First quarter of fiscal 2018

IR meeting

August 8 , 2018
KYORIN Holdings, Inc.
President Minoru Hogawa

- **Overview of consolidated results**
  - consolidated results, and progress of the main products
- **Consolidated Financial Results and Forecast**
- **Changes in Capital Policy**

Overview of consolidated results

Outline of First Quarter Consolidated Financial Results for the Fiscal Year Ending March 31, 2019

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(¥ billion)	First quarter Jun / 2017	First quarter Jun / 2018	YoY		Progress to Interim term forecast(%)
			Change	change (%)	
Net sales	26.5	**25.1**	−1.4	−5.0	50.1
Operating income	2.6	**1.3**	−1.3	−49.1	69.5
Ordinary income	2.8	**1.6**	−1.2	−43.1	72.6
Net income	2.4	**1.1**	−1.3	−55.0	71.8

Highlights of Business Performance ①　(Sales)

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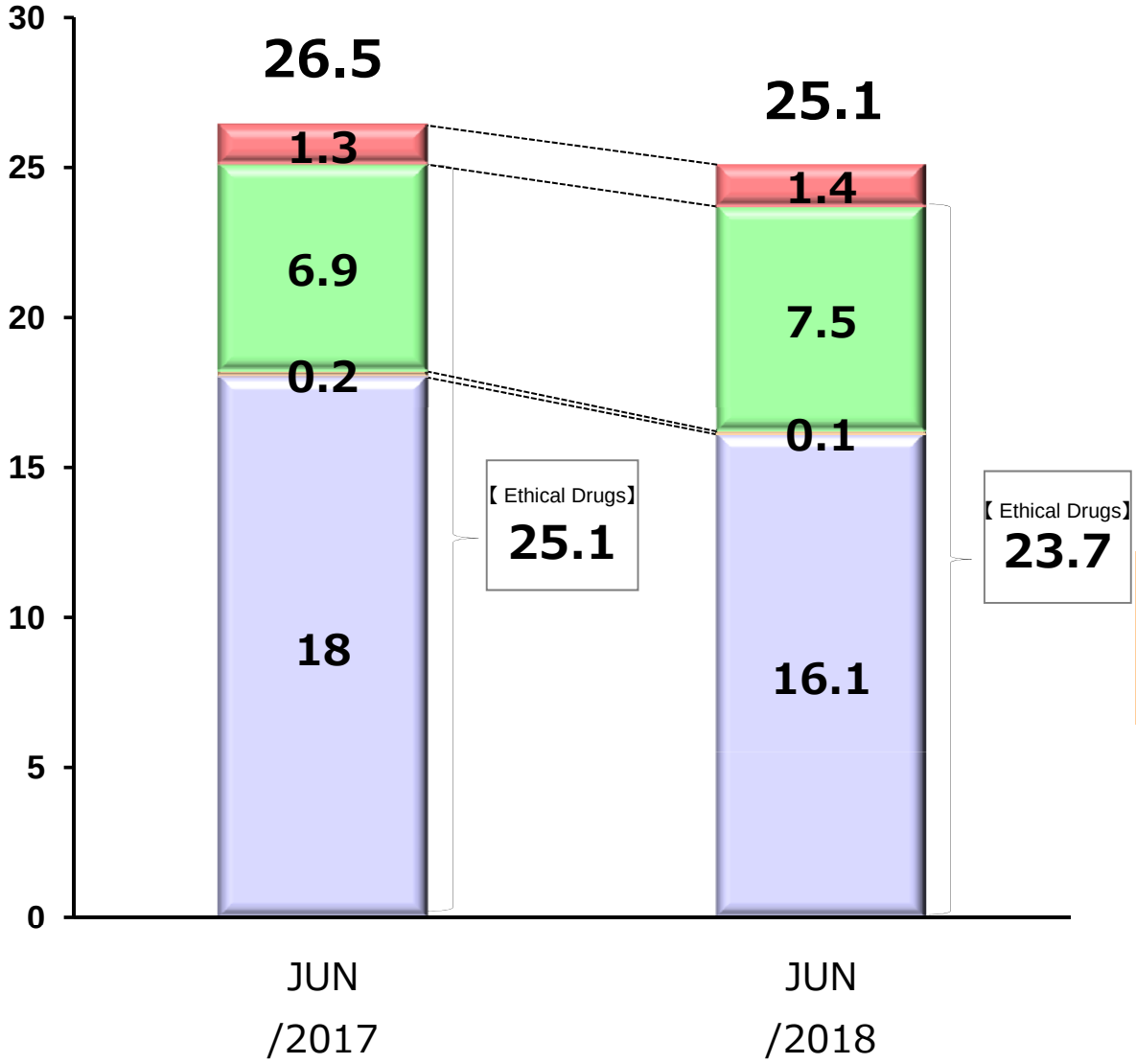
Sales （Units: ¥ billion）



【Net Sales ¥ −1.4bln】

Healthcare Business ¥+0.1bln

・Growth of RUBYSTA and Milton

【Ethical Drugs Sales ¥ −1.4bln】

Generic drugs ¥+0.6bln

・Increase of MONTELKAST AG sales
・Sales to other companies decreased

Ethical drug sales overseas ¥− 0.1bln

Income related to Gatifloxacin decreased

Ethical drug sales in Japan ¥ −1.9bln

・Despite steady growth in Flutiform and Desalex sales
・Decreased by the expiration of the patent for KIPRES.

Main Product Sales Update

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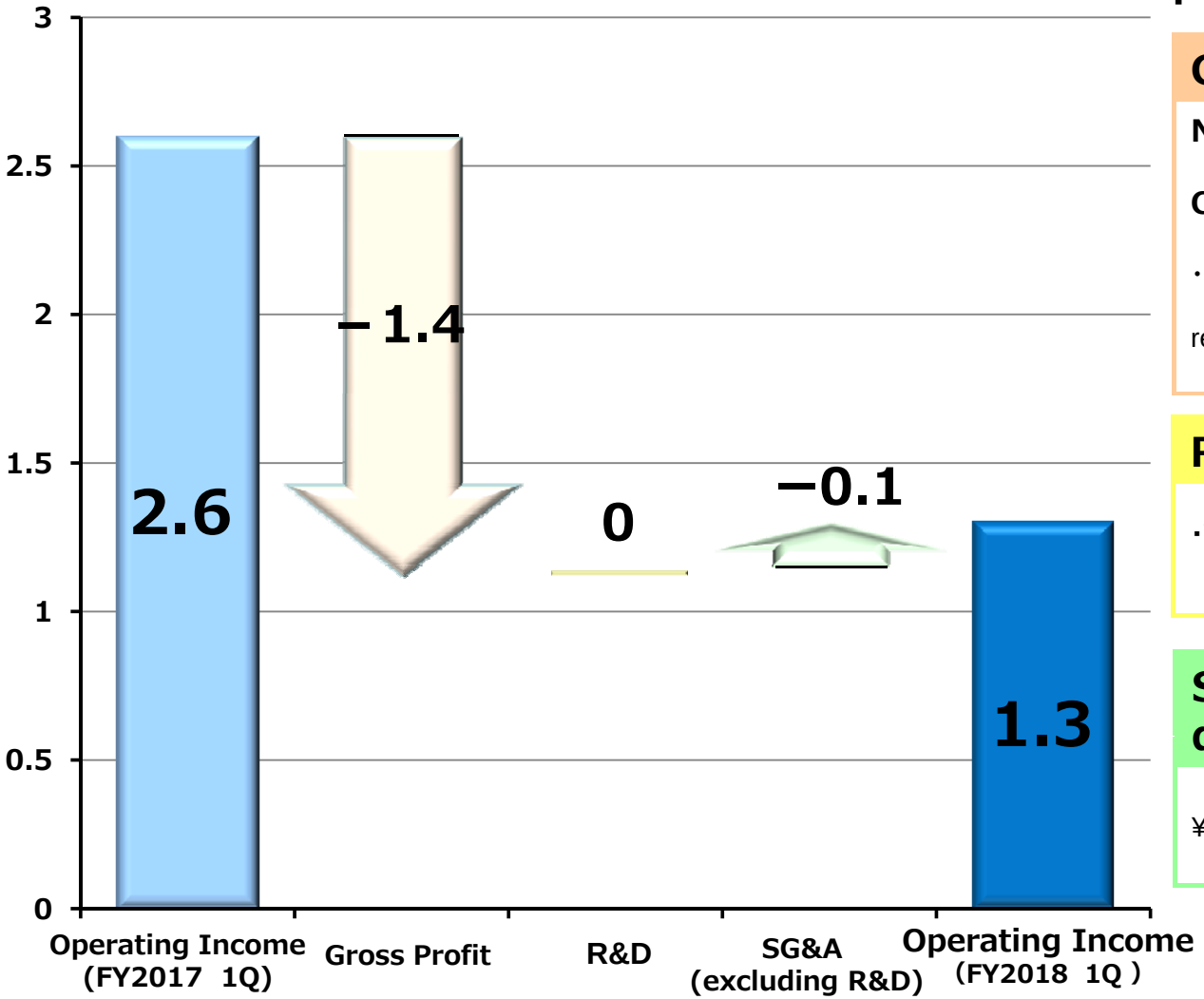
（Units: ¥ billion）

