THE BEST OF NATURE AND SCIENCE

Business Results for Fiscal 2023

May 10, 2024

TSUMURA & CO.

Agenda

01 Moving Towards Realizing the Long-Term Management Vision—TSUMURA VISION “Cho-WA” 2031

02 Business Results for Fiscal 2023 and Earnings Forecast for Fiscal 2024

03 Progress in US development (TU-100)

THE BEST OF NATURE AND SCIENCE

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Moving Towards Realizing the Long-Term Management Vision—TSUMURA VISION “Cho-WA” 2031

President & Representative Director, CEO
Terukazu Kato

Aiming to Establish a Global Standard for Pharmaceuticals Derived from Natural Ingredients

【Corporate Purpose】 “Lively Living for Everyone”　【Corporate Value】“Best of Nature and Science”

Creation of shared value with society

Science

- Creation of new value through pharmaceuticals and products derived from natural substances
- Sustainable, stable supply of pharmaceutical products such as Kampo formulations, which are traditional pharmaceuticals

Materiality (Priority issues)

Nature

- Sustainable procurement of raw materials (research on cultivation of crude drugs, etc.)
- Recycling use of resources (recycling of water and crude drug residue)
- Preservation of biodiversity (restoration of forests, soil, water sources)
- Climate change countermeasures (realization of carbon neutrality)

Health

- Expansion of access to high-quality pharmaceuticals and products derived from natural substances
- Expansion of the standardization of Kampo treatments and building of evidence
- Initiatives for personalized Kampo treatments through cutting-edge technology
- Contribution to health suitable for each individual’s life stage (treatment, pre-symptomatic disease, healthcare (prevention))

Reinforcement of business foundations

- Strengthening and enhancement of corporate governance
- Utilization of diverse human resources
- Cultivation of a corporate culture that draws out potential abilities through dialogue

Realization of a Global Quality for Pharmaceuticals Derived from Natural Ingredients

Pharmaceutical requirements: Possesses therapeutic benefits (efficacy) but no side effects (safety)

Degree to which requirements are fulfilled: Confirmed in studies (clinical trials)

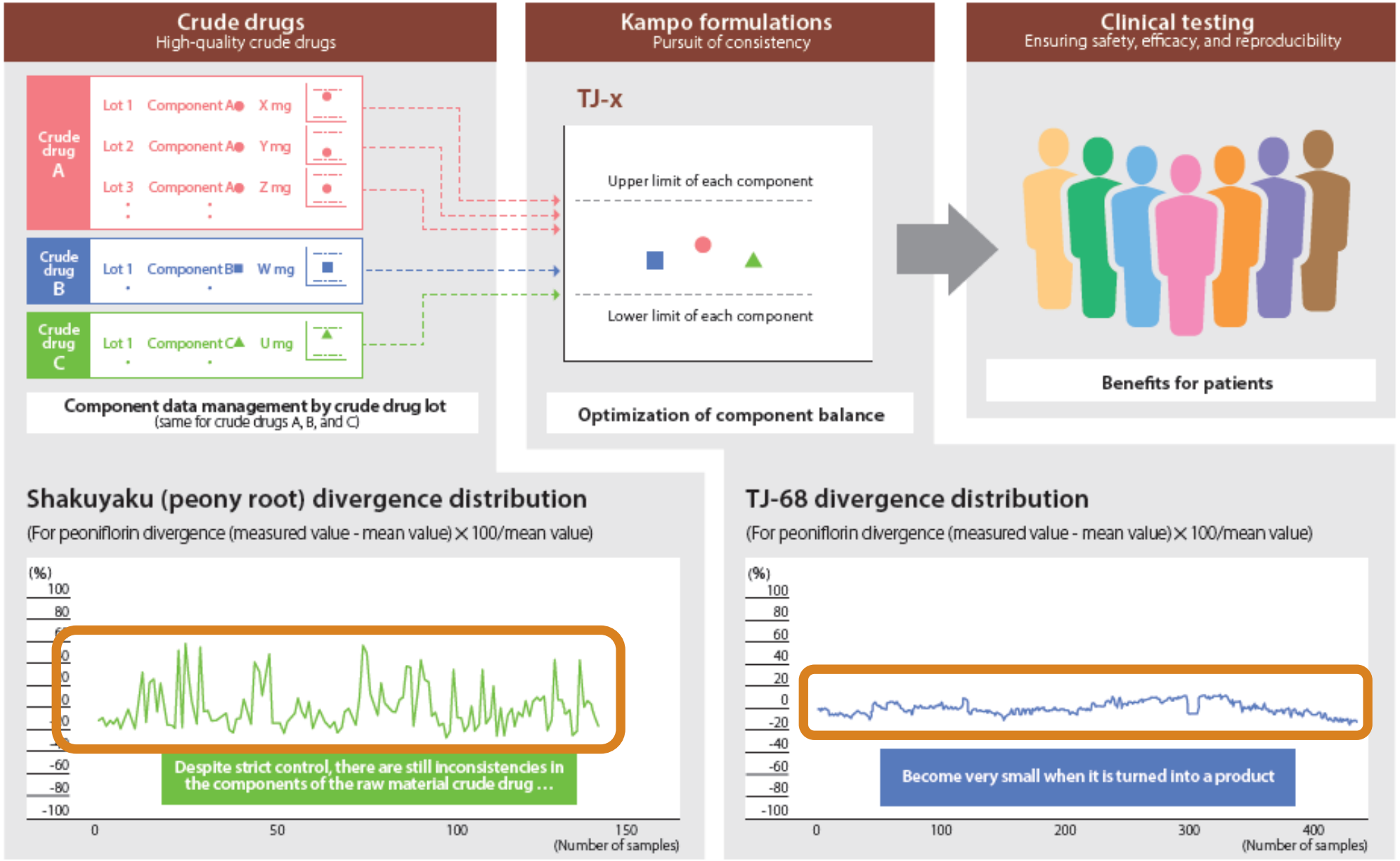
Investigational new drug (IND): Gold standard quality

The efficacy and safety of pharmaceutical products is guaranteed through the constant supply to the front lines of medicine of pharmaceutical products that are equivalent to INDs evaluated in clinical trials.

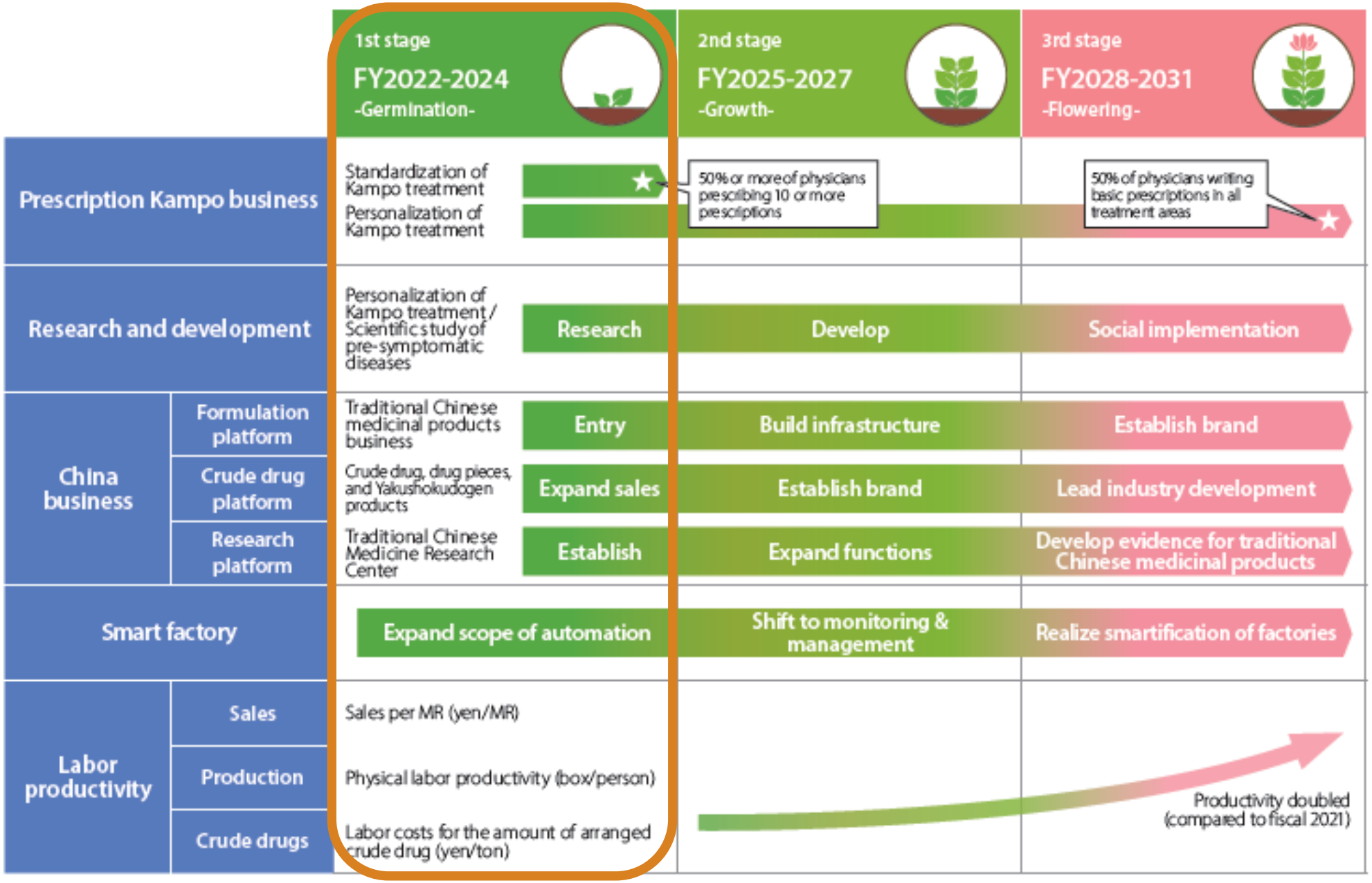
Good quality pharmaceutical products are
those products for which the efficacy and safety is guaranteed to be constantly equivalent to those that have been clinically confirmed
⇒ Pharmaceutical products that have been standardized to guarantee their medical reproducibility

Dr. Yukihiro Goda, Honorary Director, National Institute of Health Sciences (NIHS)

Standardization to guarantee medical reproducibility [High level of difficulty]



Roadmap for achieving the TSUMURA VISION “Cho-WA” 2031



Three Important Medical Domains that are Urgent Issues in Japan

D Drug-fostering program formulations G "Growing" formulations

Geriatric health

Symptoms associated with frailty

- G Ninjin'yoeito
- G Kamikihito
- G Hochuekkito
- D Goshajinkigan

+Associated formulations

Psychiatric and neurological disorders

- D Yokukansan

+ Associated formulations

Peripheral symptoms in patients with cardiovascular diseases

- G Goreisan

+Associated formulations

Digestive system diseases

- D Daikenchuto
- D Rikkunshito

+ Associated formulations

Cancer (supportive care)

Mitigation of side effects, etc.

- D Rikkunshito
- D Hangeshashinto
- D Goshajinkigan
- G Kamikihito
- G Hochuekkito

+ Associated formulations

Women's health

Diseases specific to women

- G Kamishoyosan
- G Kamikihito

+ Associated formulations

Other diseases and symptoms

- D Daikenchuto
- G Goreisan

+ Associated formulations

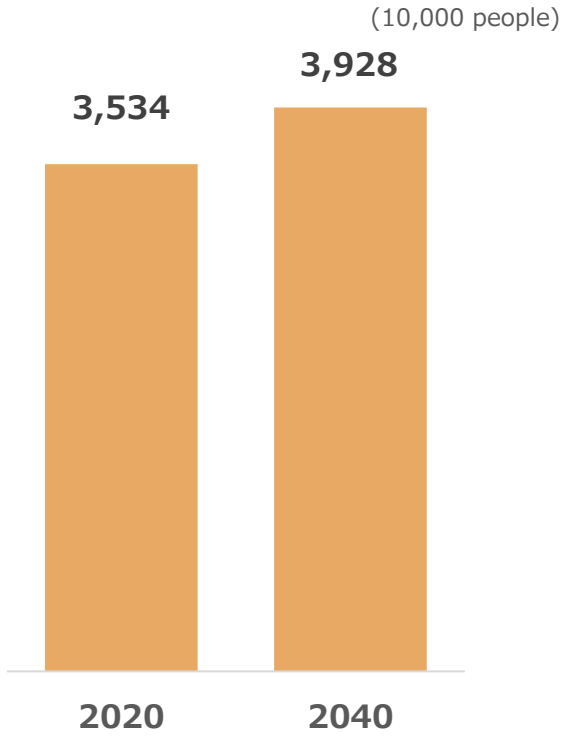
Increasing trend of diseases in related fields with the increase in the elderly population

Estimated that the number of patients with dementia , chronic heart failure and frail is trending upward in tandem with the increase in the number of elderly

Elderly Population

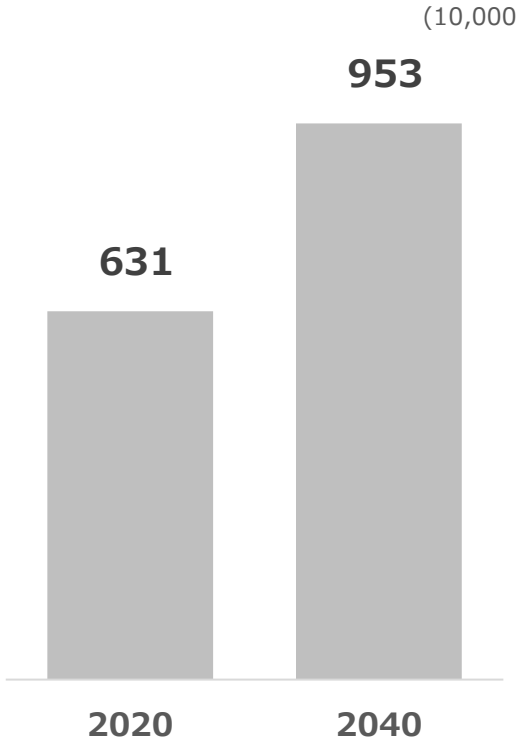
Domain related to the elderly

Estimate of the population aged 65 and older



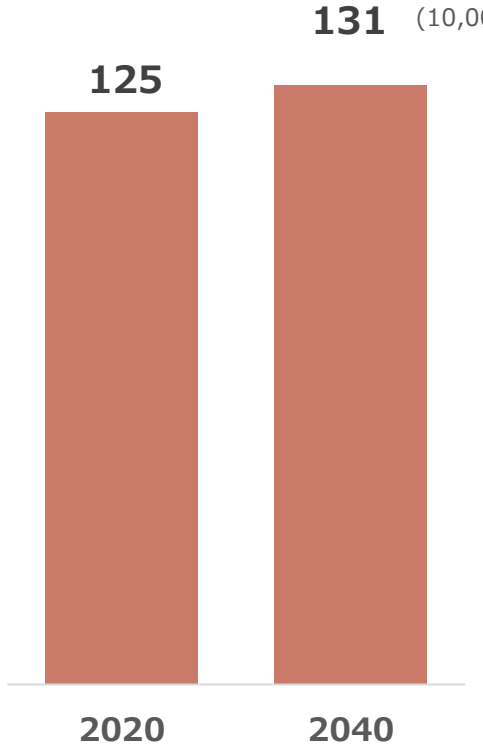
Prepared by Tsumura based on a population estimate for Japan (National Institute of Population and Social Security Research)

