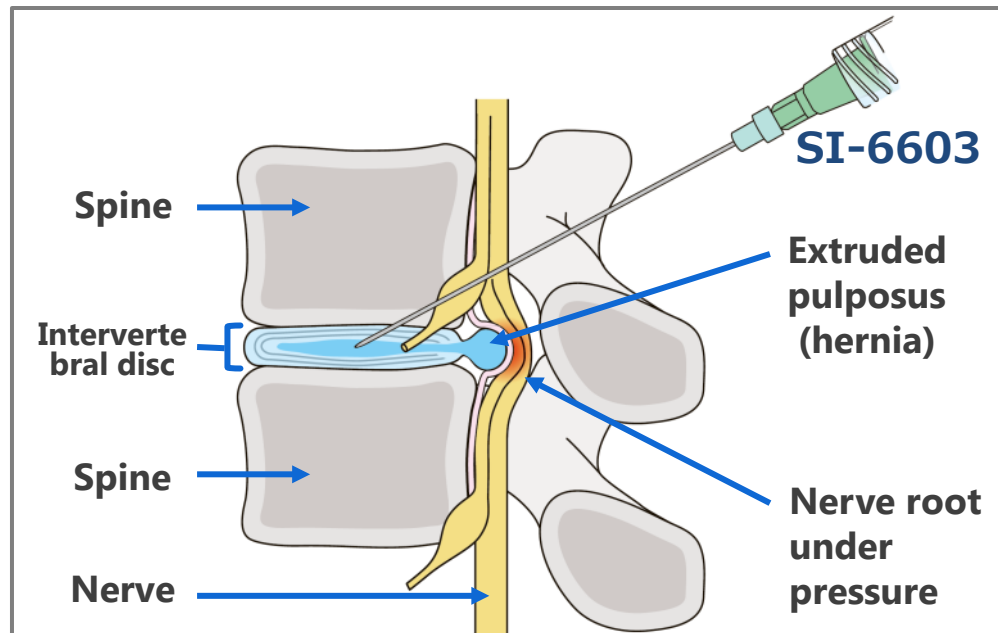
Aiming for the early, continuous introduction of new products that meet high treatment needs, focusing on glycoscience as an area of specialization



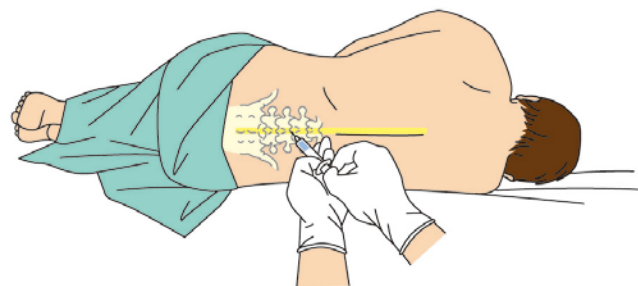
GAG: Glycosaminoglycans (One of the constituents of complex carbohydrates)

# 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



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



## 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)

# 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**



# 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

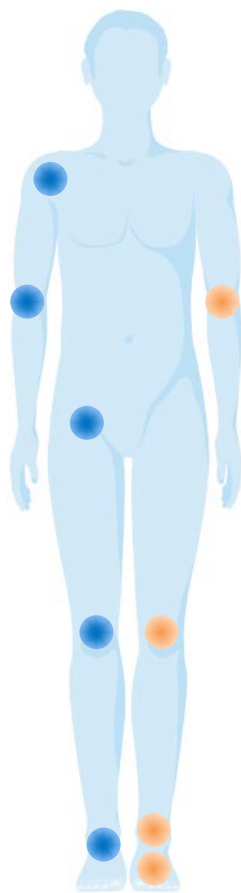
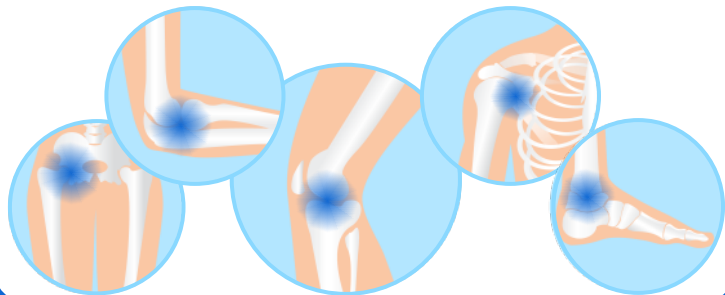
A disease in which joint tissue deteriorates due to abrasion of the articular cartilage, leading to inflammation and pain