	Jun/2017	Jun/2018	change	change（%）	Progress to Interim term forecast(%)
Flutiform (Combination drug for asthma treatment)	2.8	**3.0**	+0.2	+9.4	52.5%
Uritos（Kyorin） (Overactive bladder)	1.9	**1.7**	−0.2	−8.8	50.1%
Desalex (Antiallergic Agent)	0.5	**1.5**	+1.0	+230.8	48.6%
Kipres （LT receptor antagonist）	2.0	**1.6**	−0.4	−23.1	53.7%
For children	3.1	**1.7**	−1.4	−45.7	57.6%
Pentasa (Ulcerative colitis and Crohn's diseasetreatment)	4.0	**3.5**	−0.5	−12.4	47.2%
Mucodyne （Mucoregulant）	2.1	**1.7**	−0.4	−22.5	51.4%
MONTELUKAST Tablets "KM"	2.7	**3.3**	+0.6	+21.9	68.1%

Highlights of Business Performance ② （Income ）

（ Units: ¥ billion）



【Operating Income ¥－1.4bln】

Gross Profit decreased

Net Sales :
decreased ¥1.4bln year on year
Cost of sales ratio :
Increased 2.6% year on year

・Decreased in sales of drugs due to drug price revisions. (Kyorin Pharmaceutical drug price revision rate: 7% range)
Rising cost of sales ratio

R&D expenses is flat

・¥2.5billion（FY20171Q）
⇒ ¥2.5billion(FY20181Q)

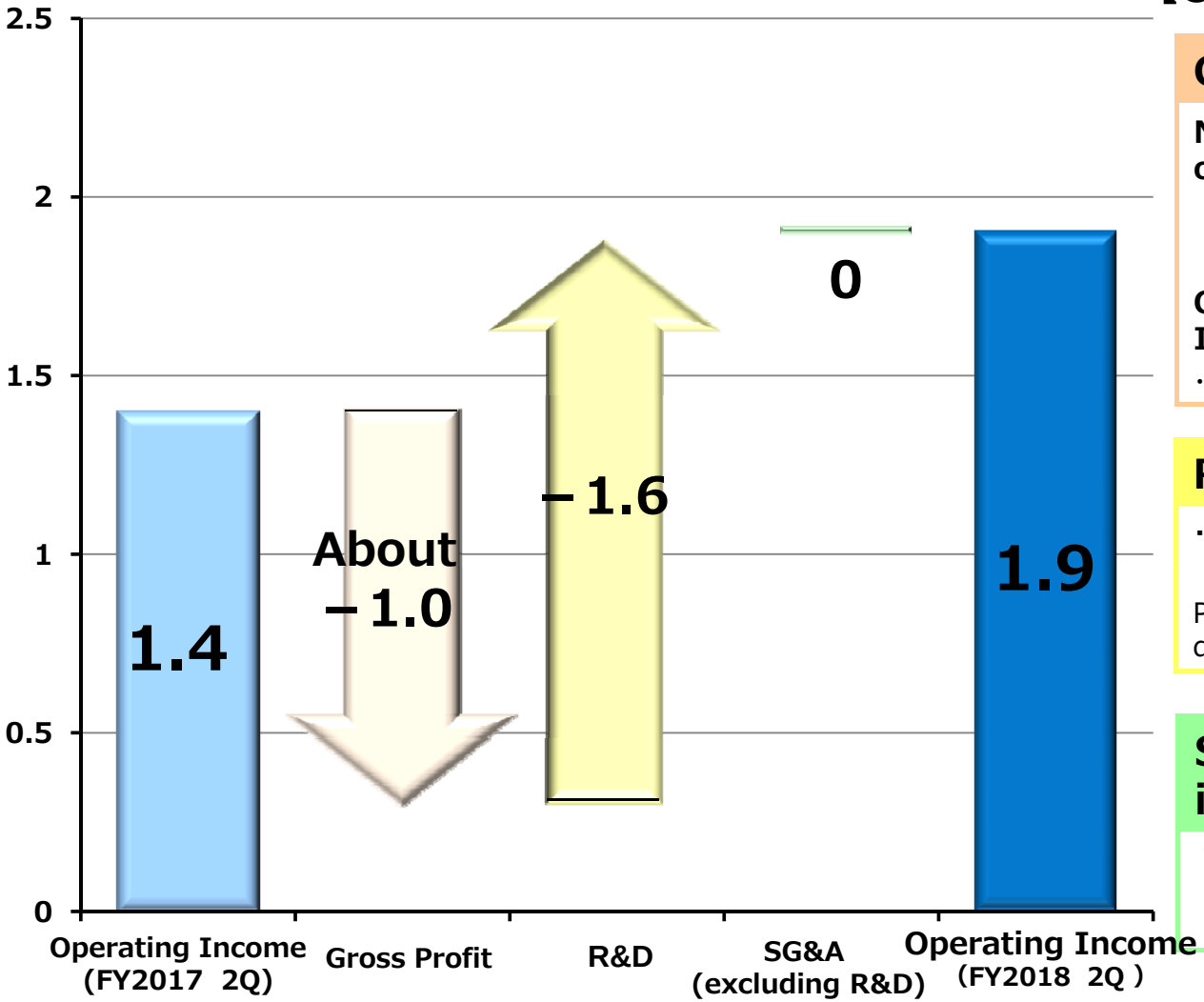
SG&A(excluding R&D) decreased

・Decrease of Labor costs ¥9.5billion(FY2017 1Q）
⇒ ¥9 4billion(FY2018 1Q)

Progress to Interim term forecast(%)
Operating Income : 69.5%

Forecast of Business Performance Second quarter (Income)

（Units: ¥ billion）



【Operating Income ¥＋0.5bln】

Gross Profit decreased

Net Sales： decreased ¥0.6bln year on year

・Despite steady growth in Flutiform and Desalex sales

Cost of sales ratio : Increased about1.5% year on year

・decrease in loss on retirement of inventories.

