SHIONOGI & CO., LTD.

Third Medium-Term Business Plan

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SHIONOGI & CO., LTD.
President and Representative Director
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Forward-Looking Statements

- This presentation contains forward-looking statements. These statements are based on expectations in light of the information currently available, assumptions that are subject to risks and uncertainties which could cause actual results to differ materially from these statements.
- Risks and uncertainties include general domestic and international economic conditions such as general industry and market conditions, and changes of interest rate and currency exchange rate. These risks and uncertainties particularly apply with respect to product-related forward-looking statements. Product risks and uncertainties include, but are not limited to, completion and discontinuation of clinical trials; obtaining regulatory approvals; claims and concerns about product safety and efficacy; technological advances; adverse outcome of important litigation; domestic and foreign healthcare reforms and changes of laws and regulations. Also for existing products, there are manufacturing and marketing risks, which include, but are not limited to, inability to build production capacity to meet demand, unavailability of raw materials and entry of competitive products.
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- This material contains information on pharmaceuticals (including compounds under development), but this information is not intended to make any representations or advertisements regarding the efficacy or effectiveness of these preparations nor provide medical advice of any kinds.

Agenda

- Review of the 2nd medium-term business plan
- Overview of the 3rd medium-term business plan
  - Vision
  - Basic strategies
    - Steady growth mainly through enriched pipeline
    - Investments in the new growth drivers
    - Therapeutic areas to be focused on
  - Enhancement plans for each value chain component
- Financial goals

Review of the 2nd Medium-Term Business Plan

Status on the Achievements of the 2nd Medium-Term Business Plan

S·O·N·G for you!

Energizing R&D

- Pipeline
  - Selected 17 DCS compounds and advanced 9 compounds to FTIH
  - Advanced 7 compounds to Phase II and beyond (more than target of 5 compounds)
- Build-up of target therapeutic areas
  - In addition to strong expertise in infectious disease, strengthened metabolic syndrome and pain areas
  - Grown to the level where able to enrich pipeline
- Aggressive alliance
  - Achieved remarkable solid results for anti-HIV drug by co-development with GSK
  - Facilitated collaborative research with Purdue Pharma L.P. and created new DCSs in pain area
  - Established Shionogi Innovation Center in Hokkaido University campus
  - Launched collaborative industry-academia initiatives for discovering drug seeds (FINDS, FLASH):

DCS: Drug candidate selection
FTIH: First trial in human
FINDS: PHarma-INnovation Discovery competition Shionogi
FLASH: PHarma-Link between Academia and SHionogi

Status on the Achievements of the 2nd Medium-Term Business Plan

SONG for you!

Beefing up domestic sales

- Maximized the value of Crestor
  - Grown to be the core product with net sales of 23 billion yen
- Continuously launched new products
  - Launched 11 products in Japan

Steady overseas business development

- Established sales network in the USA through acquisition of Sciele Pharma, Inc.
  - Launched new 3 products in FY2009
  - Changed the name to “Shionogi Pharma, Inc.” (SPI)
- Expanded export of antibiotics to Europe, USA and Asia
  - Prospect in FY2009: 8.6 billion yen (about 4 times compared to FY2004)
- Strengthened capacity/capability of Shionogi USA. Inc. by investing in talent

Assignments Not Achieved during the 2nd Medium-Term Business Plan

- Company-wide
  - Royalty-dependent to non-dependent business structure
  - Expansion of overseas sales network and development of globally competent human resources
- Research
  - Enhancement of drug seed discovery and early phase research programs
  - Improvement of predictive performance for clinical efficacy
- Development
  - Emphasis on the differentiation strategy and enhancement of product evaluation capability
  - Quick strategic planning and decision making for global development
- Manufacturing
  - Continuing emphasis on quality improvement
- Domestic sales
  - Achievement of net sales goal and reduction of the selling expense
- Indirect department
  - Reduction in general administrative expense