Estimate for dementia



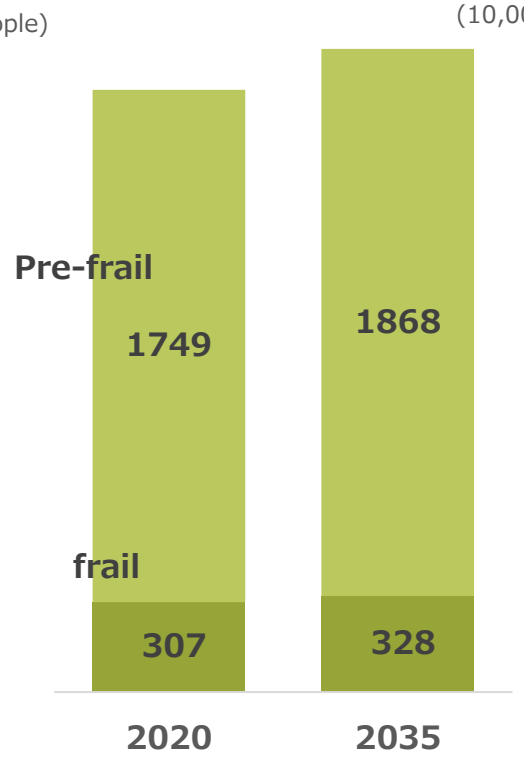
Prepared by Tsumura based on the Comprehensive Strategy for the Promotion of Dementia Measures (Ministry of Health, Labour and Welfare)

Estimate for chronic heart failure



Prepared by Tsumura based on Okura Y et al.Circ J 2008;72:489-491

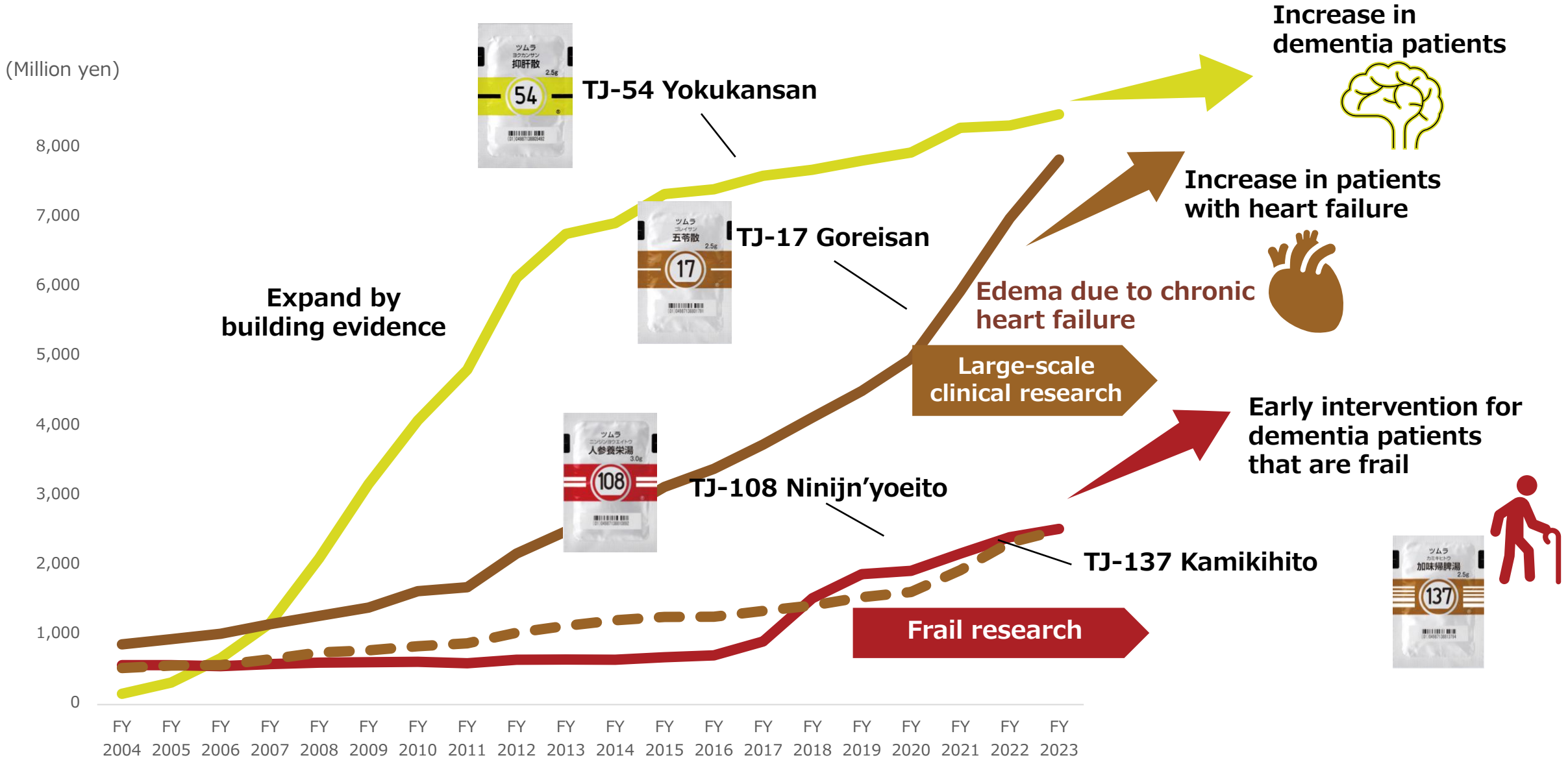
Estimate for frail (including pre-frail)



Prepared by Tsumura based on the Tokyo Metropolitan Institute of Gerontology and Geriatric Medicine 2020

Domain related to the Elderly, Contributing to the Extension of a Healthy Life Expectancy

Research pipeline for drug-fostering program formulations and growing formulations



China Business : Milestones in Each of the Platforms

Vision for the China business:
Contributing to the health of the citizens of China

	First medium-term management plan FY2022-2024	Second medium-term management plan FY2025-2027	Third medium-term management plan FY2028-2031	
Formulation platform	**Enter the traditional Chinese medicinal products business** M&A of a traditional Chinese medicinal products company Apply for classical prescriptions	**Build a foundation for the traditional Chinese medicinal products business** External sales ratio: More than 50%	**Establish a brand as a traditional Chinese medicinal products company** Industry top 10	Sales outlook RMB **7** billion or more
Crude drug platform	**Increase sales of crude drugs, drug pieces, and Yakushokudogen product** External sales ratio: More than 50%	**Establish a brand for crude drugs, drug pieces, and Yakushokudogen products** Expand sales routes to public hospitals (including M&A)	**Crude drug and drug piece company that leads the industry's Development** Leading share in China	Sales outlook RMB **3** billion or more
Research platform	**Establish the Traditional Chinese Medicine Research Center**	**Expand the functions of the Traditional Chinese Medicine Research Center**	**Build evidence in traditional Chinese medicinal products**	

China Business/Crude Drug PF: Products/Services Owing to High-Quality Crude Drugs

FY 2019
Net sales 330 million yen

FY 2023
Net sales 18.7 billion yen

Crude drug PF vision
Sales image
3 billion yuan
(Approx. 60.0 billion yen)

01 Acquire recognition for crude drug quality by expanding sales channels, mainly for raw material crude drugs

- **2019**
  Sales function: Established Pingcun (Shenzhen) Med
  Manufacturing function: Pingcun Zhongying (Hebei) Pharmaceutical Co., Ltd.
- **2020**
  Core functions: Acquisition of Ping An Tsumura Pharma Inc.

Raw material crude drugs

- ■ Sales growth underpinned by a CAGR of 30% (First Medium-Term Management Plan)
- ■ Expand customers that recognize the value of our quality

02 Expand high value-added services and sales to a high profit-margin customer base

- ■ Expand drug pieces, drug piece added-value services
- ■ Develop new products based on the concept of Yakushokudogen

Drug pieces (Crude drug pieces)

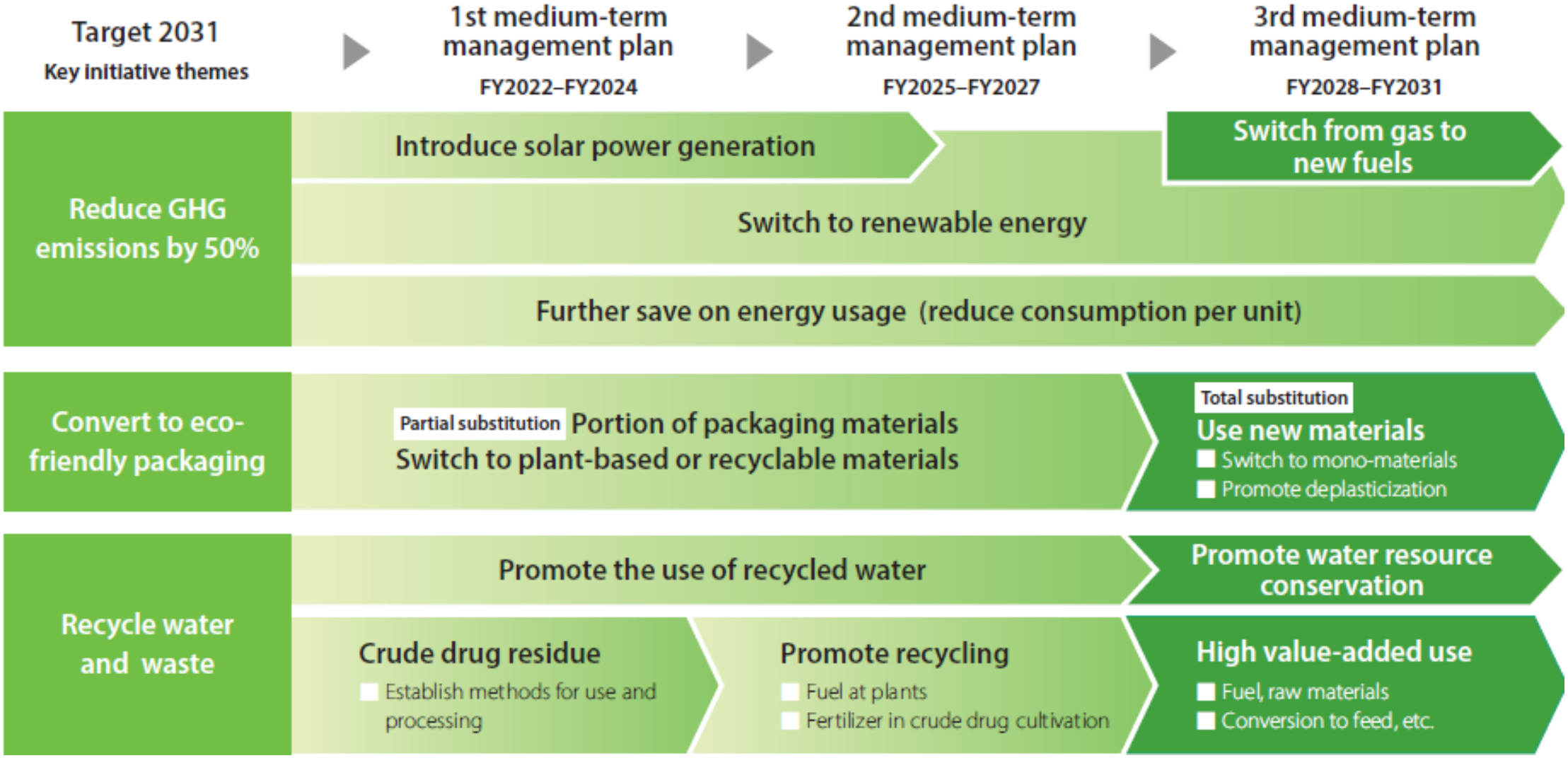
Fluid extract for use by traditional Chinese doctors

New Yakushokudogen products

Strengthen crude drug procurement function for Japan and for China (fortify collaboration systems with local production companies)

Sustainability Targets 2031

Sustainability Vision : Living with nature for tomorrow.