R&D expenses decreased

・¥7.2billion（FY2017 2Q)
⇒¥5.5billion(FY2018 2Q forecast)

Previous year: R & D expenses increased due to the development pipeline progress

SG&A(excluding R&D) increased

¥19.0billion(FY2017 2Q）
⇒Roughly flat against the same period last year (FY2018 2Q forecast)

Consolidated Financial Results and Forecast

Consolidated Financial Results Forecast for the Year Ending March 31, 2019

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（Units: ¥ billion）

			FY2017	FY2018 (forecast)	Y/Y Change	Y/Y Change(%)
Net sales			110.6	**114.4**	+3.8	+3.4
Ethical drugs business			104.7	108.4	+3.7	+3.5
	Sales of new ethical drugs		77.0	80.9	+3.9	+5.0
		Japan	73.7	79.9	+6.2	+8.4
		Overseas	3.3	1.0	−2.3	−70.1
	Generic drugs		27.7	27.4	−0.3	−0.9
Healthcare Business			5.9	6.0	+0.1	+1.1
Operating Income			8.8	**8.6**	−0.2	−2.5
Ordinary Income			9.3	**9.2**	−0.1	−1.6
Net Income			6.6	**6.6**	0	+0.4

【for reference: year on year】

① Increase sales of our main products Flutiform and Desalex, and increase sales of Nasonex.
② Reduction of gross operating income: The cost rate is up by about 4 point.
③ Reduction of selling, general and administrative expenses (SGA): R&D cost is reduced (forecast a reduction of 2.6 billion yen from the previous year, to 11.6 billion yen). The rate of SGA (excluding R&D cost) has declined by about 1% from the previous year.
④ Method of depreciation: Expect a change from the declining-balance method to the straight-line method.

Forecast of Mainstay Product Sales

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（Units: ¥ billion）

	FY2017	FY2018 (forecast)	Y/Y	
			Change	Change(%)
Flutiform (Combination drug for asthma treatment)	11.9	**12.3**	+0.4	+4.1
Uritos（Kyorin） (Overactive bladder)	7.2	**6.8**	−0.4	−4.7
Desalex (Antiallergic Agent)	4.9	**8.1**	+3.2	+65.3
Kipres for adult （LT receptor antagonist）	8.3	**6.0**	−2.3	−26.8
Kipres for children （LT receptor antagonist）	10.5	**7.2**	−3.3	−30.9
Pentasa (Ulcerative colitis and Crohn's diseasetreatment)	15.3	**14.5**	−0.8	−5.0
Mucodyne （Mucoregulant）	8.7	**7.2**	−1.5	−16.5
Nasonex （Spray type allergic rhinitis remedy）	−	**10.1**	+10.1	−
MONTELUKAST Tablets "KM"	11.7	**9.8**	−1.9	−16.4

Changes in Capital Policy

Changes in Capital Policy

Before the change

・While maintaining the sound financial base, we adopt the capital policy ensuring both growth investment and stable return to shareholders.
As for the return to shareholders, we aim for “stable dividends” on a basis of the present dividend standard.

Reason of the Changes in Capital Policy

◇Considering the perspective of the recovery of the corporate earnings caused by the implementation of our key strategies.
◇ Taking into consideration the current capital market conditions and the financial situation of the Company, we decided to change the policy from capital accumulation to capital efficiency improvement
◇We aim to continue this new shareholder return policy unless there is a special change in the business environment.

Changes in Capital Policy and Shareholder Return Policy

Basic idea

■Please note that there is no change in our business strategy towards the realization of the medium-term business plan “HOPE100-Stage 2-”, and we will continue to make our best efforts to achieve our target figures in that business plan by investing for continuous growth.
■ We aim to further improve the shareholder's value and increase efficiency of capital to strengthen the return to shareholdersby strengthening shareholder return taking DOE (shareholders' equity dividend rate) into account

Shareholder Returns

Basic Policy(After the change)

・While maintaining the sound financial base, we aim to improve the capital efficiency through growth investment and returns to shareholders.
・We will maintain stable dividends taking DOE (Dividend on Equity ratio) into account.

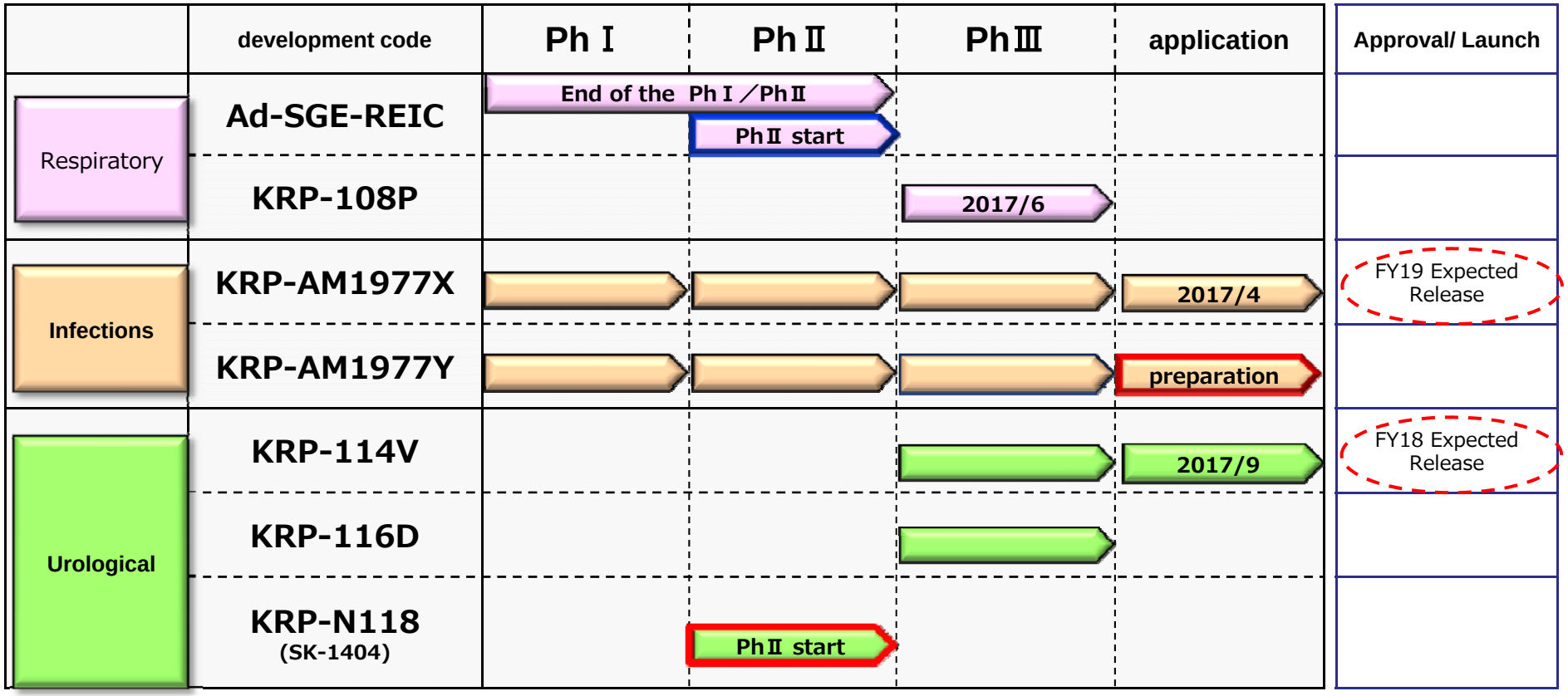
Dividends

	FY2017	FY2018 (orginal forecast)	FY2018 (revise forecast)
Dividend per share (Yen)	¥58 (Year-end ¥38)	¥58 (Year-end ¥38)	¥75 (Year-end ¥45)
Consolidated payout ratio(%)	65.9%	65.7%	84.9%

※ We revised the dividend forecast for the fiscal year ended March 2007, which was announced on May 10, 18, to July 31, 18.

Drug Developmet Pipeline: Progress in FY2017, schedule of FY2018

schedule of FY18　　progress in FY18 1Q



【Licensing development】　※ For KRP-AM 1977 X, additional nonclinical studies are required and will be carried out.