Overview of the 3rd Medium-Term Business Plan

New image Shionogi aims for during the 3rd medium-term business plan

SONG for the Real Growth

***S**peed*

Quick decision and implementation

***O**pen Mind*

Flexible mind and out of box thinking

***N**ever-Failing Passion*

Persistent passion

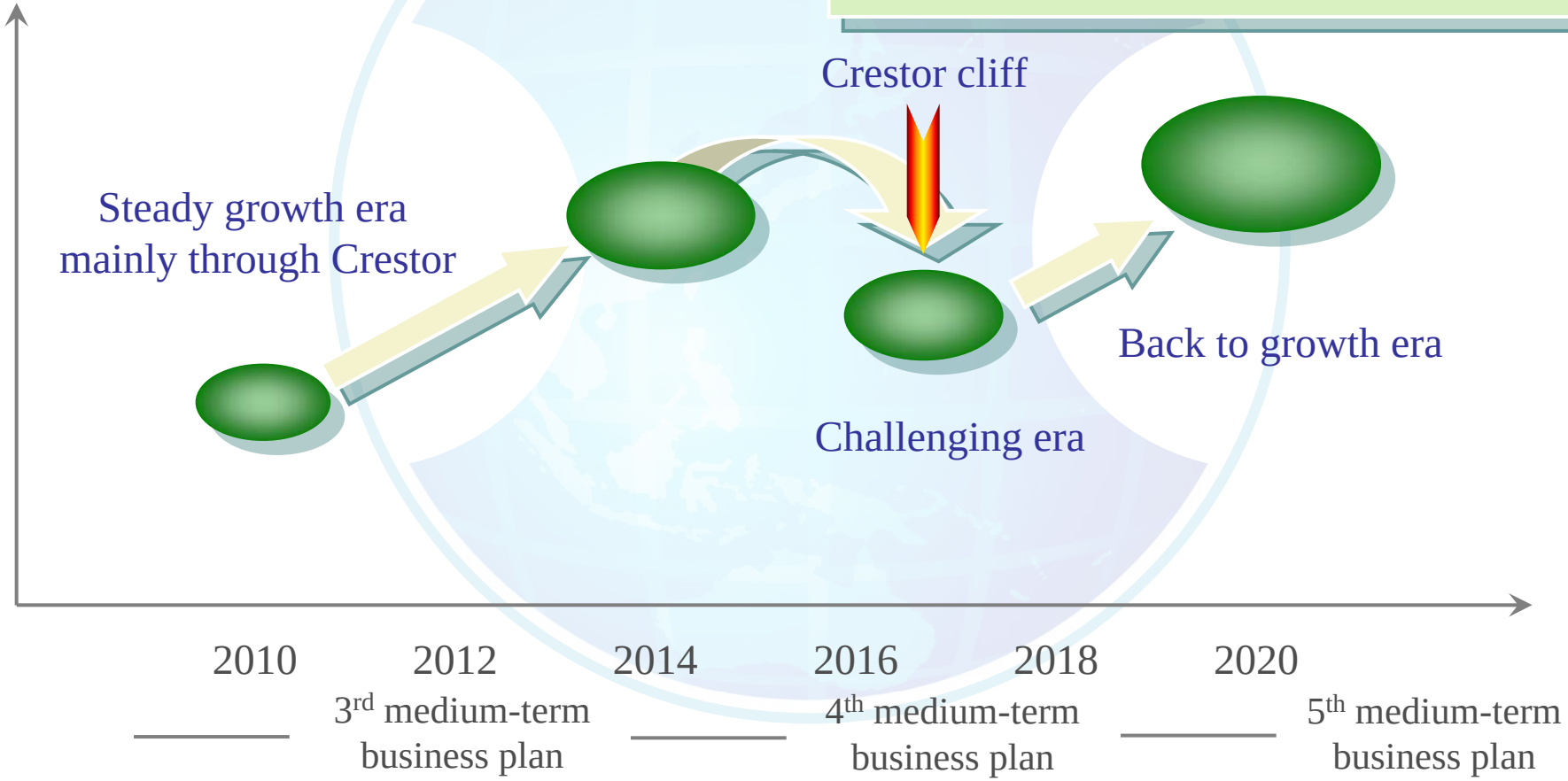
***G**lobal Perspective*

Higher and broader perspective

Shionogi Mid and Long-Term Vision

Goals for
the next 10 years

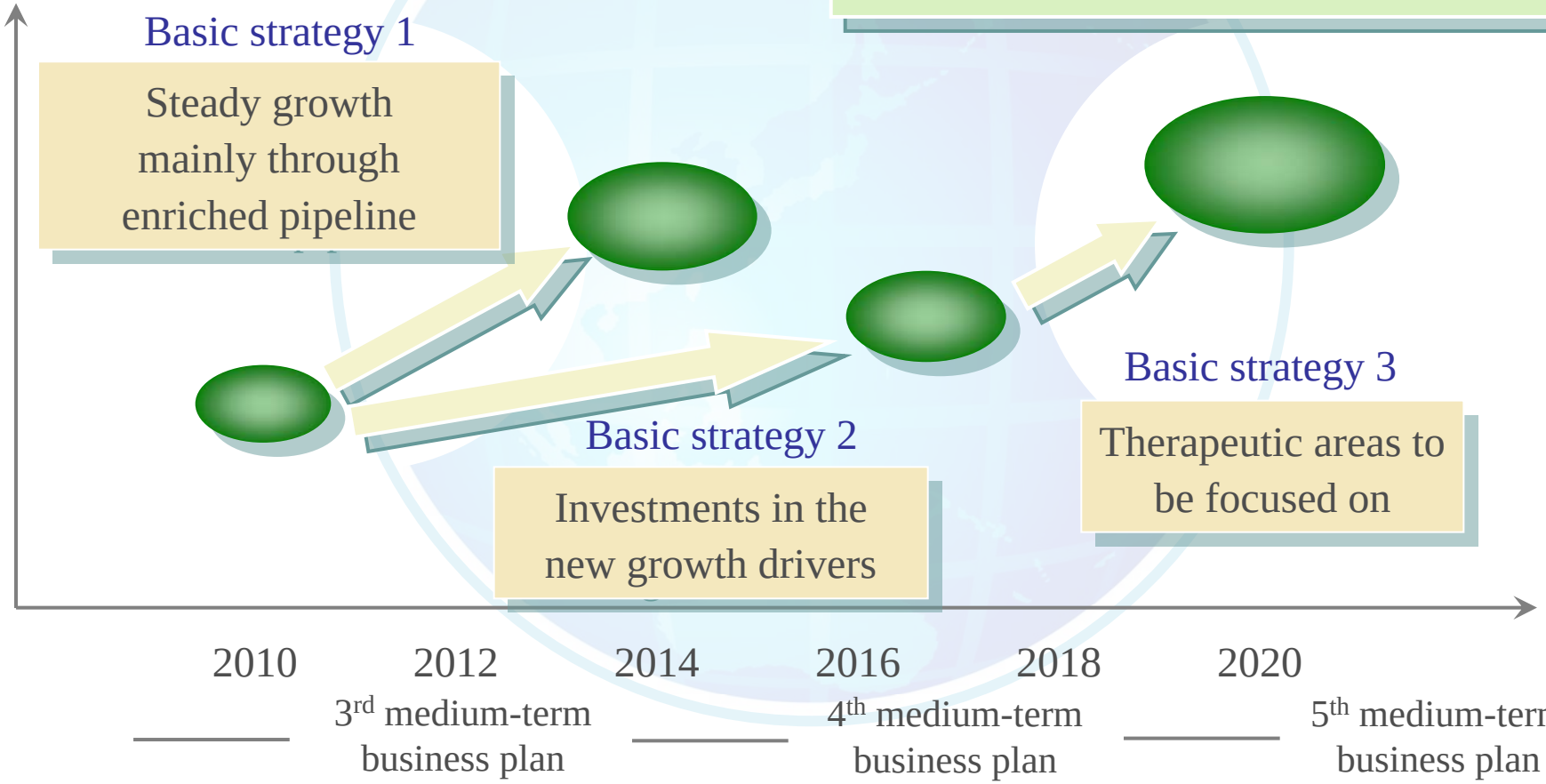
Consolidated net sales: 600 billion yen
Operating margin: More than 25%
Overseas net sales ratio: More than 50%



Basic Strategy in the 3rd Medium-Term Business Plan

Goals for
the next 10 years

Consolidated net sales: 600 billion yen
Operating margin: More than 25%
Overseas net sales ratio: More than 50%



Basic Strategy 1

Steady Growth Mainly through Enriched Pipeline

Realize Positive Revenue Spiral through "New Drugs"

Introduction of the new drug pricing policy, "The premium pricing for the development of new drugs and elimination of off-label drug use"

Generate revenue by launching excellent new drugs to the clinical practice

Invest in the new drug development of the next generation

Conversion of revenue structure ⇒ Establish robust revenue foundation independent from the "Legacy products"

8 new products at the beginning of the 3rd medium-term business plan

Crestor Irbetan Cymbalta	Pirespa, Differin Rapiacta, Finibax Oxycontin/Oxinorm

Realize steady growth by expanding sales of 8 new products

Maximize the Value of Globally-Proven Products

Position the following 3 products as the key strategic product among 8 new products

Crestor, Irbetan, Cymbalta

Net sales target: Total 100 billion yen with 3 products

- Crestor
  - Based on the sufficient evidence, establish a position as “The strongest statin in history” and “The statin that promotes efficient plaque regression”
- Irbetan
  - Build presence in the metabolic syndrome area based on its potent antihypertensive effect
  - Expand sales based on the sufficient evidence interrelating among brain, heart and kidney
- Cymbalta
  - Aim to position Cymbalta as the drug that will best help patients suffering from depression
  - Expand indication to diabetic neuropathic pain

Global Growth of Crestor

SONG for you!