### 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:**

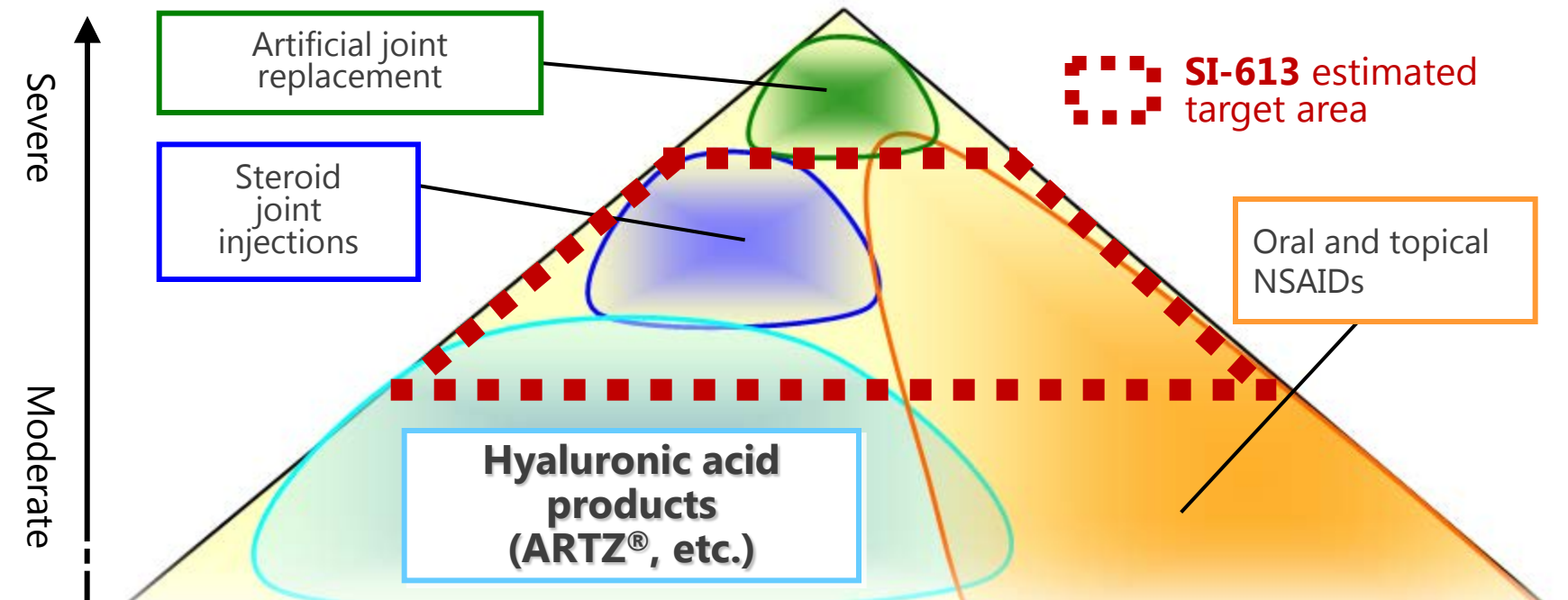
**Approx. 0.9 million**

(Seikagaku estimate for the above four diseases in Japan)



# SI-613 Estimated Target Patients

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



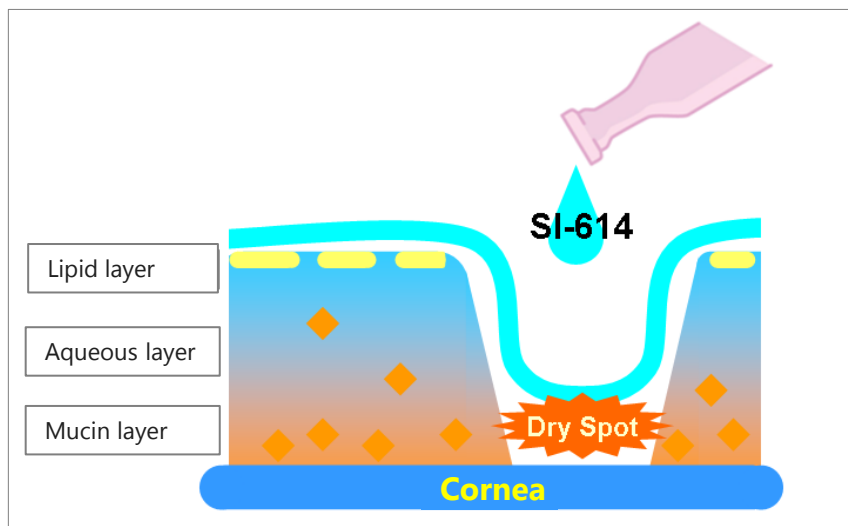
**Target market size in Japan**  
\* Including applications outside the knee