Compound/Code	Licensee	Stage	Features
FPR2 agonist program	BMS	**Ph Ⅰ**	FPR-2 agonists that mainly inhibit the migration of neutrophils and exhibit anti-inflammatory action.　Therapy area：Non-disclosure
KRP-203	Derivation activity restart	**Ph Ⅰ**	Sphingosine-1-Phosphate Receptor Agonist .　Therapy area：GvHD
	Because Novartis (licensee) decided to discontinue development of KRP-203 for strategic reasons,kyorin receive the return of development rights.		

Accelerate regrowth with new drug group and new products

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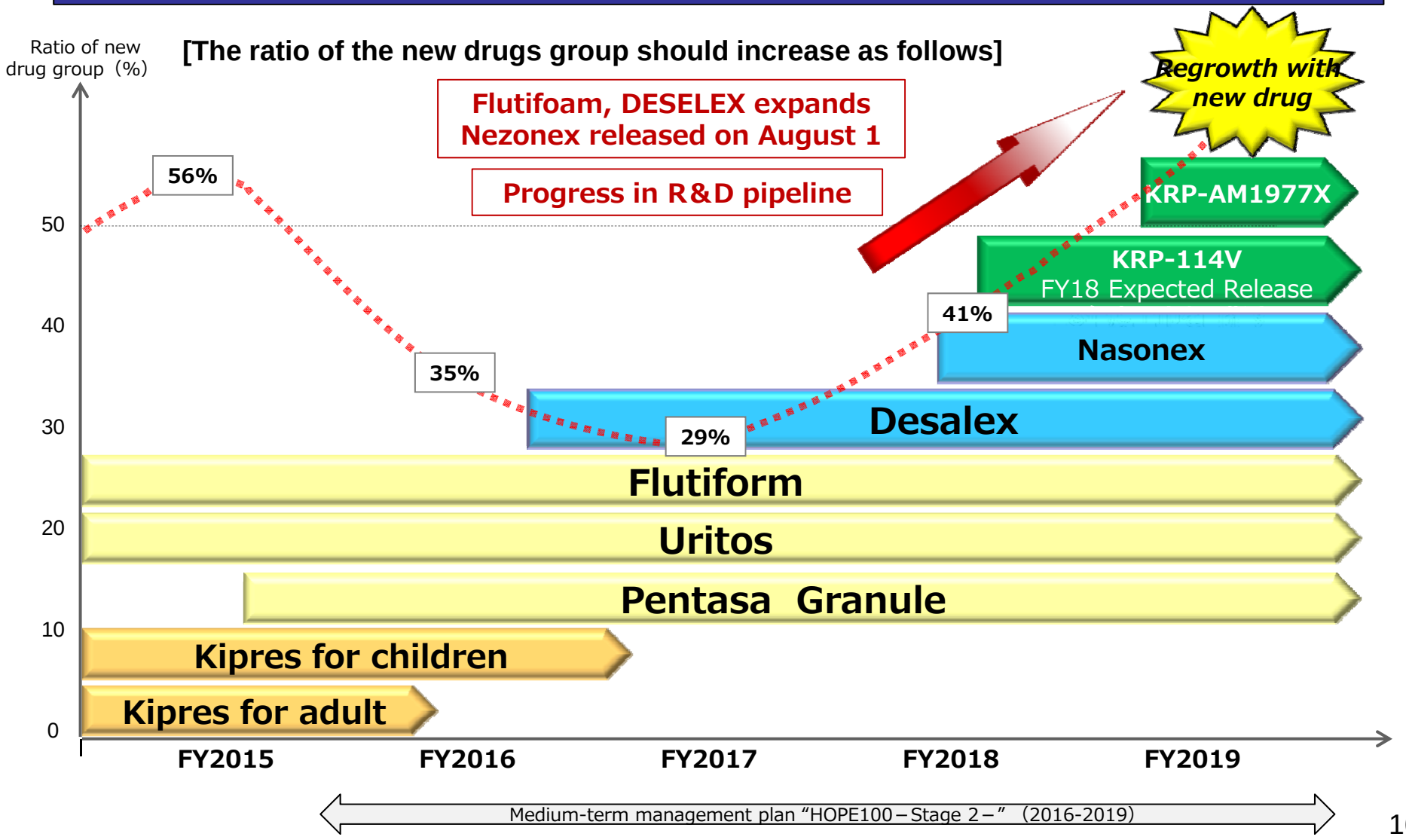
・Maximize the dissemination of Flutiform, Desalex, PENTASA Granules, Uritos and Nasonex.
・Launch and disseminate KRP-114V and KRP-1977X.



Approach to Drug Discovery and Status of R&D Pipeline

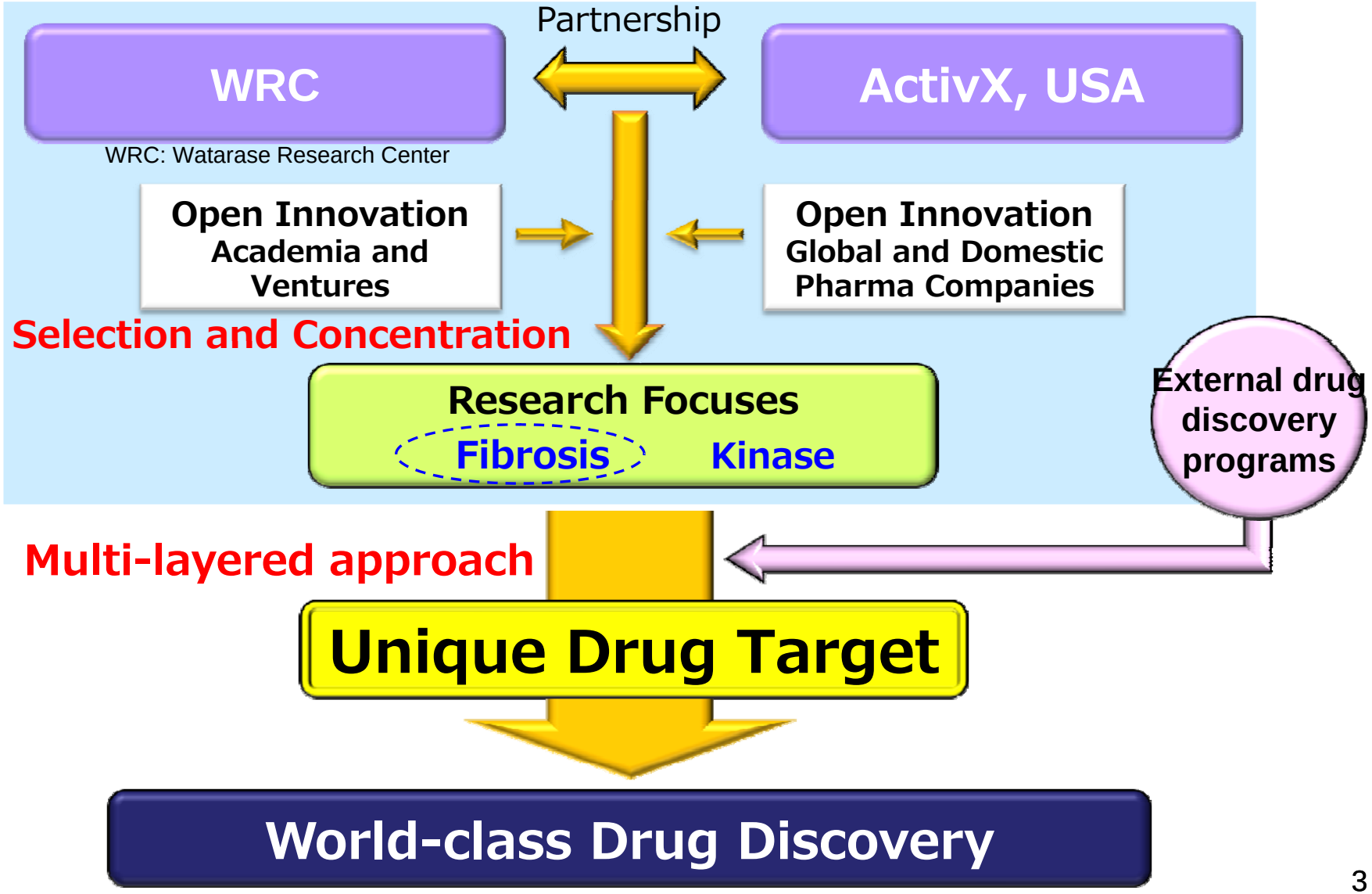
Kyorin Holdings, Inc.
August 8, 2018

Shigeru Ogihara, Senior Executive Director
(Senior Executive Director and General Manager, Discovery Research HQs, Kyorin Pharmaceutical Co., Ltd)