A challenge for No. 1 in domestic market

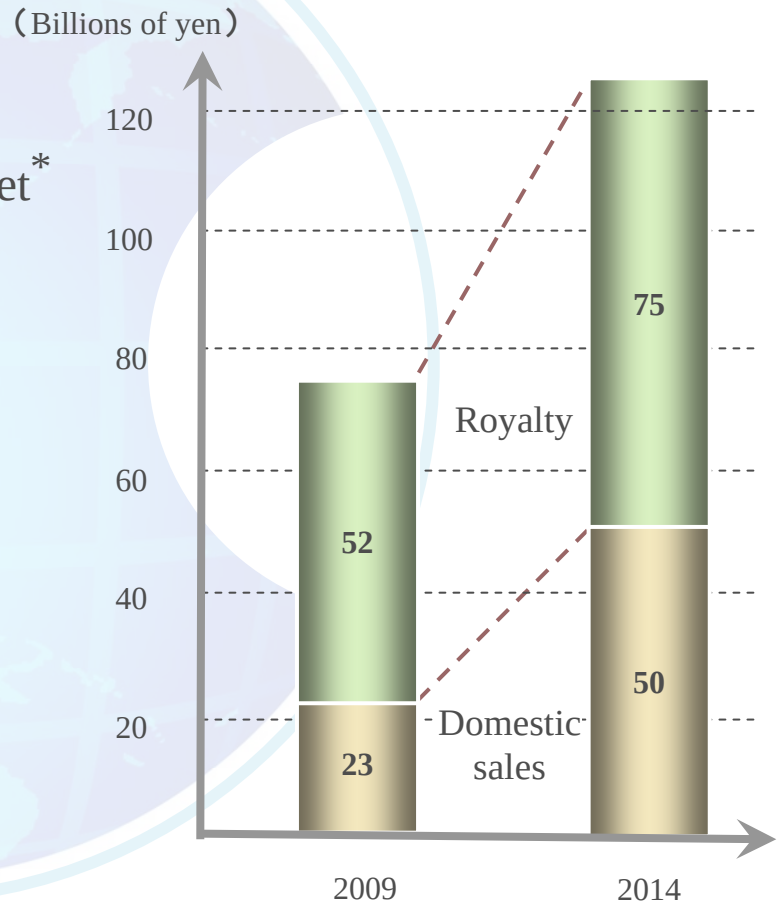
Continue high-quality collaboration with AZ

- FY2011 Establish top share in statin market*
- FY2014 Net sales target: 50 billion yen