Improve Evaluations by Environment-related Rating Agencies

FY2021

First Medium-Term Management Plan FY 2022 - FY 2024

Second Medium-Term Management Plan FY 2025 - FY 2027

Third Medium-Term Management Plan FY 2028 - FY 2031

Acquire SBT certification

Application　Certification acquisition　Execute certification plan

B-

Improve CDP climate change evaluation

B or higher　A- or higher　A- or higher

Declaration of support

Expand information disclosure based on TCFD recommendations

Analysis and disclosure of basic content　Further improve the level of analysis and disclosure

CDP 2023 evaluation ranking
Climate change: A⁻　Water security: A⁻

Request response addressing “climate change” and “water security”

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Business Results for Fiscal 2023 and Earnings Forecast for Fiscal 2024

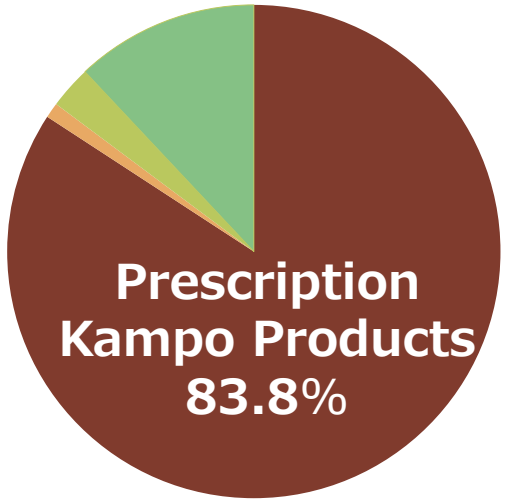
Director, and CFO
Muneki Handa

Business Results for FY 2023

【Million yen】	Revised forecast for FY 2023 (Revised on February 6)	FY2023 results	Vs.planned	YoY	
				Amount	Change
Sales	**152,000**	**150,845**	**99.2%**	**+10,801**	**+7.7%**
Domestic business	133,300	132,099	99.1%	+7,400	+5.9%
China business	18,700	18,745	100.2%	+3,400	+22.2%
Operating profit	**19,500**	**20,017**	**102.7%**	**(899)**	**(4.3)%**
Domestic business	20,100	20,531	102.1%	(658)	(3.1%)
China business	(600)	(514)	–	(240)	–
Ordinary profit	**22,400**	**23,493**	**104.9%**	**+40**	**+0.2%**
Profit attributable to owners of parent	**16,200**	**16,707**	**103.1%**	**+225**	**+1.4%**
PL translation rate (CNY)	19.00	19.83	–	+0.28	–

*Forex rate at the time overseas subsidiaries' PLs were incorporated; differs from the import rate for raw material crude drugs

Ratio to total sales



- China business : Crude Drug Platform 12.4%
- Domestic business : OTC Kampo etc. 2.9%
- Domestic business : Other prescription pharmaceuticals 0.9%

Key Points in Performance

Net sales and profits at each level nearly in line with revised plan

Net sales	150,845	million yen	Achievement rate	99.2%	YoY	+7.7%

- **Domestic business** Total sales of the 129 prescription Kampo products : 126,357 million yen,up 5.9% year-on-year
  Total sales of OTC Kampo formulations and other healthcare products : 4,439 million yen, up 11.9% year-on-year
- **China business** Raw material crude drugs, drug pieces, Yakushokudogen products, etc. : 18,745million yen,up 22.2% year-on-year

Operating profit	20,017	million yen	Achievement rate	102.7%	YoY	(4.3)%
Operating profit margin	13.3	%	vs. Plan	+0.5pt	YoY	(1.6)pt

Cost-to-sales ratio: 54.4%, down 0.5pt vs. plan and a rise of 3.2pt year-on-year

Versus plan: Manufacturing input was small for powdered extracts at the Tianjin Plant Year-on-year: Impact mainly due to a rise in crude drug procurement expense, depreciation in the value of the yen against major currencies, and raw material expenses continuing to trend at a high level

SG&A ratio: 32.4%, up 0.2pt vs. plan and down 1.4pt year-on-year

Year-on-year: Sales growth absorbed growth investments, including the DX of R&D and the Kampo Value Chain

Ordinary profit	23,493	million yen	Achievement rate	104.9%	YoY	+0.2%

- Foreign exchange gain primarily related to loans to overseas subsidiaries: 2,193 million yen, up 684 million yen year-on-year

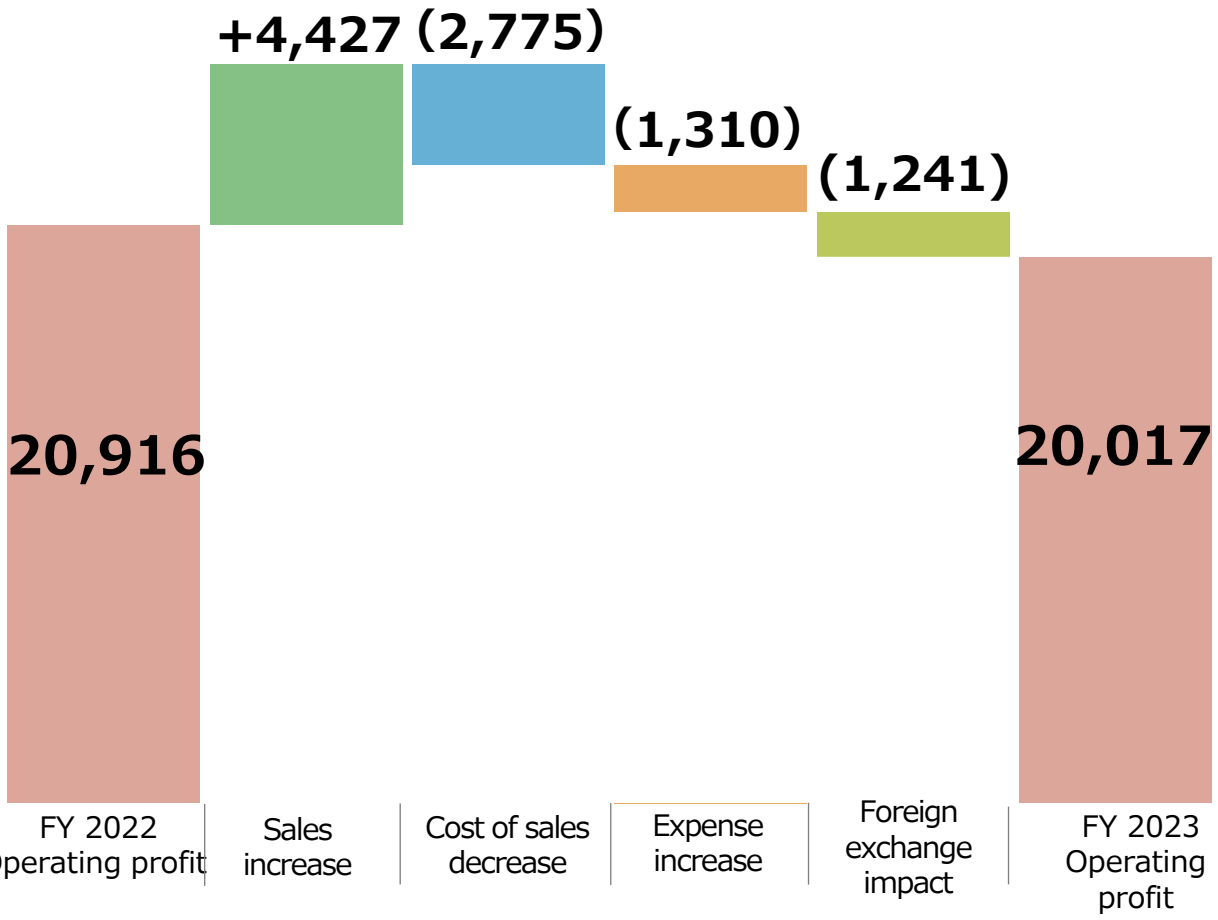
*Foreign exchange gains of 1,338 million yen were recorded at the time of the February 7 revised forecast revision.

Profit attributable to owners of parent	16,707	million yen	Achievement rate	103.1%	YoY	+1.4%

Posted extraordinary loss (impairment loss and COVID-19 related loss) in the prior fiscal year

Factors Triggering Changes in Operating Profit (YoY)

(Million yen)



Sales increase: +4,427 million yen	
Domestic business	+3,900
China business	+527
Decrease in cost of sales: (2,775) million yen	
Domestic Business Sales Composition (including NHI price revision impact)	+2,178
Domestic business: Crude drug procurement cost (of which unrealized profit was (2,109))	(4,361)
Domestic business: Raw material expenses	(871)
Domestic business: Processing expense, etc. (of which energy expense was +526, other productivity improvements, etc.)	+982
China business: Increase in sales ratio	(703)
Expense increase: (1,310) million yen	
R&D cost	(683)
Salary allowance	(224)
Sales promotion expense	(175)
Depreciation (of which there was a decline in one-off expense at the Tianjin Plant +720)	+474
Other (of which system introduction expense, etc. (371), activities expense (402))	(702)
Foreign exchange (yen depreciation) impact: (1,241) million yen	

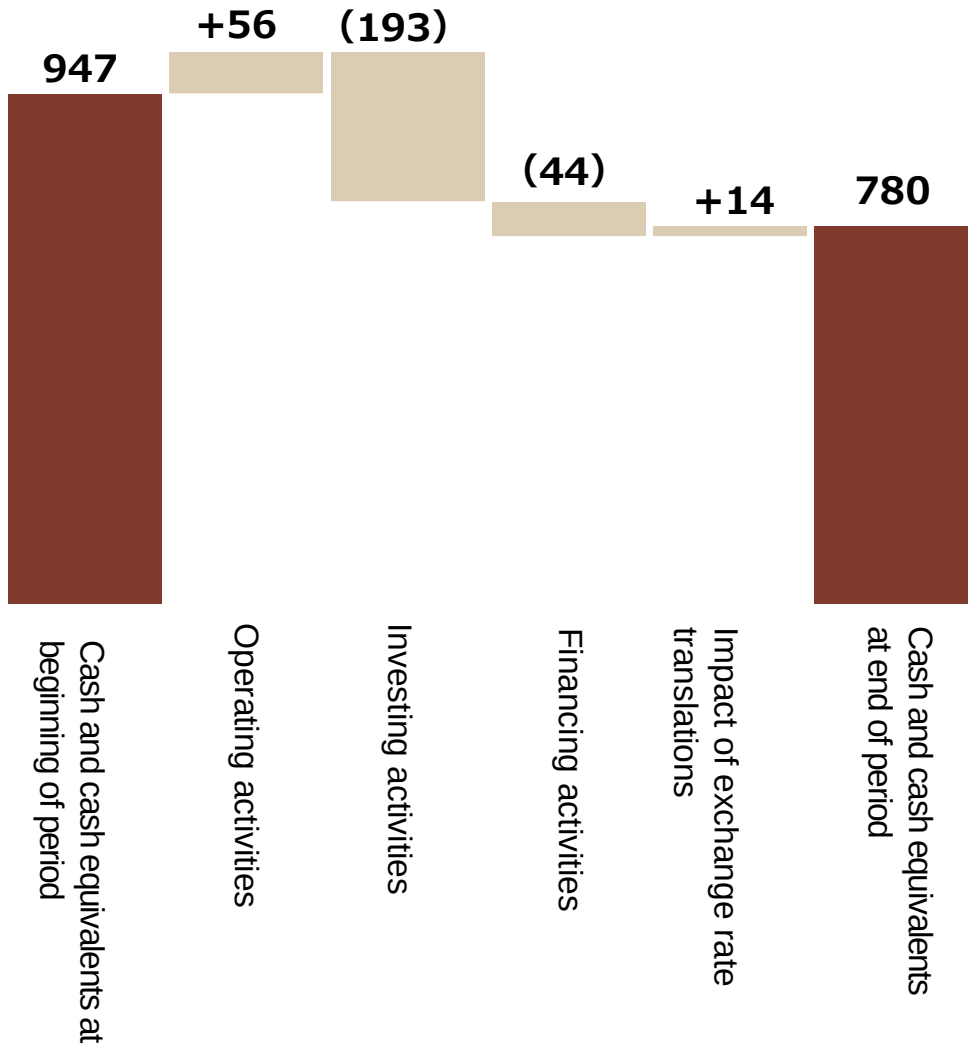
Financial Condition/Cash Flow Position for FY 2023

(Million yen)

	FY 2022 (March 2023)	FY2023 (March2024)	Change
Total assets	**396,813**	**428,254**	**31,440**
Current assets	268,320	281,292	12,971
Non-current assets	128,492	146,961	18,469
Total liabilities	**124,566**	**132,889**	**8,322**
Current liabilities	47,205	68,557	21,352
Non-current liabilities	77,361	64,332	(13,029)
Total net assets	**272,246**	**295,364**	**23,118**
Equity ratio	63.5%	63.2%	(0.3)pt

	FY 2022 (March 2023)	FY2023 (March2024)	Change	Of which, Exchange rate
Inventories	**101,726**	**117,617**	**15,889**	589
Merchandise and finished goods	11,257	12,139	881	290
Work in process	14,430	18,309	3,878	142
Raw materials and supplies	76,038	87,168	11,130	156

(100 million yen)

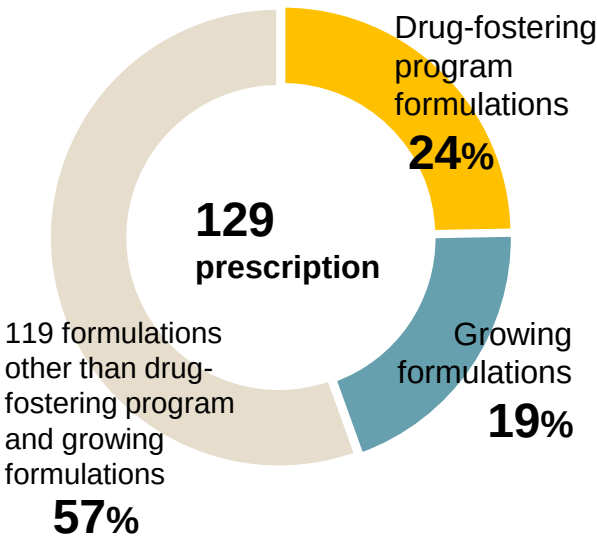


Domestic Business : Sales of Drug-fostering Program Formulations/Growing Formulations

(Million yen)

	Net sales Ranking	Product No./formulation name	FY 2022	FY 2023	YoY	
Drug-fostering program formulations	1	100 Daikenchuto	9,739	9,851	+111	+1.1%
	3	43 Rikkunshito	7,300	7,454	+153	+2.1%
	4	54 Yokukansan	7,380	7,447	+66	+0.9%
	9	107 Goshajinkigan	3,421	3,698	+276	+8.1%
	24	14 Hangeshashinto	1,390	1,448	+57	+4.2%
Total sales for drug-fostering program formulations			29,233	29,899	+666	+2.3%
Growing formulations	2	41 Hochuekkito	7,727	7,956	+228	+3.0%
	5	17 Goreisan	6,208	6,869	+660	+10.6%
	6	24 Kamishoyosan	5,050	5,117	+66	+1.3%
	17	108 Ninjin'yoeito	2,128	2,305	+177	+8.3%
	18	137 Kamikihito	2,067	2,290	+223	+10.8%
Total sales for growing formulations			23,182	24,539	+1,356	+5.9%
Total sales for 119 formulations other than drug-fostering program and growing formulations			66,946	71,918	+4,971	+7.4%
Total sales for 129 prescription Kampo products			119,362	126,357	+6,994	+5.9%

Ratio to total sales



China Business: Crude Drug Platform Business Sales Expansion

By expanding sales of Crude Drug Platform , we have achieved our business plan in China.