- **Approach to first-in-class drug discovery through “selection and concentration” scheme: Focus on fibrosis research**

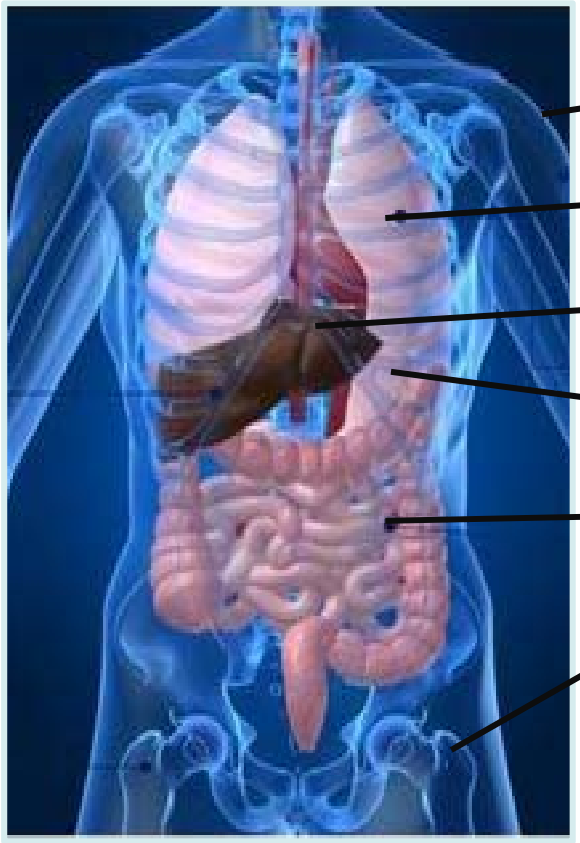
- **Status of R&D pipeline**

Approach to “First-in-class” Drug Discovery



Organ Fibrosis

- ✓ Functional damage of organs by excessive accumulation of collagens and so on
- ✓ Cause of the onset is not clear, and progression is irreversible.
- ✓ Development of effective drugs is required.



Skin (scleroderma: 20k)[b]

Lung (IPF: 13k)[a]

Liver (NASH: 7 million)[a]

Pancreas (Chronic pancreatitis: 44k)[c]

Kidney (Diabetic nephritis: 2.8 million)[a]

Bone marrow: (Myelofibrosis: 1.5k)[c]

Estimated number of patients in Japan (as of Jan 2018)
a: Datamonitor Healthcare
b: Japan Intractable Diseases Information Center
c: Disease guidelines

Outline of Organ Fibrosis

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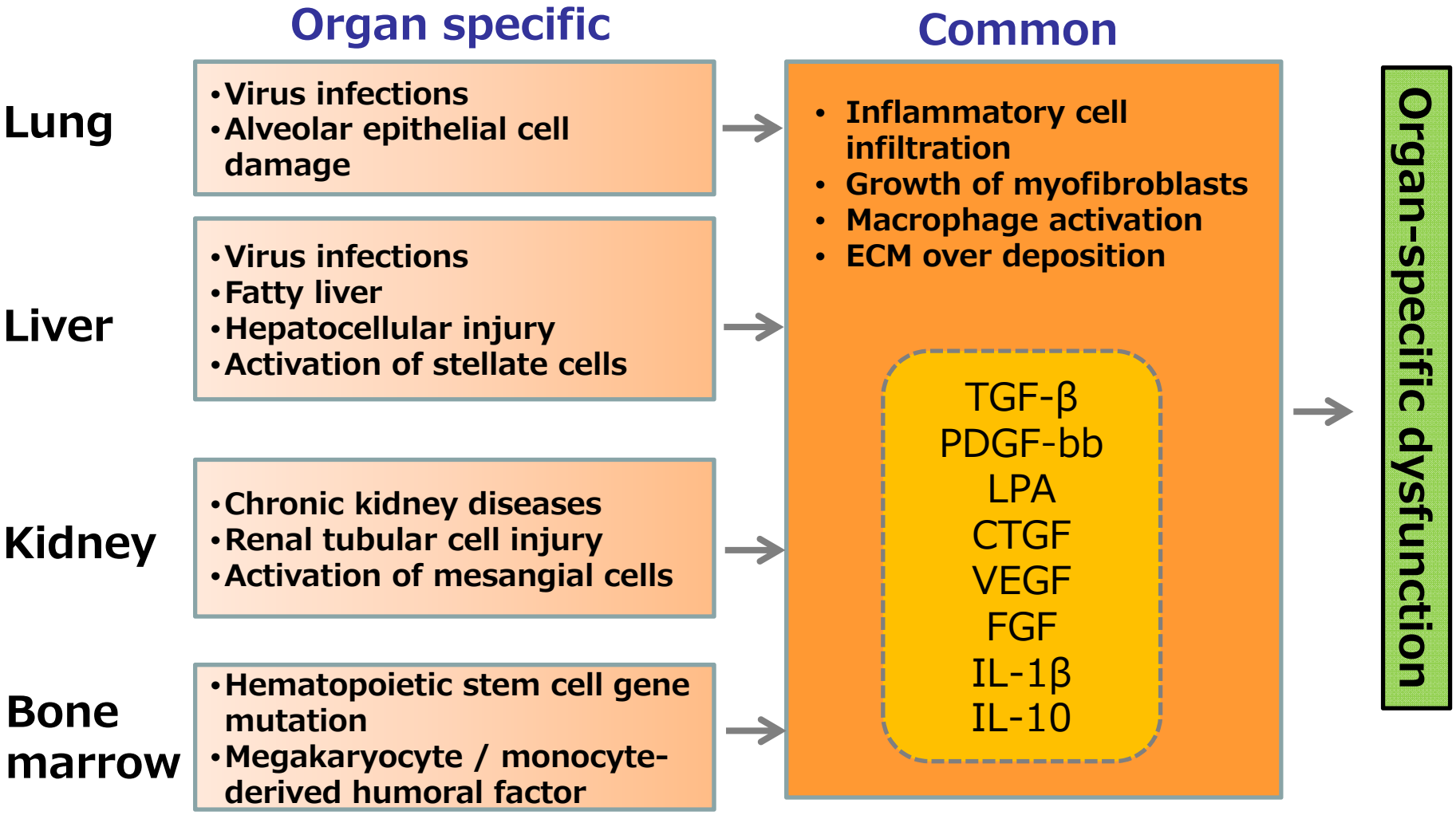
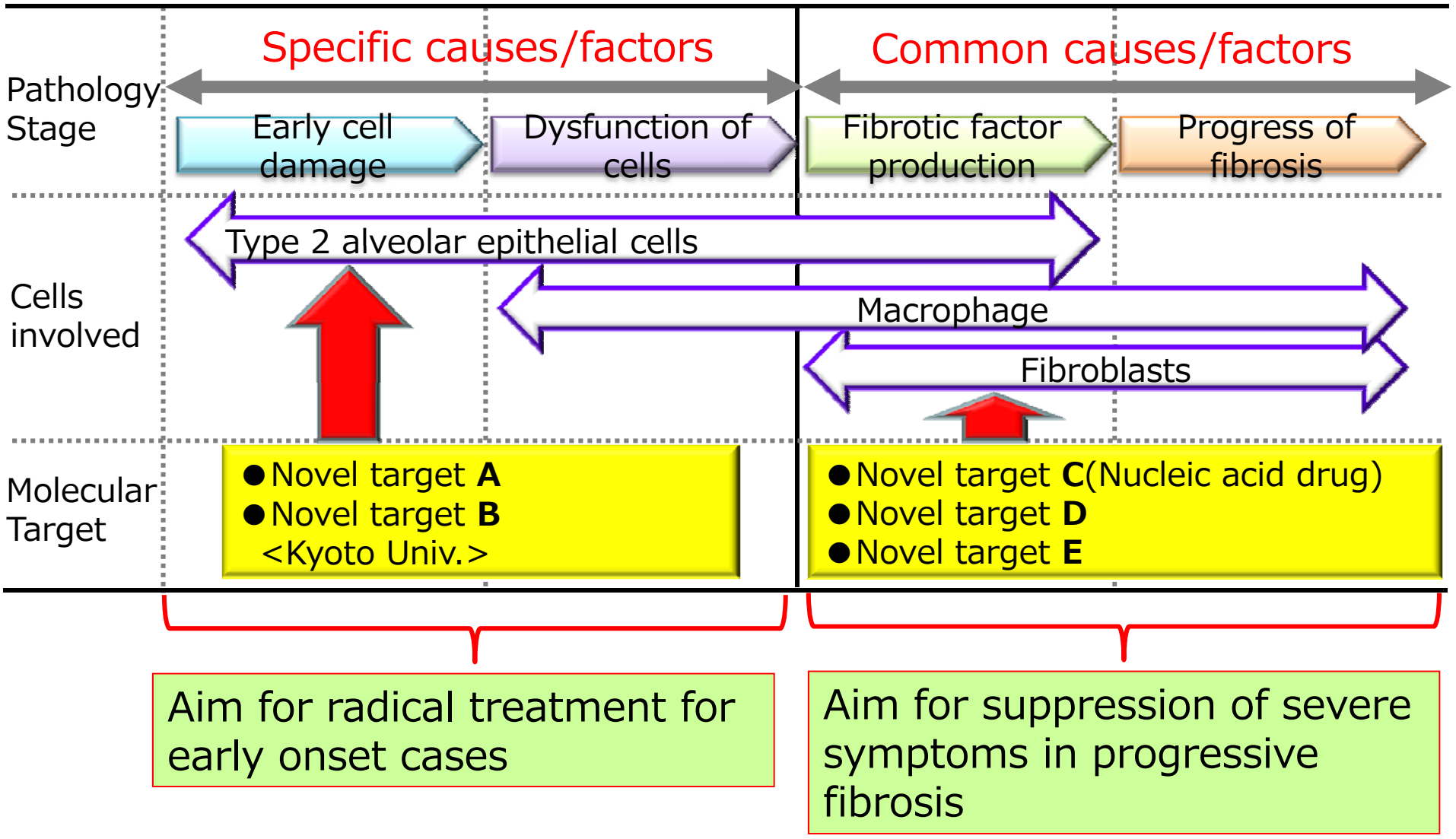
For organ fibrosis, there are common causes and factors irrespective of organ and organ specific ones