Increase in royalty revenue

Further sales expansion by AZ through collaboration with Abbott

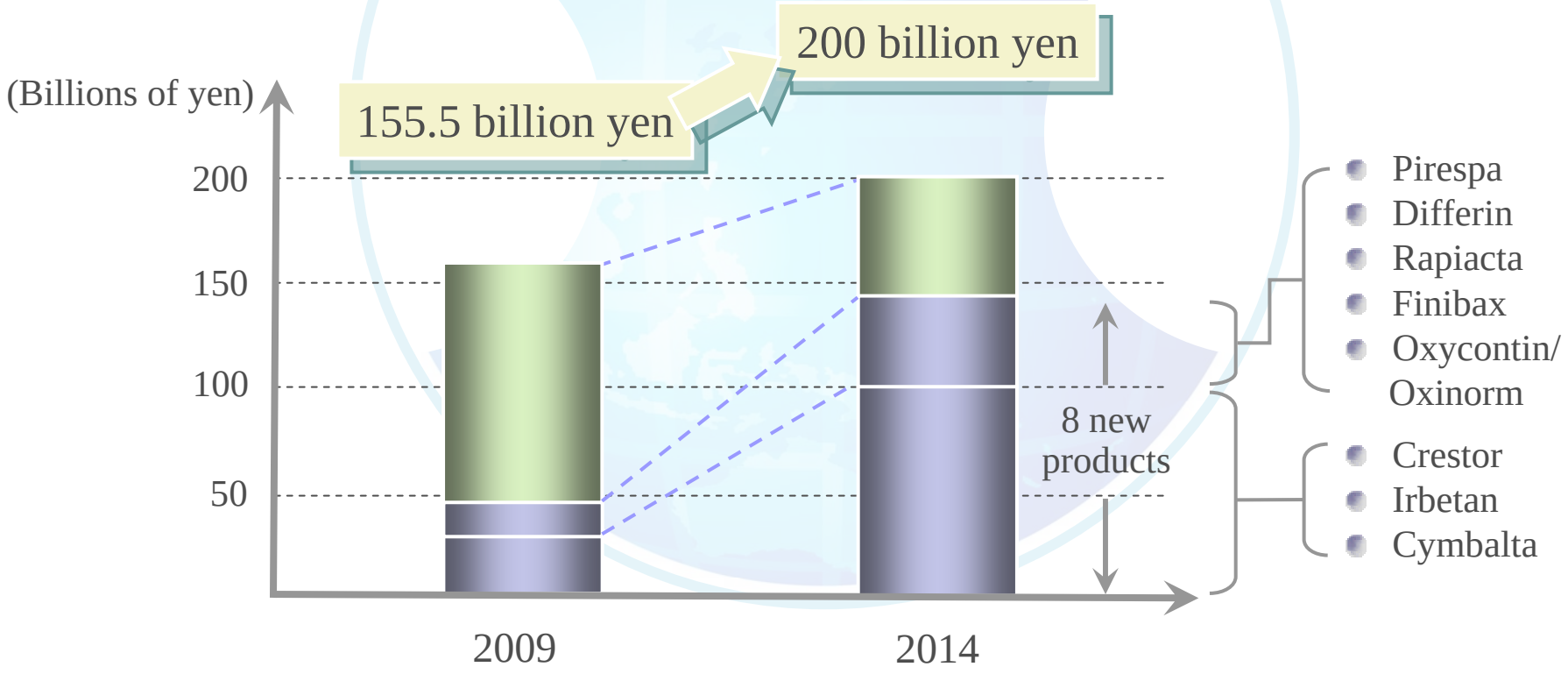
FY2014 forecast: More than 75 billion yen