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

\*Numbers in this slide are estimated by Seikagaku, as of March 31, 2017 42

# 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
- Plan to conduct a PIII study after a sales partner has been decided

### Expected Features :

- SI-614 is a modified hyaluronate produced by Seikagaku's proprietary technology
- SI-614 Improves symptoms of dry eye by protecting the ocular surface and promoting corneal epithelial wound healing
- Many factors are involved in dry eye, and SI-614 has the potential to provide a therapeutic option based on a new mechanism unavailable from products with anti-inflammatory mechanisms now on the market in the U.S.

# 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 )
<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 U.S. : Knee Osteoarthritis	Japan	Ono Pharmaceutical Co., Ltd.	Max. ¥10.0 billion (¥2.0 billion)
	U.S.	Searching	—
<b>SI-613-ETP</b> Enthesopathy	Japan	Ono Pharmaceutical Co., Ltd.	*included in the above
<b>SI-614</b> Dry eye	U.S.	Searching	—
<b>SI-449</b> Adhesion Barrier	Japan	—	—

# 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

# 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**

# 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)

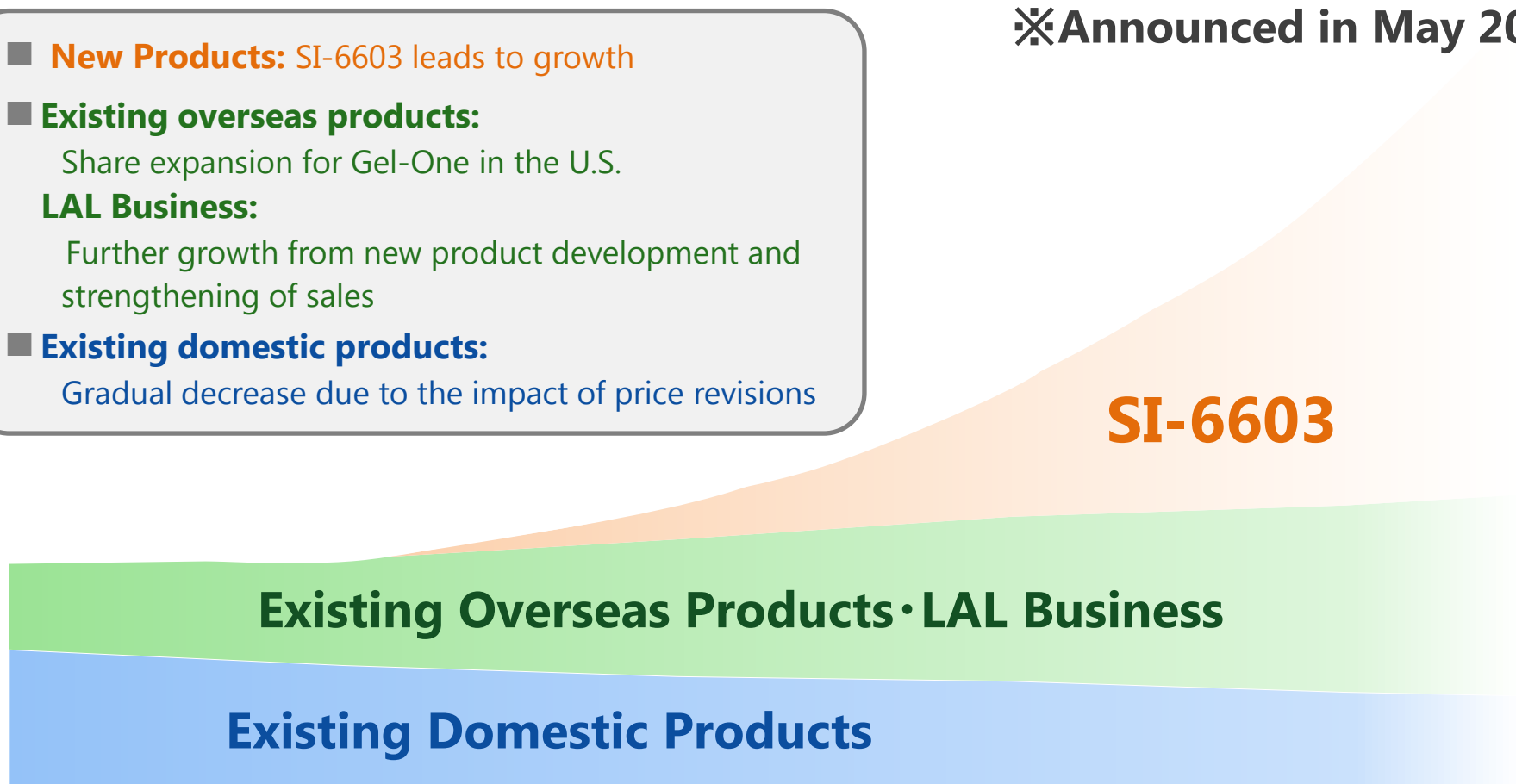
▶ **Expected shortfall for numerical target, despite some progress on R&D pipeline**