Drug Discovery for Pulmonary Fibrosis



Status of R&D Pipeline

Status of R&D Pipeline

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Highlights in FY2018　　As of July 31, 2018

	Projects	Ph1	Ph2	Ph3	NDA	Appr/Launch
Respiratory	**Ad-SGE-REIC** Gene therapy (MPM)	Ph1／Ph2 ended	Ph2 start June 2018			
	KRP-108P Asthma combo. inhaler			June 2017		P.9
Infections	**KRP-AM1977X** Fluoroquinolone				Apr 2017	Aim for launch in FY2019
	KRP-AM1977Y Fluoroquinolone				Preparation	
Urology	**KRP-114V** OAB treatment				Sept 2017	Aim for launch in FY2018
	KRP-116D IC treatment			Mar 2017		P.13
	KRP-N118 **(SK-1404)** Nocturia treatment		Ph2 started			

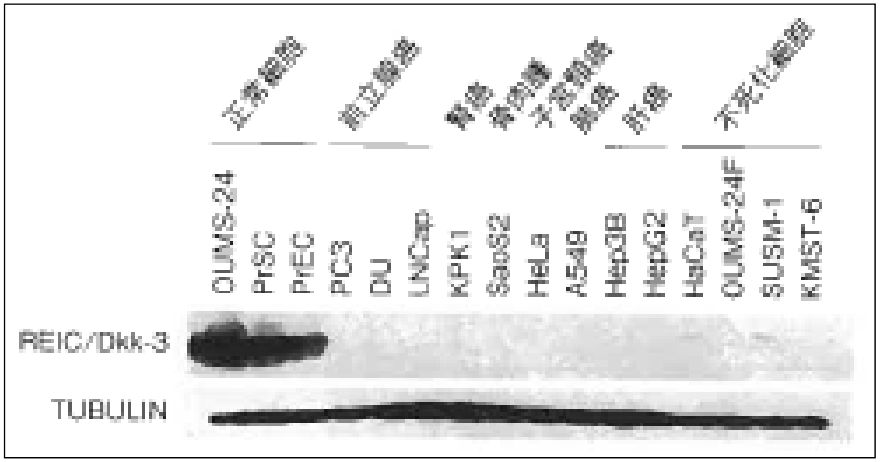
※Additional non-clinical studies for KRP-AM1977X ongoing

【Status of out-licensing items】

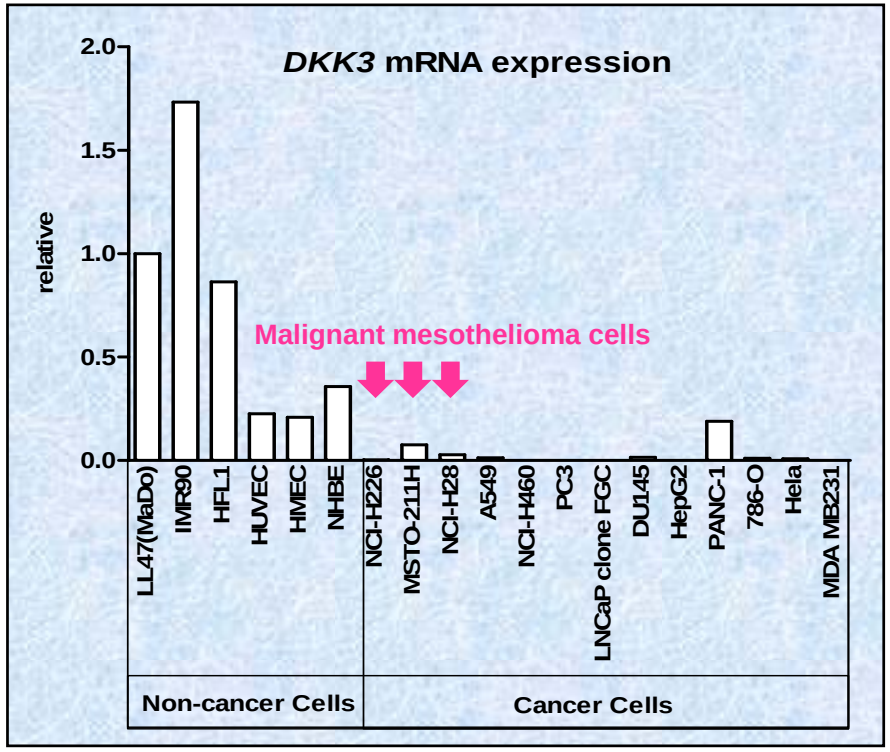
Projects	Licensed to	Stage	Features
FPR2 agonists	BMS	**Ph1**	FPR2 agonist: Mainly suppresses the migration of neutrophils and shows anti-inflammatory action Target disease: Undisclosed
KRP-203	Re-start of out-licensing	**Ph1**	S_1P receptor agonist Target disease: GvHD
	Novartis ceased the development from the strategic viewpoint and returned development rights to Kyorin. P.15		

Outline of Ad-SGE-REIC

Expression of REIC protein in various cancer cells



Igaku no ayumi. 2018; 265(5); 422-428.