*: prescription base, brand total

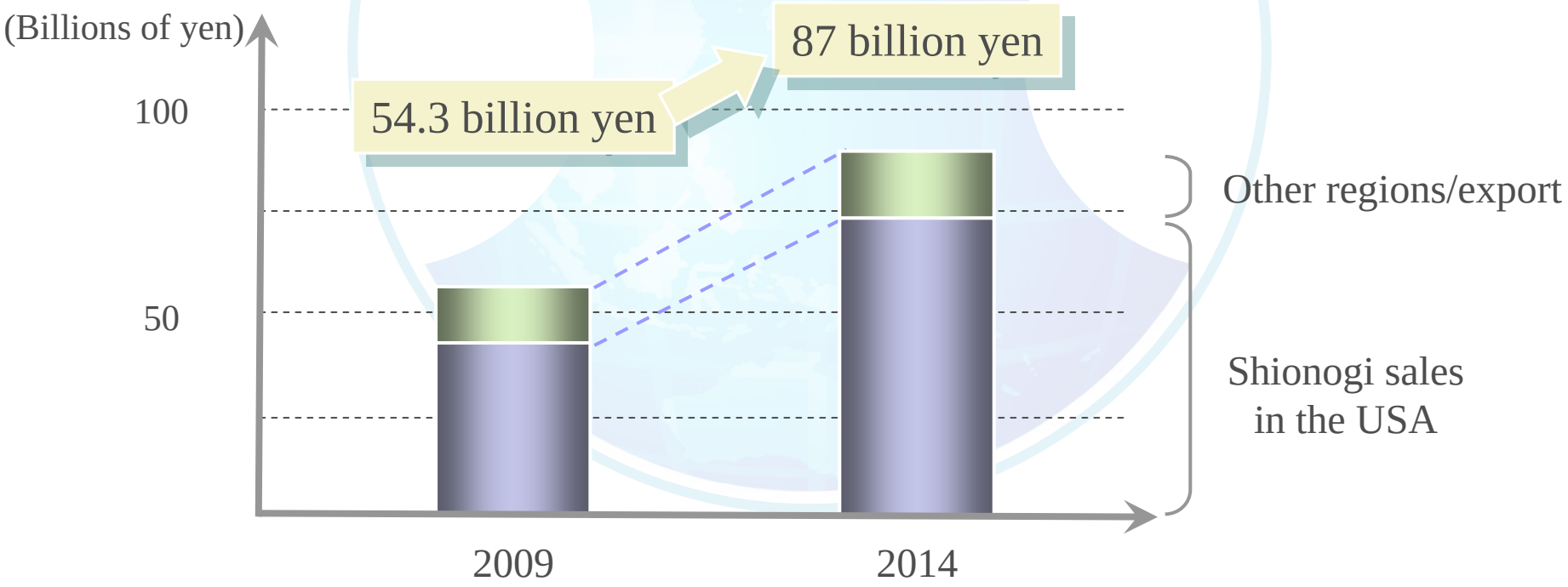
Domestic Sales Forecast

- Net sales target: 200 billion yen
  - 25% increase compared with FY2009
- More than 70% of net sales generated by 8 new products
  - From legacy product dependent to newer product dependent growth



Overseas Sales Forecast

- Net sales target for marketed and products in development: 87 billion yen ($1=90 yen)
  - Exclude additional sales through strategic business development deals
- Expand consolidated overseas net sales ratio excluding royalty to approximately 30%
  - FY2009: 24% ⇒ FY2014: 29%



Basic strategy 2

Investments in the New Growth Drivers

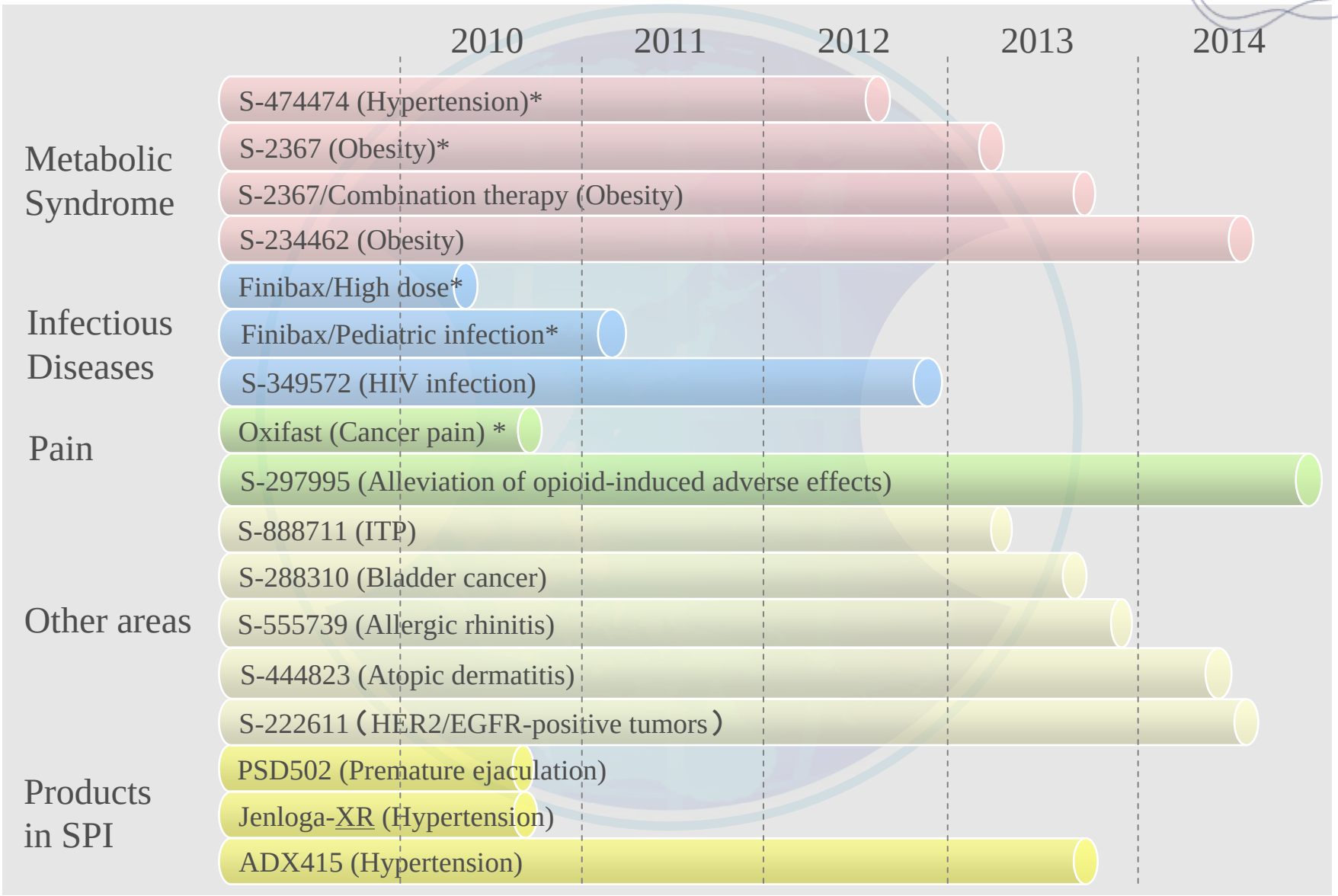
Portfolio Management of Development Products and Numerical Targets