22.2% growth*

Chinese business	**Net sales**	**18.75 billion yen**
Crude drug platform	Operating profit	0.98 billion yen
Formulation platform, IT infrastructure investments, etc.	Expenses, etc.	
Chinese business	**Operating profit**	**(0.51) billion yen**

***Local currency basis: 20.4% growth**

✓ Operating profit in the crude drug platform continued to increase

Crude drug platform products

Raw material crude drugs

Sales to traditional Chinese medical products companies as a raw material

Drug pieces

Sales for prescription-use and as an OTC to hospitals and pharmacies

Yakushokudogen products

Sales of health food products made from crude drugs to general consumers

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Earnings Forecast for Fiscal 2024

FY 2024 Earnings Forecast

Forecast of increased sales and profit /First Medium-Term Management Plan is expected to achieve its numerical targets

[Million yen]	FY 2023 Results	FY 2024 Earnings Forecast	YoY Amount	YoY Change
Net sales	**150,845**	**185,000**	**+34,154**	**+22.6%**
Domestic business	132,099	163,400	+31,300	+23.7%
China business	18,745	21,600	+2,854	+15.2%
Operating profit	**20,017**	**39,500**	**+19,482**	**+97.3%**
Domestic business	20,531	39,490	+18,958	+92.2%
China business	(514)	10	+524	–
Ordinary profit	**23,493**	**39,500**	**+16,006**	**+68.1%**
Profit attributable to owners of parent	**16,707**	**28,500**	**+11,792**	**+70.6%**
Income statement exchange rate (JPY/RMB)	19.83	**21.00**	**+1.17**	–
ROE	**6.4%**	**10.0%**		
EPS	**219.83円**	**375.35円**		

First Medium-Term Management Plan Numerical targets (fiscal 2024)

Net sales: **¥162.0**billion

Operating profit: **¥29.0**billion

ROE: **8%**

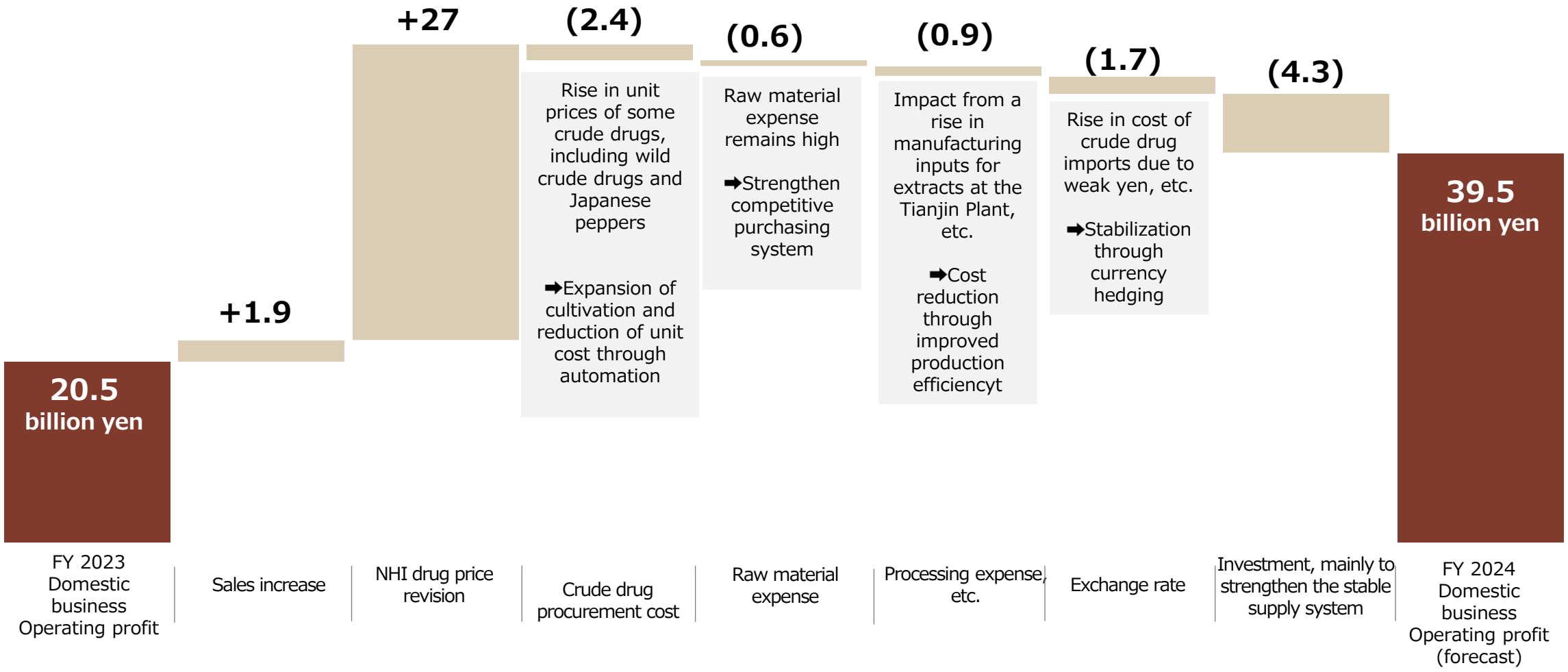
Versus the First Medium-Term Management Plan

Although there was negative impact from a rise in a portion of crude drug expenses, mainly wild crude drugs, a depreciation in the yen's value against major currencies, and ongoing high expenses for raw materials and energy, we expect to achieve all our indicators (sales, operating profit, ROE) in the First Medium-Term Management Plan owing to a boost in drug prices reflecting the recalculation of unprofitable products

(Note) ・Foreign exchange impact (non-operating profit) was not factored into the earnings forecast given the difficulty to reasonably calculate this impact based on the status of the forex market.

FY 2024: Factors Triggering Changes in Operating Profit in the Domestic Business

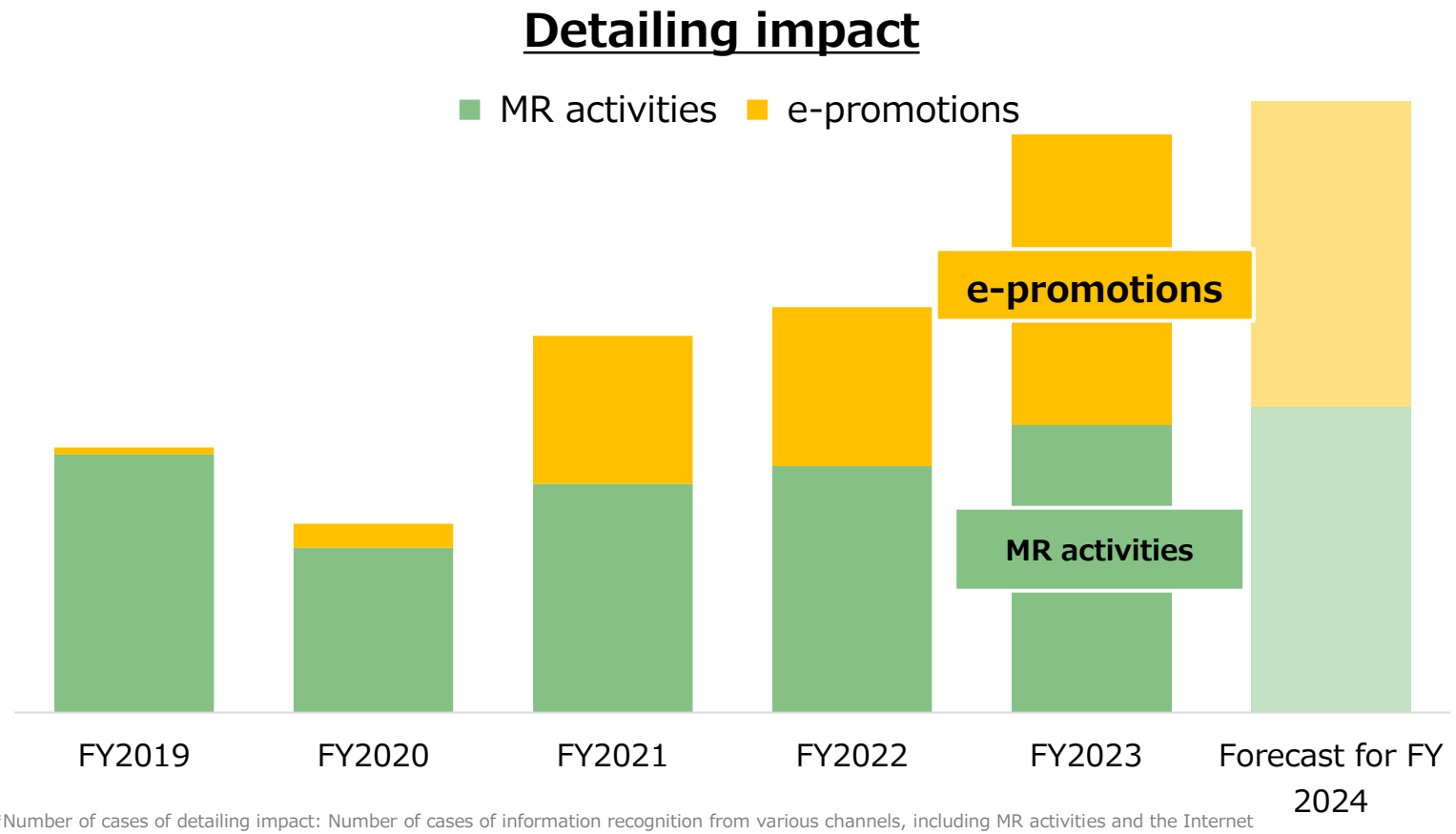
- **Although factors in the external environment, including inflation, continue to be harsh, we look for profit growth owing to NHI drug price revisions (recalculation of unprofitable products)**
- **Plan to implement investment, mainly to strengthen the stable supply system**

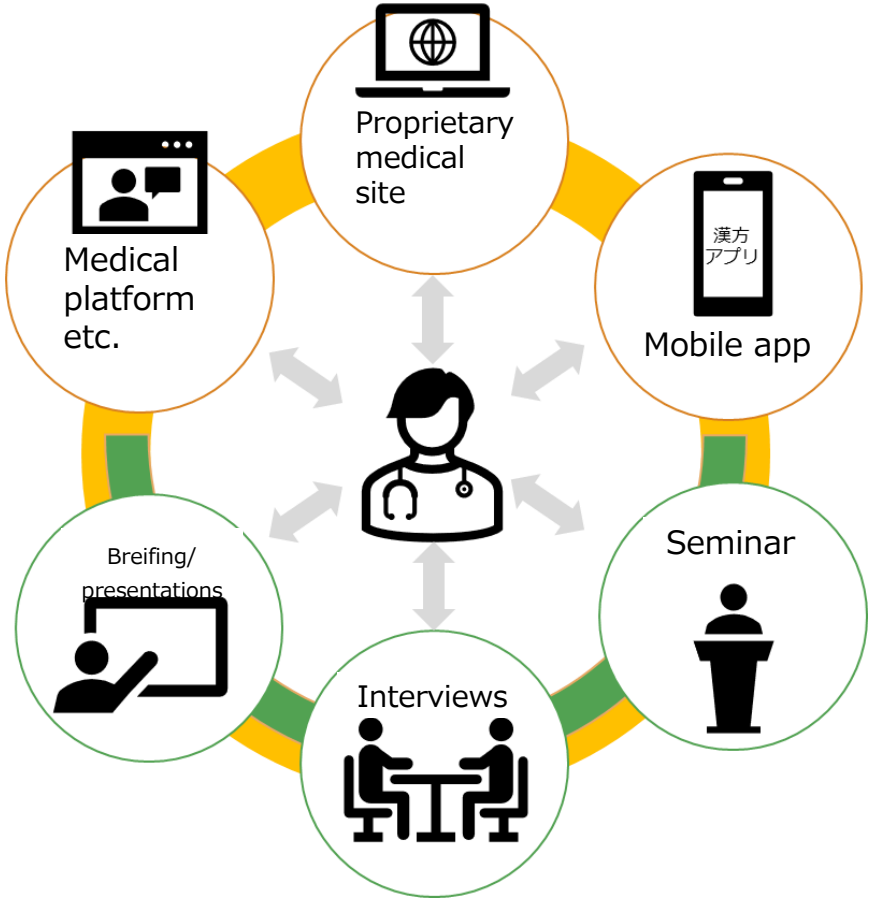


Domestic Business :The Status of Expansion for Information Provision Activities

In FY 2023, detailing impact rose 140% versus the previous year, in particular e-promotion growth was up 180%

In FY 2024, we plan to further expand information provision activities, mainly through e-promotions





*Number of cases of detailing impact: Number of cases of information recognition from various channels, including MR activities and the Internet
*e-promotions: Information provision, mainly through online lectures and video streaming
*MR activities: Information provision via MRs + in-person lectures