Internal data

Expression of REIC in normal and cancer cells

It has been confirmed that expression of REIC protein is downregulated in various cancer cells.

Outline of Ad-SGE-REIC

Mechanism of Action

Ad-SGE-REIC is a gene therapy product in which the cancer-suppressing gene REIC/Dkk-3 discovered in Okayama Univ is mounted on an adenoviral vector as a therapeutic gene.

Selective cytotoxicity against cancer cells
By forcibly expressing REIC in cancer cells, selective cell death (apoptosis) of cancer cells is induced.

Activation of anticancer immunity
By differentiation induction of dendritic cells and cytotoxic T cells (CTL cells), activation of anticancer immunity is induced.

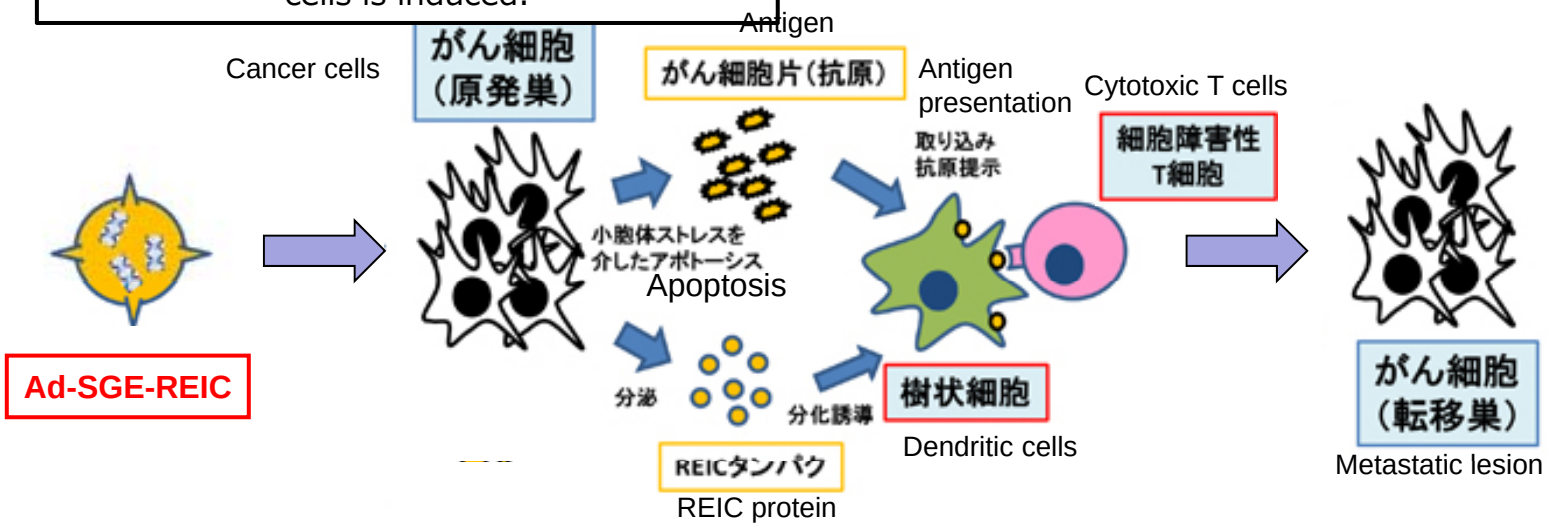
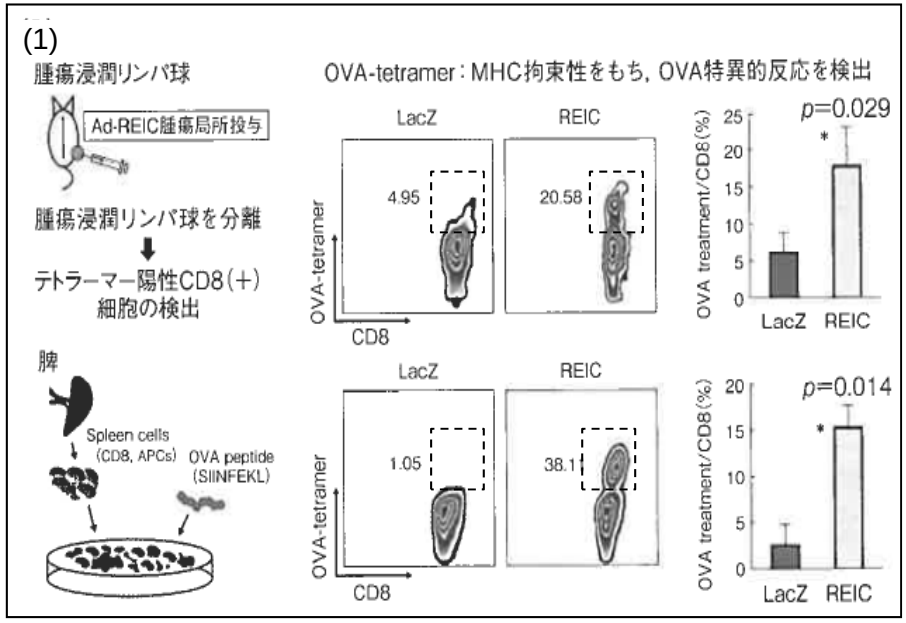


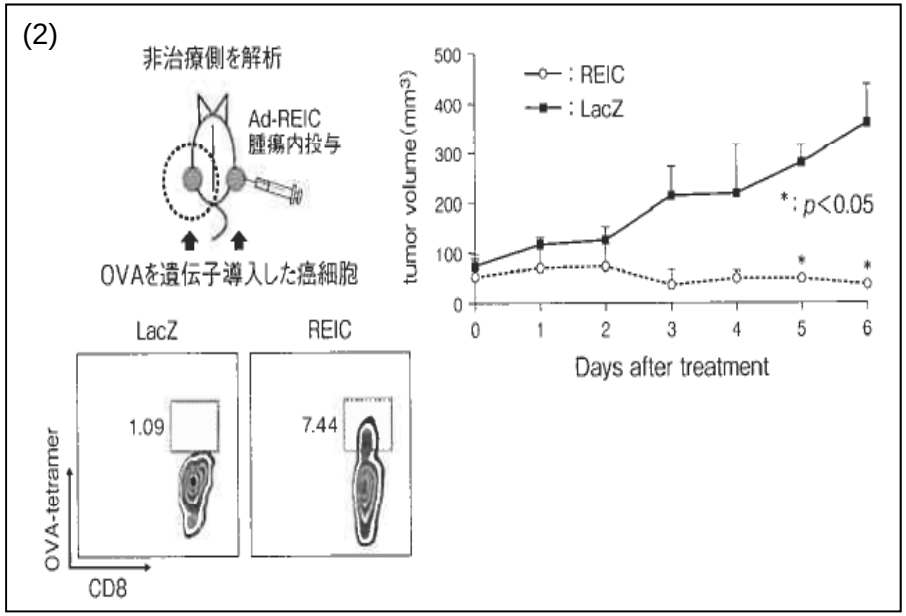
Figure: Attributed to Okayama Univ.