- Persistence with portfolio management of development products
  - Reassess the potentials of all development products every 6 months
  - Reassess the investment allocation for each product and focus strategically on the priority products
- Contingency Plan
  - Back-up strategy
    - Create seamlessly back-up/follow-up compounds
    - Promote rapid decision-making and enhance flexibility in resource allocation
  - In-license strategies
    - Prioritize late-stage development products in the target areas
    - Assume Shionogi direct sales overseas
    - Strengthen business development activities by integrating Japan and US business development

Numerical target for the 3rd medium-term business plan

- Globally develop more than 5 products in the late stage (Ph 2b and beyond)
- Achieve NDA submission overseas for 4 products (originate from Shionogi or Japanese research institutes), and launch of more than one product by FY2014

Schedule for NDA Submission in Each Therapeutic Areas



ITP: Immune thrombocytopenia , * Domestic clinical development

Core Development Products: S-349572

- Anti-HIV drug
  - Integrase inhibitor expected to demonstrate high therapeutic efficacy
  - Good in vitro resistance profile, including low cross resistance and higher genetic barrier to resistance compared with first generation integrase inhibitors
  - Good pharmacokinetic profile exerting sufficient efficacy with once daily oral administration
  - Low risk of drug-drug interaction and good safety profile
- Aim to develop as the drug with wide therapeutic indication for treatment-naïve, treatment-experienced but integrase-naïve, and integrase-resistant patients
  - HIV patients worldwide: 33.4 million
  - HIV patients in major countries: 1.8 million
  - Market forecast of anti-HIV drugs in major countries (in 2017): $15.3 billion
- Schedule
  - FY2010: Initiation of Phase 3 study

Core Development Products: S-2367/S-234462

- Anti-obesity drug
  - Receptor antagonist for Neuropeptide Y Y5, new target
  - Weight reduction met the criteria in the FDA's draft guidance by year-long treatment
  - Showed sustainable weight reduction without rebound and favorable safety profile
  - Developing combination therapy with orlistat to aim stronger weight reduction
  - Developing a follow-up compound (S-234462) possessing more significant anti-obesity activity with mono therapy
- Aim to develop as the first line drug for the treatment of obesity
  - Obese subjects worldwide: 1.6 billion (BMI≧25), 0.4 billion (BMI≧30)
  - Obese subjects in USA: 72 million
  - Morbid obese patients in Japan: 3 million
  - Market forecast of anti-obesity drug in major countries (in 2018): $3-5 billion
- Schedule (S-2367)
  - FY2010: Completion of dosing in Phase 2 study in Japan with mono therapy; Completion of dosing in Phase 2 study in the USA with combination therapy
- Schedule (S-234462)
  - FY2010: Initiation of Phase 2 study in the USA

Core Development Products: S-297995

- Drug for the treatment of opioid-induced gastrointestinal symptoms
  - Orally active peripheral opioid receptor antagonist
  - Showed anti-emetic and anti-constipation effects in the non-clinical studies
  - Not affect on the analgesic effect of opioid
- Has a potential to become an alleviator enable to relief opioid-induced various adverse effects
  - Patients taking opioid analgesic in the USA: 4.7 million
  - Incidence rate of opioid-induced constipation: About 40%
  - Market forecast in major countries of alleviator for the opioid-induced adverse effect (in 2018): More than $6 billion
- Schedule
  - FY2010: Completion of Phase 2a study