INTAGE Healthcare Inc. survey, Impact Track

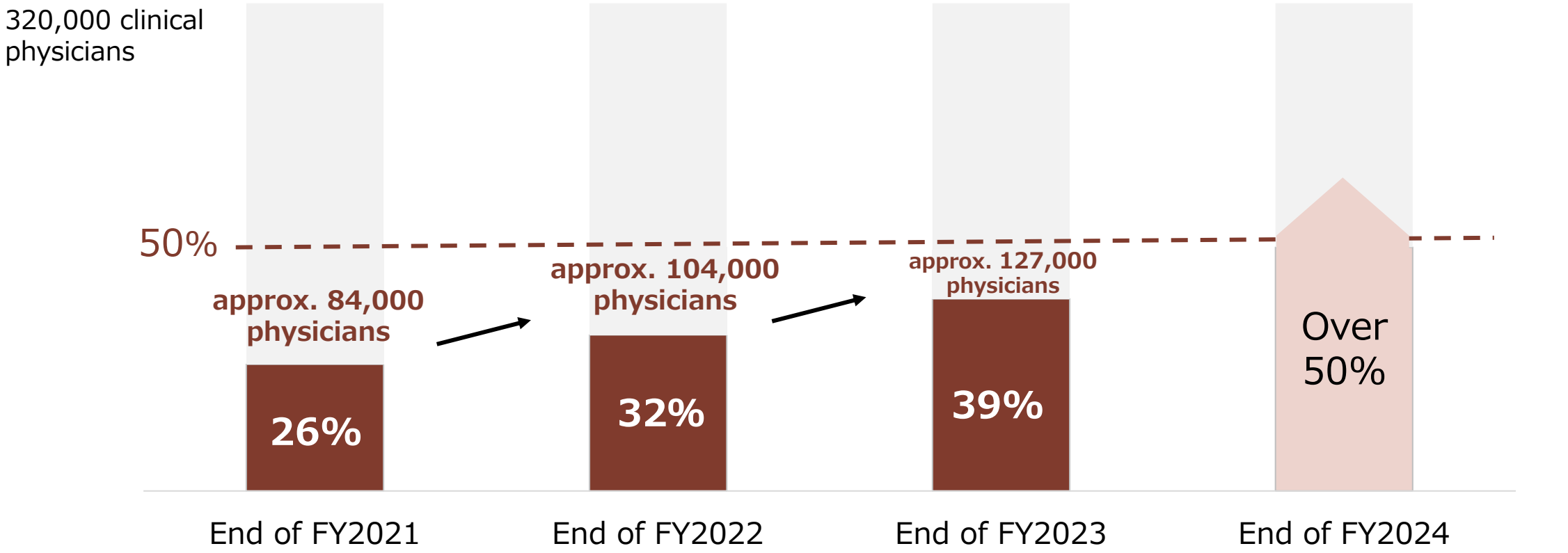
Domestic business: Trends in the Number of Physicians Writing 10 or More Prescriptions for Kampo Pharmaceuticals

The number of physicians writing 10 or more prescriptions for Kampo pharmaceuticals increased by approximately 23,000 physicians, a ratio of 39%

Aim to achieve a ratio of 50%-plus, owing to the implementation of hybrid promotions

*Trend in the number of physicians writing 10 or more prescriptions for Kampo pharmaceuticals

*Survey by Tsumura



First Medium-Term Management Plan

China business: Achieve operating profit

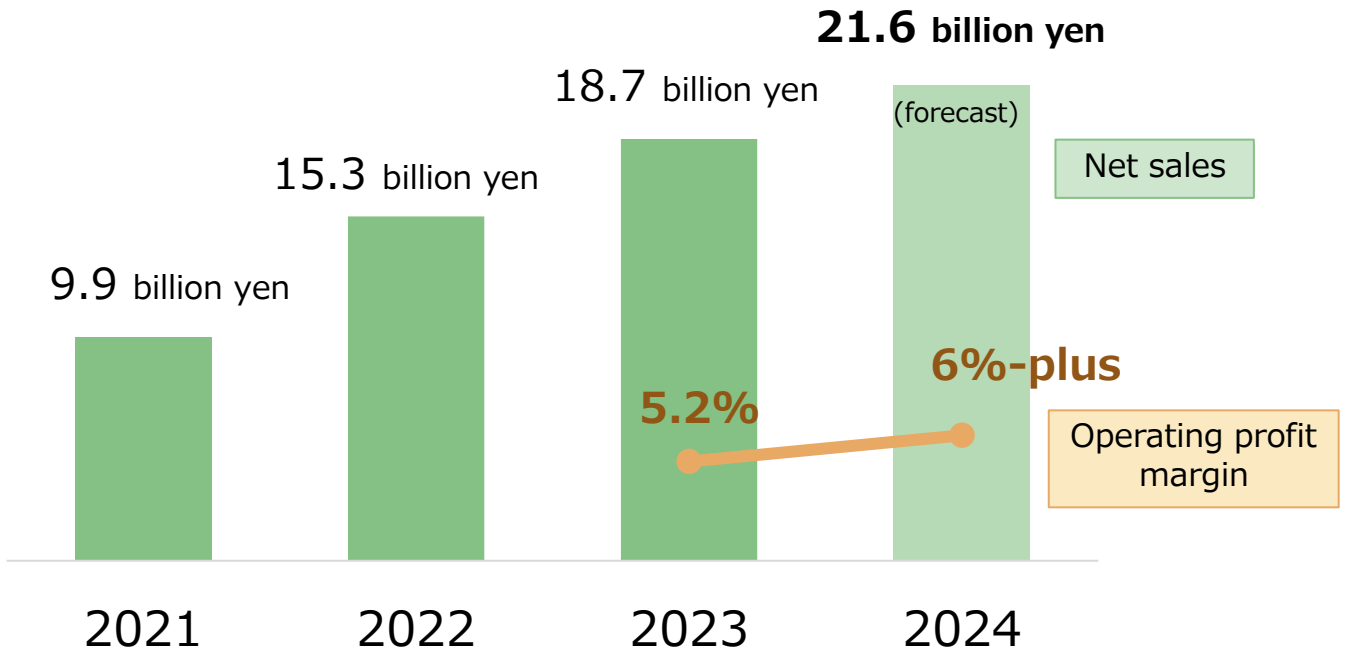
- **In the crude drug platform, we estimate sales CAGR of 30%**
- **In FY 2024, we plan an improvement in the operating profit margin owing to an expansion in scale that focuses on profitability**

Crude drug platform policy

“Expand scale focusing on profitability”

- Emphasis on improving profit margins
- Expand sales mainly to business partners that recognize the value of high quality

Net sales and operating profit margin in the crude drug platform



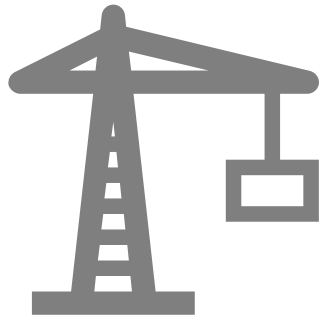
Invest to further strengthen the stable supply system

■ Accelerate the bolstering of production capacity, Improved productivity through automation, newly establish a warehouse, etc.

Capex 34.0 billion yen

***Approx. +15.0 billion yen YoY**

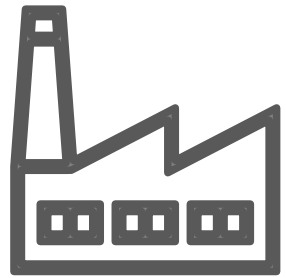
Main investment activities	Total investment	FY 2024 investment amount	Period
Tianjin Plant Phase 2 and Phase 3 construction (Manufacturing of Kampo powdered extracts)	25.0 billion yen	9.5 billion yen	FY 2021 - FY 2026
Newly establish a manufacturing process for Kampo powered extracts, and a granulation packaging process	68.0 billion yen	10.5 billion yen	FY 2024 - FY 2027
Yubari Tsumura Expand a crude drug warehouse	2.5 billion yen	1.5 billion yen	FY 2023 - FY 2025



■ Additional manufacturing costs

Expense: +2.5 billion yen YoY

Main activities	FY 2024 increase in value
Hike headcount to newly establish manufacturing line, etc.	+1.0 billion yen
Strengthen prevention and maintenance, secure warehouse, etc.	+1.5 billion yen



Initiatives for the Visualization of Non-financial Value of Tsumura's Business Operations

(1) Value of pharmaceutical products derived from natural ingredients

(2) Value in the Kampo value chain

(3) Value of the organization and human capital

Approach for Visualization Using an Optimal Analytic Method

- Impact Accounting
- Yanagi model*1
- Value relevance Analysis*2
- VTA (Value Tree Analysis)
- Other

*1: Model developed by Ryohei Yanagi employed in the "CFO Policy (CHUOKEIZAI-SHA HOLDINGS, INC. 2020)"
*2: One analytic method in Digital ESG Data Analytics of ABEAM Consulting Ltd.

Initiatives for the visualization of the relevance of pre-financial capital and corporate value improvement

Goal: Visualization of the relevance of initiatives related to pre-financial capital and the corporate value improvement
Analyze issues through visualization to contribute to the improvement of initiatives

Analytic method: Overview (Yanagi model) analysis *1
・Value relevance analysis (Implement analysis: ABEAM Consulting Ltd., Digital ESG Data Analytics)

◆ Example of analysis: Results of overview analysis (excerpt)

Employment

◆ Promotion rate (female employees)

1% increase → PBR improved 0.27% after two years

Employee health

◆ Health checkup rate

1% increase → PBR improved 12.72% after three years

Work-life balance

◆ Paid leave acquisition rate (All employees)

1% increase → PBR improved 7.37% after two years

◆ Average number of days of childcare leave taken (female employees)

1% increase → PBR improved 1.25% after one year

◆ Average period of childcare leave taken (female employees)

1% increase → PBR improved 0.28% after two years

Implemented the aforementioned analysis (overview analysis/value relevance analysis) in FY2023 In the overview analysis, confirmed items with a positive correlation to pre-financial capital and PBR.
Implementing a detailed analysis of the results. In accordance with the analytical results, extract issues from each initiative to contribute to improvements. Results of detailed analysis is scheduled to be disclosed. Plan to continue to implement this analysis.

*1: Analysis using the ABEAM Consulting Ltd. Digital ESG Platform in accordance with the model developed by Ryohei Yanagi based on the “CFO Policy (CHUOKEIZAI-SHA HOLDINGS, INC. 2020)”

ROE Improvement: Quickly Realize a Positive Equity Spread Early On and Expand

Announced on November 7, 2023

ROE = **Earnings power** × **Total assets turnover rate** × **Financial leverage**

FY 2024 Target Level

ROE 10%

Existing businesses
ROE of 8% or more

- **Earnings power**
  - Net sales growth
  - Reduce cost of goods sold
  - Curb the SG&A ratio
  - The China business aims to secure a profit margin that is equivalent to or higher than the profit margin in the domestic business
- **Total assets turnover rate**
  - CCC improvement
  - Manageable level of cash and deposits
  - Sale of cross-shareholdings
  - Improving capital investment efficiency etc.
- **Financial leverage**
  - Secure financial soundness and pursue an optimal capital composition
  - Use interest-bearing debt
  - Equity ratio of 50%-plus

***Cost of equity: approx. 7%**

Calculate using the CAPM Risk free rate: 2%; Risk premium: 6%, β value: approx. 0.8

*Equity spread = ROE − Cost of equity

Capital Efficiency Improvement: Initiatives to Improve the Balance Sheet

Improved B/S by curtailing the collection site for accounts receivables and decreasing cross-shareholdings

Curtail the collection site for accounts receivables

Negotiate with business partners on collection sites for accounts receivables and

Reduce in stages by approximately 20%

Decrease cross-shareholdings

Based on a policy with a principle of zero

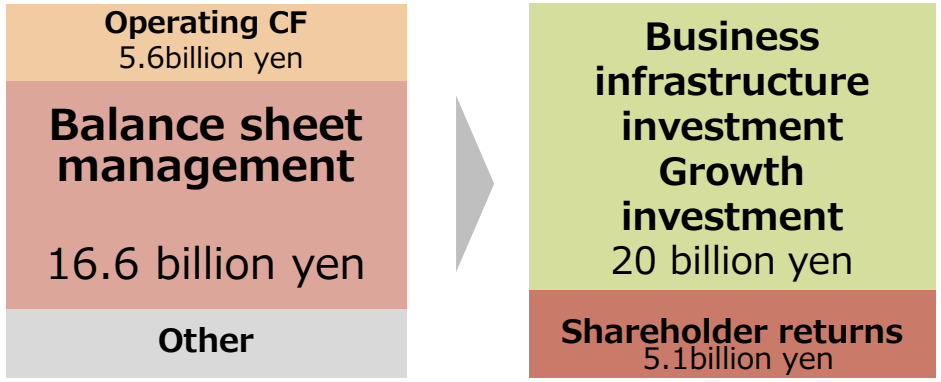
From FY 2024, aim to realize full-fledged reduction and cut by half early on

*Excluding shares with a purpose of forming a capital and business alliance

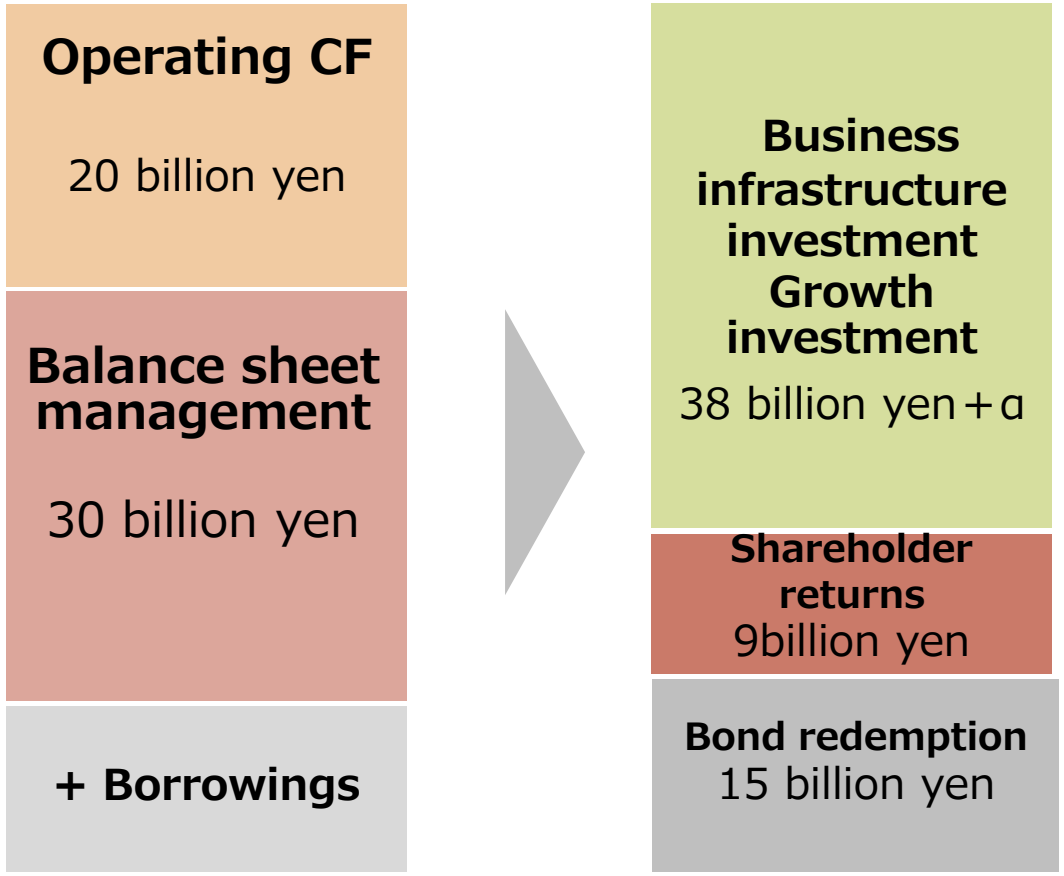
Cash allocation

In addition to the Operating CF, create cash by improving the balance sheet, and allocate to the further growth of shareholder returns and business operations