# 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



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

## 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

3

## 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

GAG: Glycosaminoglycans (A major component of complex carbohydrates)

# Our Business Segment

## Pharmaceutical Business

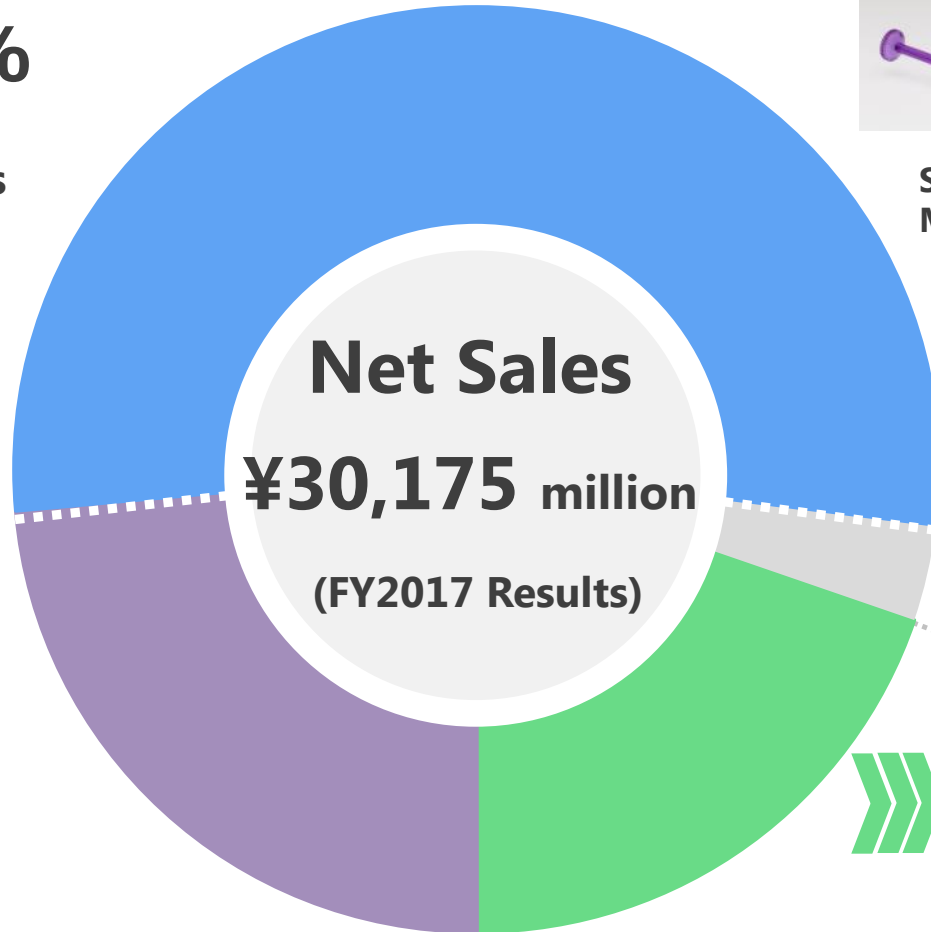
80.3%

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%

Bulk Products



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.)



## ■ **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.



**SEIKAGAKU CORPORATION**