It is expected that the REIC proteins are forcibly expressed in tumor cells, resulting in the direct effect on the cancer lesion spreading in the thoracic cavity of malignant pleural mesothelioma and the indirect effect on the remote lesion due to the activation of anticancer immunity.

Anti-cancer Immunity Activation by Ad-SGE-REIC

Mouse subcutaneous tumor model





Strain: E.G7-OVA

. *Igaku no ayumi* 2018; 265(5); 422-428.

(1) Increase in cancer antigen-specific cytotoxic T cells was confirmed both in the tumor treated with the product and in the spleen.

(2) Increase in cancer antigen-specific cytotoxic T cells and anti-tumor effect were confirmed in the tumor in untreated side.

It was confirmed that Ad-SGE-REIC shows anticancer effect locally in the product-treated tumor and systemically via activation of anticancer immunity by induction of antigen-specific cytotoxic T cells.

Development status of Ad-SGE-REIC

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Ph1/2	
Study period	July 2015～
Subjects	Japanese MPM patient with standard treatment ineffective or without appropriate treatment
Objects	Primary endpoint: Safety, Estimation of maximum tolerated dose Secondary endpoint: Efficacy
Administration	Local administration to pleural tumors
Dose	Level 1: 3×10^{11} vp　Level 2: 1×10^{12} vp　Level 3: 3×10^{12} vp
No. of cases	13

MPM: Malignant pleural mesothelioma

To be presented at WCLC 2018 (September 23—26, 2018, Toronto, Canada)

Objectives of Ph 1/2 achieved and Ph2 started.

Ph2	
Study period	July 2018～
Subjects	Patients with MPM in the second treatment
Objects	Primary endpoint: Efficacy (PFS) Secondary endpoint: Efficacy (ORR, OS), Safety, etc.
Administration	Local administration to pleural tumors
Dose	3×10^{12} vp
No. of cases	30 (targeted)

PFS: Progression-free survival
ORR: Overall response rate
OS: Overall survival

- Completed responses to Cartagena Act and Clinical Trial Notification submission
- Joining in the Master Key Project
- Promote development by industry-government-academia collaboration (JST, Okayama Univ., Momotaro Gene)

P.8へ

Expansion of product line-up in urology field

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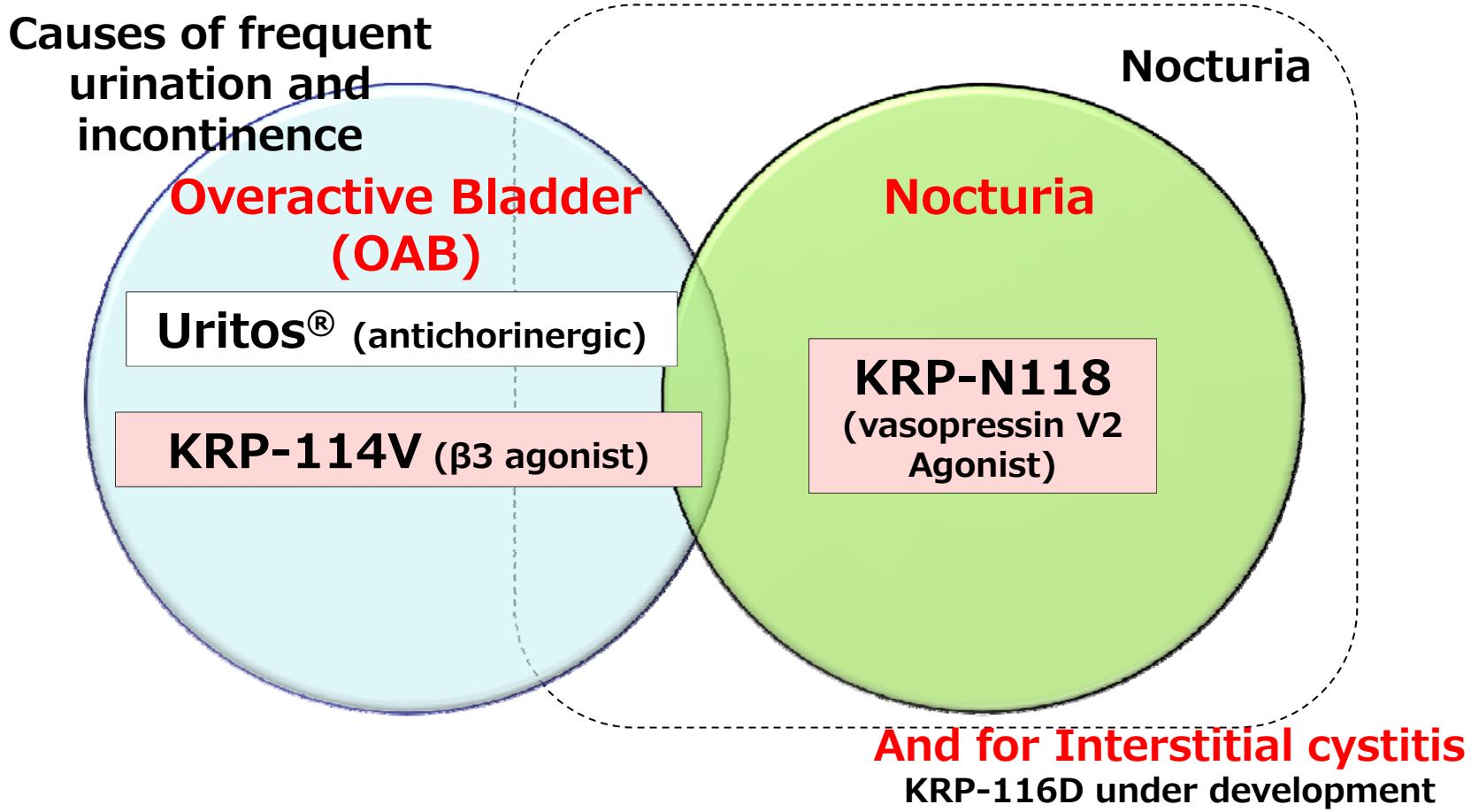

And for Interstitial cystitis
KRP-116D under development

Offer treatment options for urination trouble

(Tips)

■ **No. of OAB patients**
10.4 million (≥40 y/o) ※1

■ **No. of nocturia patients**
45 million (once/night), 8.5 million (≥3 times/night)※2

Ref. ※1:OAB guideline ※2:Honma, et al. (2003)

Outline of KRP-N118

- Indication: Nocturia caused by night polyuria
- MOA: Antidiuretic effect by promoting water re-absorption from renal collecting tubule by vasopressin V2 receptor agonistic action
- Dosage: Once daily before bedtime, oral dissolution tablets
- Features

- A small molecular compound, expecting a possibility of alleviating the variation of effects among individuals by improving oral absorbability.
- It is expected that it can be used by elderly people who have reduced renal function as this compound was mainly excreted via liver.
- By excreting promptly from the blood, the effect is exerted only during sleep, there is a possibility that side effects can be reduced.

P.8へ

Development status of KRP-203

GvHD

Ref: *ClinicalTrials.gov* (March 2018)

Stage		Targeted	Recruited	Intervention
Ph1b	Part 1	10	10	Methotrexate＋Ciclosporin
		● Novartis conducted Ph.1b (from 2013) to evaluate the preventive effect of GvHD after hematopoietic stem cell transplantation in patients with hematologic malignancy. ● GvHD prophylactic effect and the engraftment promoting effect of transplanted cells were seen and initiated part 2.		
	Part 2	20	Terminated	【KRP-203 low dose】 Methotrexate＋Ciclosporin 【KRP-203 high dose】 Methotrexate＋tacrolimus

- Novartis ceased Ph1b before the completion of scheduled cases due to development strategy reasons.
- In addition to the GvHD preventive effect, an effect of suppressing the recurrence of the blood tumor and the improvement of the survival rate were newly found. (patent filed)

Re-start of out-licensing

P.8へ