Cash allocation(FY2023)



Cash allocation(FY2024)



Shareholder returns

- In FY 2023, per-share dividend hiked to 85 yen
- In FY 2024, we expect to payout a dividend of 136 yen in accordance with the shareholder return policy
- Aim for the realization of a DOE of 5%

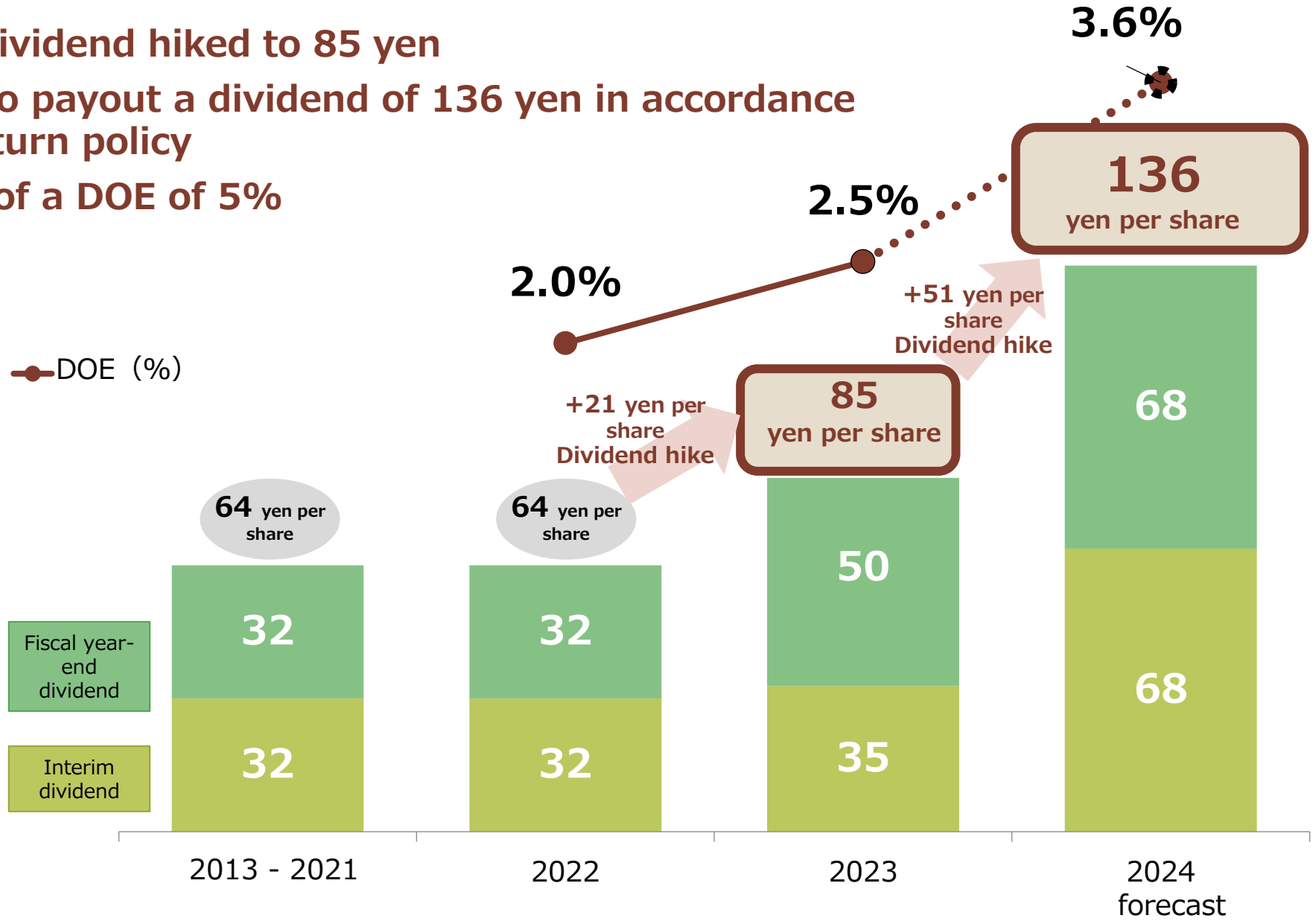
Target level

Published on November 7, 2023

DOE 5%

＝Dividend payout ratio of 50% × ROE of 10%

Existing Businesses
DOE of 4%-plus



Agenda

01 Moving Towards Realizing the Long-Term Management Vision—TSUMURA VISION “Cho-WA” 2031

02 Business Results for Fiscal 2023 and Earnings Forecast for Fiscal 2024

03 Progress in US development (TU-100)

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TSUMURA

Progress in US development (TU-100)

Head of the International Pharmaceutical Research & Development Division

Atsushi Kaneko

TU-100: Developmental and investigational drug manufactured from a crude drug with the same composition as Daikenchuto for the domestic market

Today’s Agenda

1. Complete Patient Enrollment for the Late Phase II Trial for TU-100
2. Tackle TU-100 US Development
3. Outlook Going Forward

Chapter 1
Complete Patient Enrollment for the Late Phase II Trial for TU-100

1-1. Summary and Trends for the TU-100 Trial

https://clinicaltrials.gov/ct2/show/NCT04742907?term=TU-100&cntry=US&draw=2&rank=7

Target disease: Postoperative ileus (POI)

Trial format: Multi-center, randomized, double-blind, placebo-controlled trial

Target cases: 402 cases

Group structure: 15g/day group, 7.5g/day group, placebo group

Patient enrollment period: July 2021 - March 2024 (Two years and eight months)

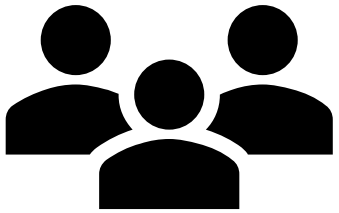
Main endpoints: Recovery time for gastrointestinal functions

The COVID-19 pandemic broke out in and after 2020. And given that rivals halted and/or suspended development,

we completed patient enrollment with a target sample size of 402 cases in March 2024!

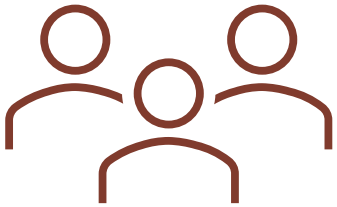
1-2. TU-100 US Development System

Proceed as an amazing “single team”



Digestive surgeons in **US**
(Global KOL well-versed in POI)

Digestive surgeons in **Japan**
(Physicians that well-versed in POI and prescribesTU-100)

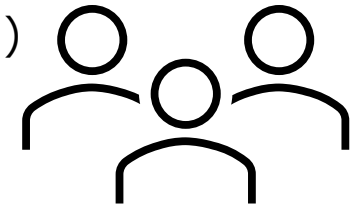


Medical consultants
(Experience in developing POI treatment)

Tsumura International Pharmaceutical Research & Development Project member

Former FDA examiner
(FDA application consultation)

World-leading global CRO



Consultant well-versed in FDA applications related to CMC

US pharmaceutical affairs consultant

CMC: Chemistry, Manufacturing and Control

1-3. Initiatives for the TU-100 Trial

Multi-center, randomized, double-blind, placebo-controlled trial, being participated in by 43 medical centers in the US

Direct and detailed communication with centers participating in the trial

Execute under a strict safety management system by setting up a data safety monitoring committee

Secure Kampo formulation manufacturing management technology and reliability to minimize lot-to-lot variation

Provide a placebo drug that utilizes the same manufacturing knowhow

Reconfirm medical needs to treat POI and **expectations in herbal medicines**

Chapter 2
Tackle TU-100 US Development

2-1. Origin of TU-100 US Development

In the US, domains in which the use of Western drug treatment is a difficult, we aim to help treatment for US patients through the development of Kampo formulations that will have a specific effect for diseases!

2-2. History of TU-100 US Development

Going from unscientific to scientifically verified

2007 - 2015
Obtaining Evidence for Daikenchuto*

- Stomach and esophagus team
- Liver surgery team
- Colon team
- Clinical pharmacology team
- Basic pharmacology

Scientific evaluation of safety and efficacy of Daikenchuto in the gastrointestinal area

2009
Daikenchuto adorned the introduction of "SURGERY," a US medical journal
Kono T, Surgery 2009

Kampo medicine symposium at the World Congress of ISS/SIC
Australia (2009)
Finland (2013)

2016
Release "**botanical drug development guidance**", which was revised by the US FDA

2016
Launch the "**Study group on the Future Vision for Kampo—Responsibility for People's Health and Healthcare**" in collaboration with industry, government, academia and related organizations

2018
Consolidate TU-100 US development into POI
Move on to late phase II trial!

Recommendations from the "Study Group on the Future Vision for Kampo—Responsibility for People's Health and Healthcare" (Section 5)
Promote **overseas deployment of Kampo formulations**

#DKT Forum: Established in 2007 with the purpose of building up clinical evidence for diseases and symptoms targeted by Daikenchuto owing to support from gastrointestinal surgeons who are KOLs. Announced research results, including at academic conferences in Japan and abroad, opportunity to promote the international development of Kampo medicine.

Boost the degree of international focus on Kampo medicines

2-3. Survey on the marketability and treatments for POI disease

POI (Postoperative ileus) is an unmet medical need

POI is a
- Pathological condition that impairs the peristaltic action of the intestinal tract due to abdominal surgery
- There are main causal factors and the progression of the disease is complex

US market evaluation of POI medicines: US HCUP database

- **The probability of POI occurring is high in digestive system surgeries**

  Colectomy: 14.90%, other types of gastrointestinal resections: 18.63%

- **The number of digestive system surgeries to continue to increase going forward**

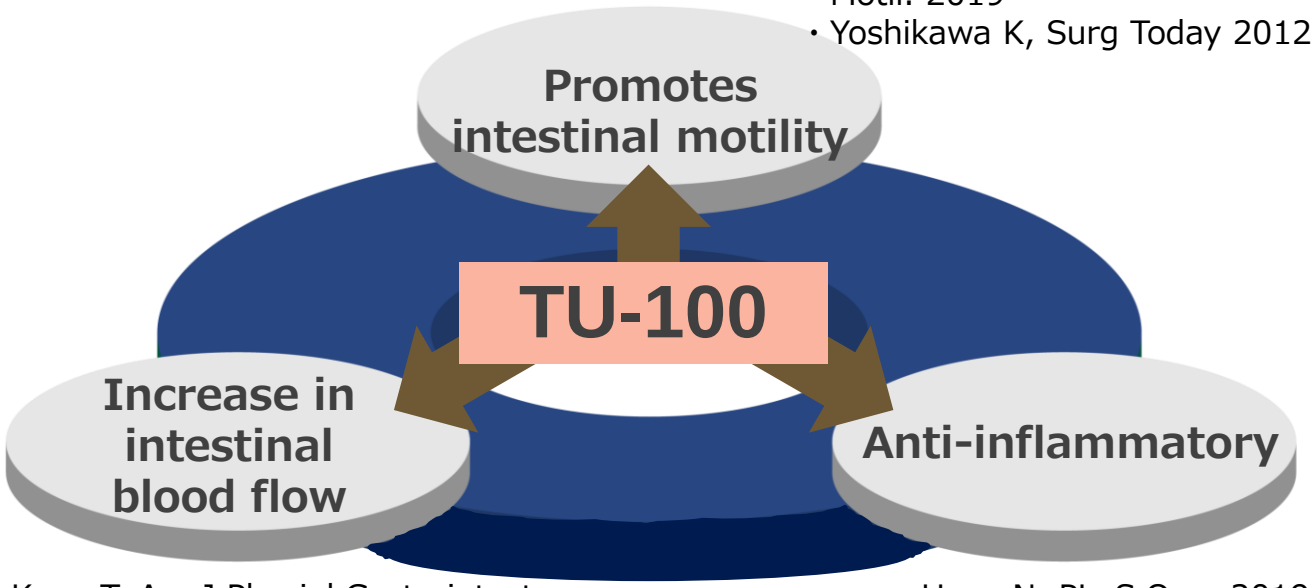
	2015	2019	2025
No. of surgeries with the potential of triggering POI	2.08 million	1.97 million	1.87 million
Portion of disgestive system surgeries	**730,000**	**750,000**	**770,000** ↑

- **The only treatment for POI is Alvimopan (μ-opioid receptor antagonist)**

This data are the results of an analysis implemented in 2021 based on IQVIA data and a survey.
IQVIA assumes no responsibility for any impact brought about from the use of these results.

2-4. Unique Mechanism of Action of TU-100

Three mechanisms of action



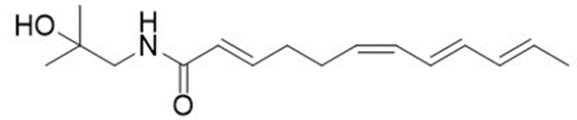
- Kubota K, Neurogastroenterol Motil. 2019
- Yoshikawa K, Surg Today 2012
- Kono T, Am J Physiol Gastrointest Liver Physiol. 2013
- Suzuki K, PLoS One. 2021
- Ueno N, PLoS One. 2019
- T Hayakawa, J Smooth Muscle Res. 1999

Pharmacological effects owing to compound actions

- ✓ **Multi-component/multi-targeted drug therapy**
- ✓ **Enrich clinical and basic research**
- ✓ **Component crude drugs and main pharmacological ingredients**

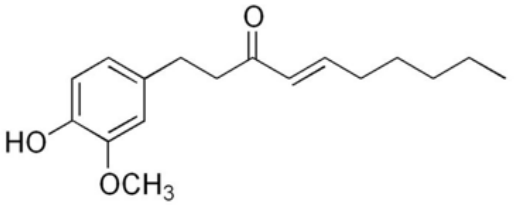
・Japanese peppers

hydroxy α-sanshool



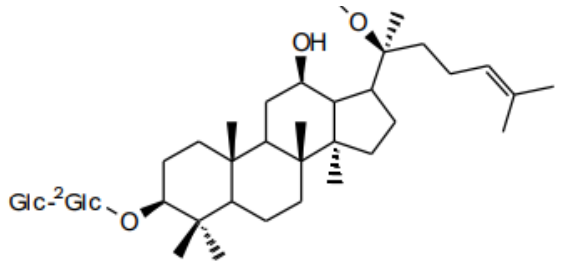
・Dried ginger

[6]-shogaol



・Ginseng

ginsenoside Rb_1



2-5. Transition in US FDA Botanical Drug Guidance

US FDA released the first edition of the "Botanical Drug Guidance" in June 2004

Guidance for Industry on Botanical Drug Products

Measures to promote the development of herbal/botanical pharmaceutical products after presenting clinical evidence on the same level as a small-molecule synthetic drug:

→ Many herbal (botanical) drug manufacturers around the world applied for clinical trials and tackled development in the US

→ Issues arise that are unique to the quality control and clinical evidence regarding herbal (botanical) medicine (product)

December 2016: Released a revised edition of the "Botanical Drug Development Guidance"

Botanical Drug Development: Guidance for Industry

Keyword: Totality of the Evidence

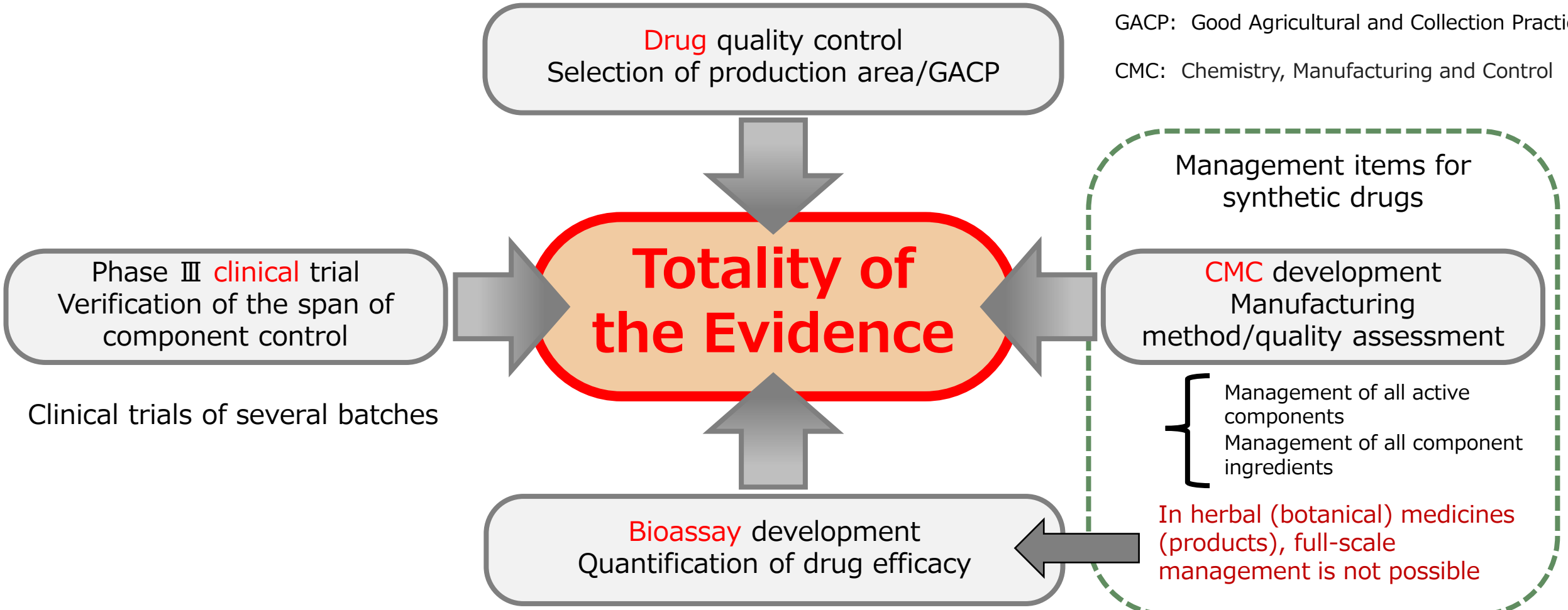
Regarding the ambiguity of safety and efficacy unique to botanical medicines (products), clarify evidence with respect to clinical evaluations, chemical/manufacturing management, management of raw material crude drugs, and biological quality control, and mutually request consistent management controls:

→ Promote development of botanical medicine (products) that fulfills the standardization of high quality, naturally including those dealing with safety and efficacy

2-6. Development Requirements for Botanical Medicines (Products) Sought by the US FDA

Source: Revised Botanical Drug Development Guidance 2016 materials released by the US FDA

Approach unique to herbal medicines with large fluctuations in quality



Evaluate everything objectively/comprehensively, and derive highly reliable quality control methods

2-7. Development Requirements for Botanical Medicines (Products) Sought by the US FDA: Drug quality control

GACP, basic structure

GACP: Good Agricultural and Collection Practice

Tsumura GACP Guidelines

Tsumura Crude Drug GACP Guidelines

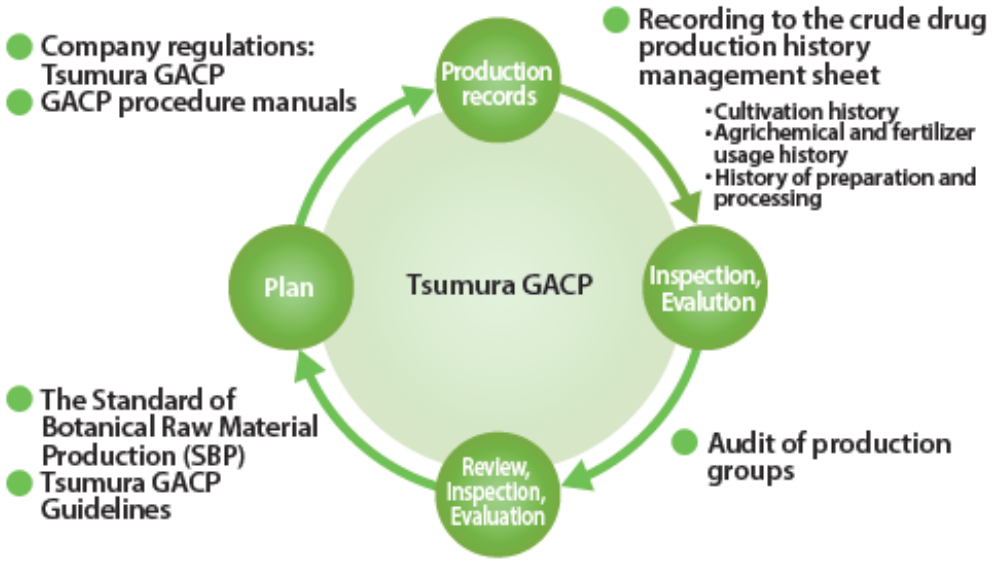
Tsumura's own guidelines
which satisfies the GACP guidelines by WHO

The Standard of Botanical Raw Material Production	Crude Drug Traceability

Education, Audit, Certification

- Education and audit to adequately operate with the "Tsumura Crude Drug GACP"
- Issuance of the "Tsumura Crude Drug GACP Certificate"

PDCA Cycle in the GACP



source: Tsumura INTEGRATED REPORT 2023

Furthermore, the FDA requires the following:

- ✓ Develop a DNA testing method to confirm original (source) plants **Scientific**
- ✓ Identify specific compounds from among plant species, and quantify as a management indicator **Specific**
- ✓ Select and fix focus on several crude drug production areas that are geographically adjacent
  → Conduct a comprehensive physical chemistry examination of each crude drug lot, acquire crude drug quality in set production areas over a 3-5 year period, and geographically manage over time the quality originating from each production area

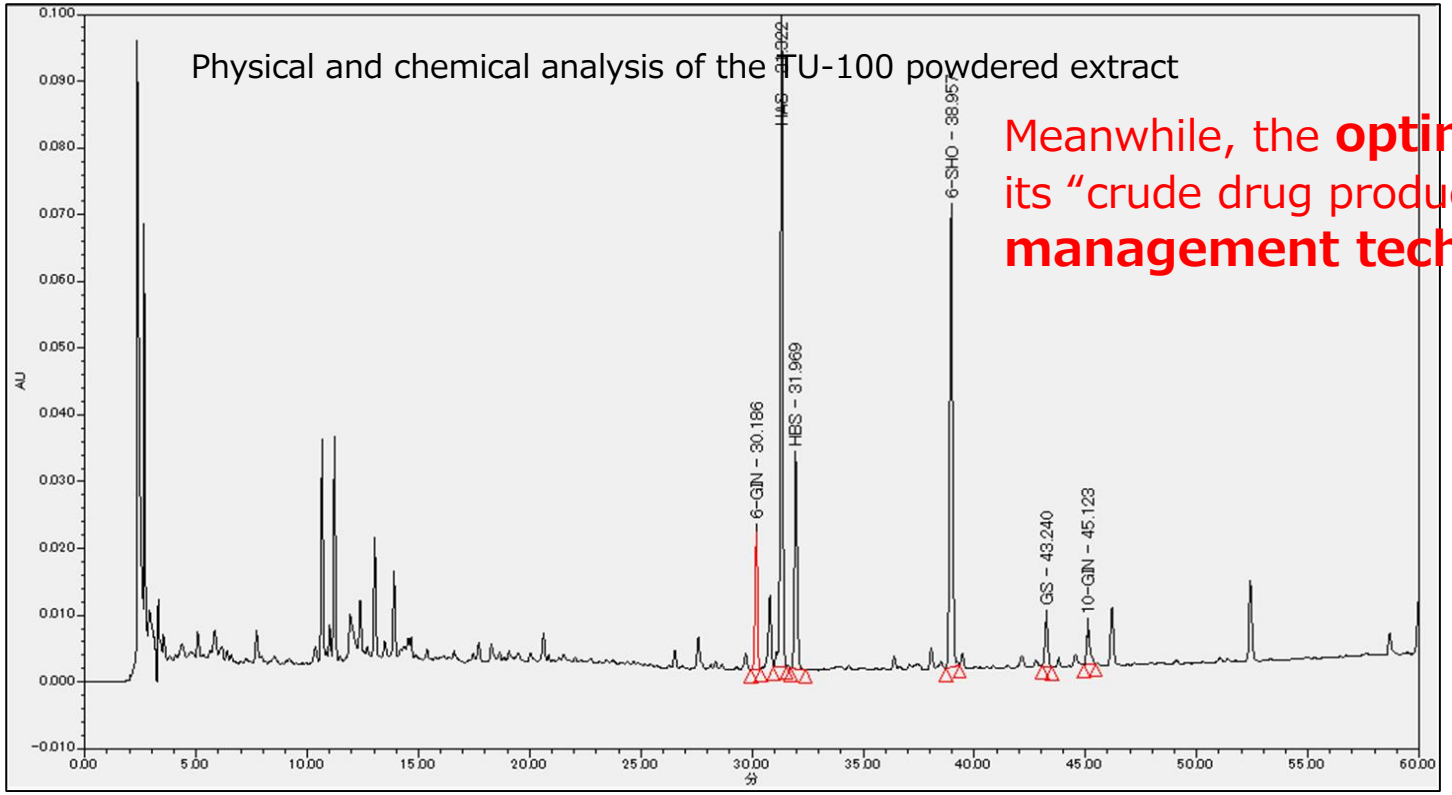
Stable supply of uniform crude drugs

2-8. Development Requirements for Botanical Medicines (Products) Sought by the US FDA: CMC development

Features of botanical medicines: Variations between lots inevitable

- Multi-components (mix of diverse compounds)
- Extremely difficult to identify all substance levels
- Differences between lots, including variety of raw material plants, cultivation areas, harvest years, weather and agricultural methods

CMC: Chemistry, Manufacturing and Control



Meanwhile, the **optimal strength** of Tsumura is its “crude drug production control/**lot management technology**”

The assessment of the validity of the width in variation is determined by making a comparison with the results of clinical trials and bioassay trials

2-9. Obtained Results and Ripple Effect owing to US Development of TU-100 ❶

Results	Ripple effect
1. Clinical trial on safety/efficacy	Acquire evidence for TU-100 and deepen understanding of pharmacology
2. Intestinal bacteria research	Accumulate knowhow for intestinal bacteria research
3. Human blood pharmacokinetics	Pioneer of the same trial method for plant extraction formulations. → Enhance package insert
4. Survey on frequency of side-effects	Quantify safety data for Kampo medicine owing to a scale of data consisting of 3,000 cases
5. Build a crude drug reference database	Establish a method for a raw material crude drug lot comparison and management using a principal component analysis
6. Systemize the quality control method in accordance with global standards	Implement PIC/S GMP andGACP in Kampo manufacturing

Expand/apply to other Kampo medicines

Improve the quality of Kampo medicine

PIC/S : Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme.
GMP: Good Manufacturing Practice. Standards related to manufacturing management and quality control GACP: Good Agricultural and Collection Practices.

2-10. Results Obtained from the US Development of TU-100❷

Build up evidence for TU-100
Accumulate pharmaceutical development knowhow

- Clinical trial on safety/efficacy
- Intestinal bacteria research
- Human pharmacokinetics trial
- Survey on frequency of side-effects
- Build a crude drug reference database
- Systemize the quality control method in accordance with global standards

Results

TSUMURA VISION
Realize “Cho-WA” 2031

[PHC] Personalized Health Care
[PDS] Pre-symptomatic Disease and Science
[PAD] Potential-Abilities Development

Positive results for the Kampo industry overall

Realize the recommendations of the “Study Group on the Future Vision for Kampo—Responsibility for People’s Health and Healthcare” (Section 5)

Recommendation 5: Promote the overseas deployment of Kampo formulations

＋

Recommendation 1: Necessity of Kampo formulations in medicine
Recommendation 2: Promote research with respect to Kampo formulations, etc.

PHC : Personalized Health Care, PDS : Pre-symptomatic Disease and Science, PAD : Potential-Abilities Development

THE BEST OF NATURE AND SCIENCE

Chapter 3
Outlook Going Forward

3-1. Short-Term Plan

- Analysis of TU-100 clinical trial data (summer)
- Address FDA inquiries on the CMC※1 development strategy
- Propose alliance activity policy

Reset the master schedule for TU-100 US development
Development activities for Phase III trial※2

※1 CMC: Chemistry, Manufacturing and Control

※2 Assuming success of late stage PII clinical trial

Inquires about these materials

Corporate Communications Dept.

Investor Relations Group

investor_madoguchi@mail.tsumura.co.jp

Cautionary items regarding forecasts

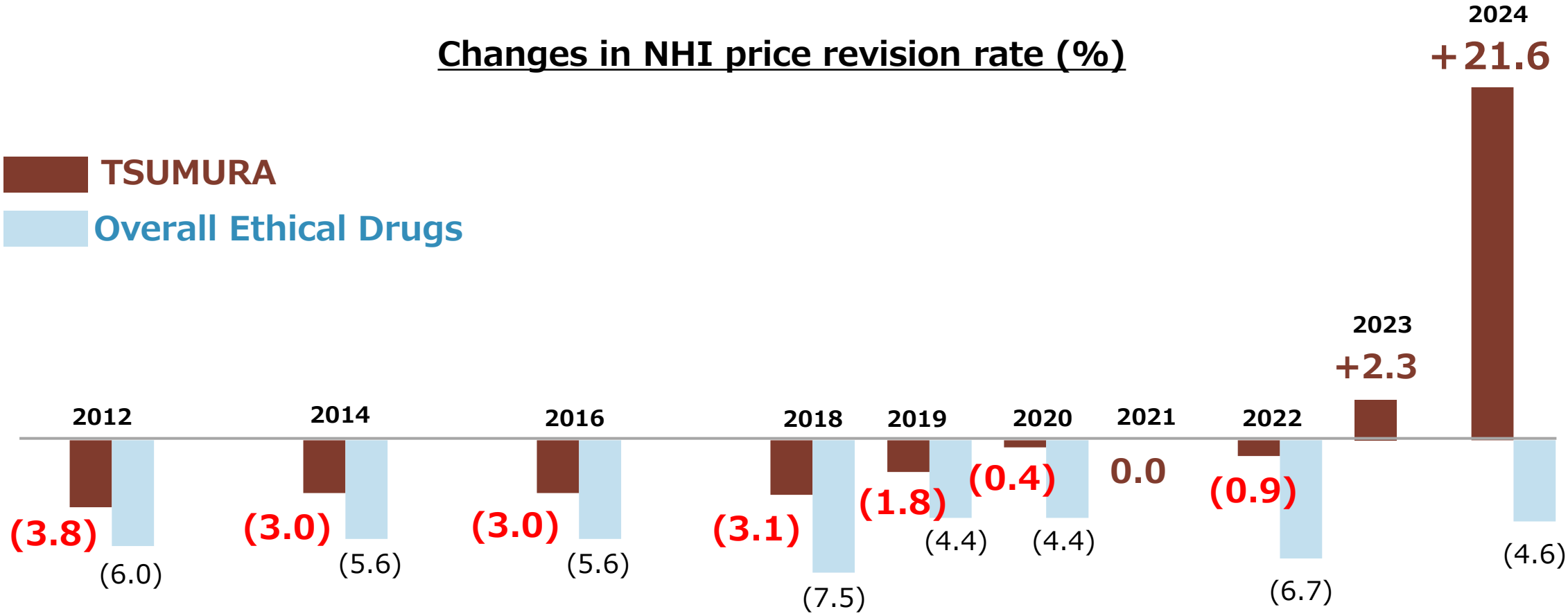
- The materials and information provided in this presentation contain so-called forward-looking statements. Readers should be aware that the realization of these statements can be affected by a variety of risks and uncertainties and that actual results could differ significantly.
- Changes in Japan or other foreign countries related to healthcare insurance systems or regulations set by medical treatment authorities on drug prices or other aspects of healthcare or in interest and foreign exchange rates could negatively impact the Company’s performance or financial position.
- In the unlikely event that sales of the Company’s core products currently on the market be halted or should sales substantially decline due to a defect, unforeseen side effect or some other factor, there could be a major impact on the Company’s performance or financial position.

THE BEST OF NATURE AND SCIENCE

Appendix

Domestic Business: NHI Price Revision Ratio

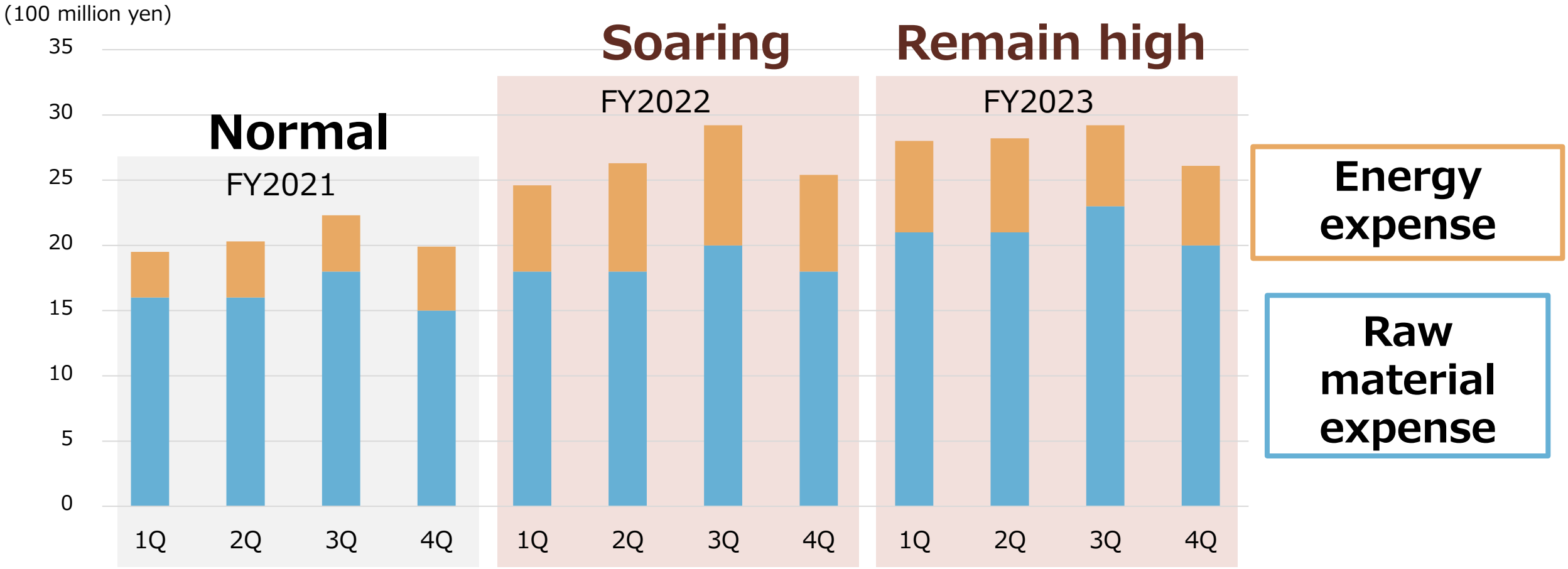
In the NHI price revision in FY2024, 66 prescriptions will be subject to re-calculation of unprofitable products, with a weighted average increase of +21.6%.



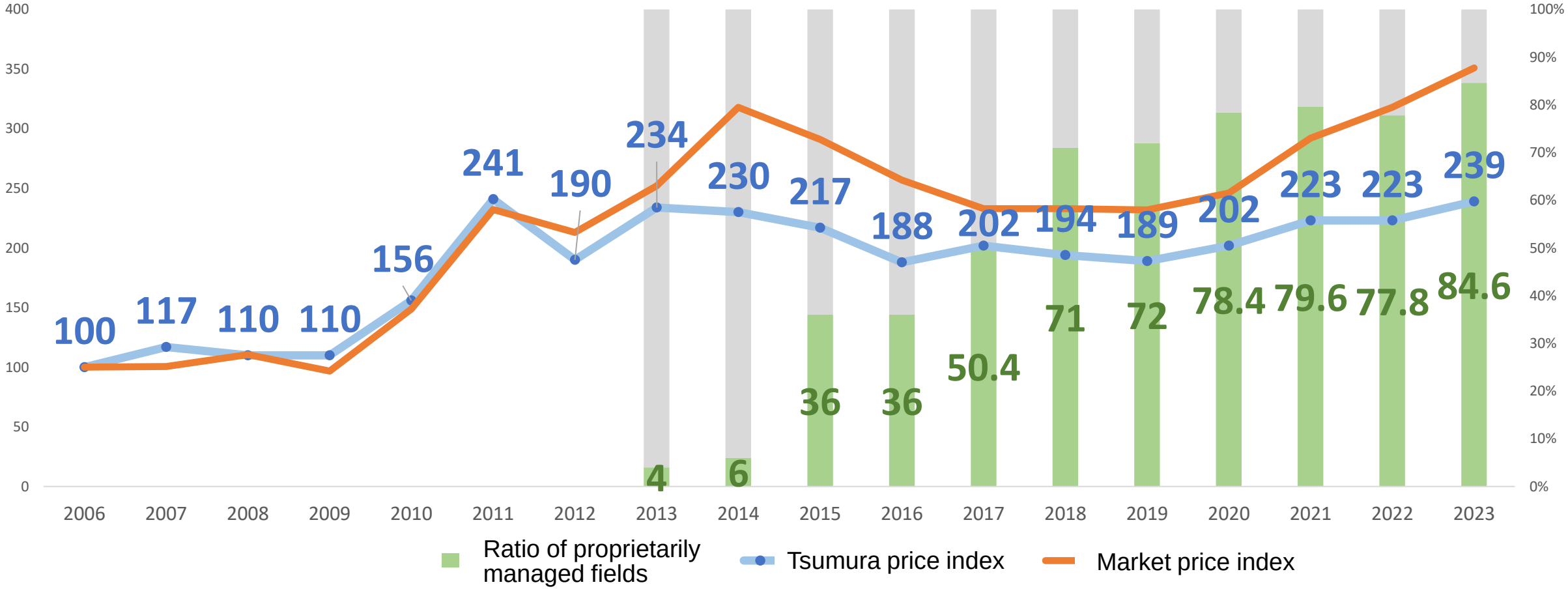
Revision rates for 2021 and 2023 are not disclosed because they are mid-year revisions.

Raw Material & Energy Expense Trends

Expense for raw materials used in the manufacturing of Kampo formulations and energy remain high level



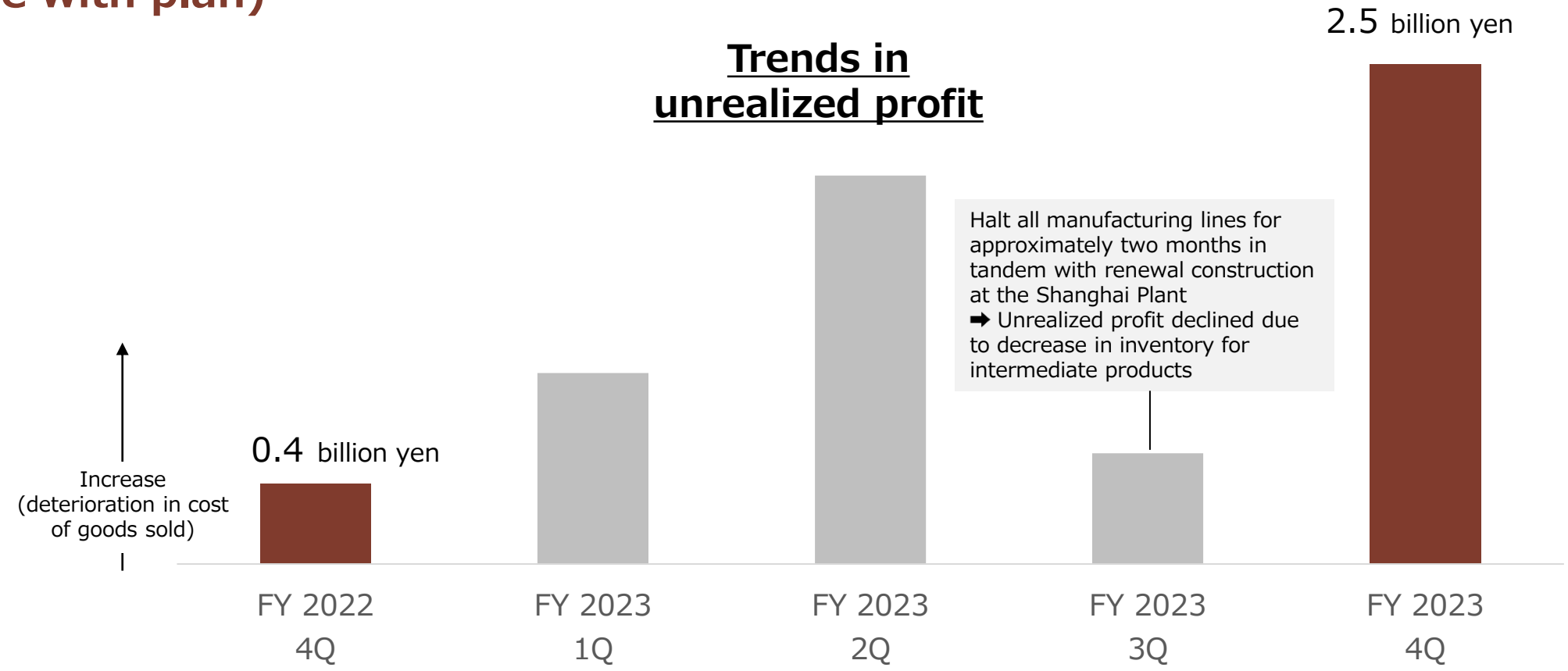
Crude Drug Procurement Costs:
Procurement Price Index of Raw Raw Crude Drugs from China



*1 Tsumura price index: Average weighted price based on the amount used by the Tsumura Group (2006 indexed at 100)
*2 Proprietarily managed fields: Direct guidance by the Tsumura Group on cultivation can be performed, making it possible to grasp costs incurred during cultivation and set prices based on this. In the medium and long term, in comparison with the market, it will be possible to realize superior and stable procurement of high quality and high value crude drugs.

Crude drug procurement cost: Trends in unrealized profit

Resume operation of a portion of manufacturing lines at the Shanghai Plant, which was shut down for renewal construction, and increase unrealized profit owing to a recovery in the inventory for intermediate products in line with the start of shipments of powdered extract from the Tianjin Plant which acquired a license (in line with plan)



Domestic Business: Increase in production capacity

- In fiscal 2024, we will increase production capacity through full operation of the first phase in Tianjin and completion of the renewal of the Shanghai plant.
- Promote construction and early operation of the 2nd and 3rd phases in Tianjin