Core Development Products: S-444823

- Drug for the treatment of atopic dermatitis (AD), eczema/dermatitis with pruritus
  - Topical cannabinoid receptor agonist
  - Strongly effective on the atopic dermatitis models
  - Demonstrate rapid onset of anti-pruritus effect and good safety profile
- Provide new alternative therapy for the treatment of atopic dermatitis
  - AD and eczema/dermatitis patients with pruritus in the USA: 9 and 33 million
  - AD and eczema/dermatitis patients with pruritus in Japan: 6 and 12 million
  - Market size of topical drugs for AD in the USA: $700 million
  - Market size of topical drugs for AD in Japan: 35 billion yen
- Schedule
  - FY2010: Completion of Phase 2a study

Portfolio Management of Development Products and Numerical Targets

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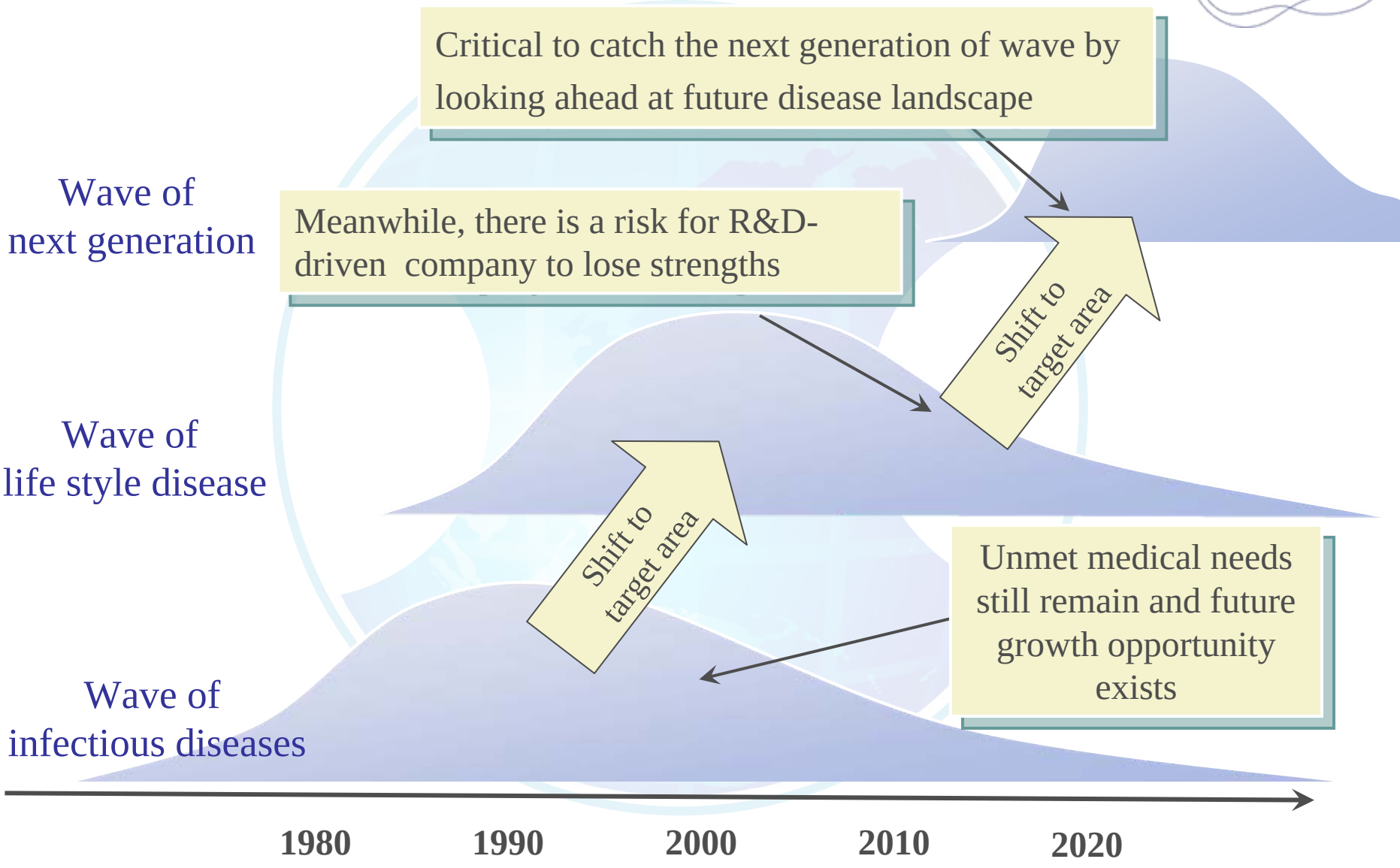
Basic Strategy 3

Therapeutic Areas to Be Focused on

Waves of Diseases Requiring Innovative New Drugs

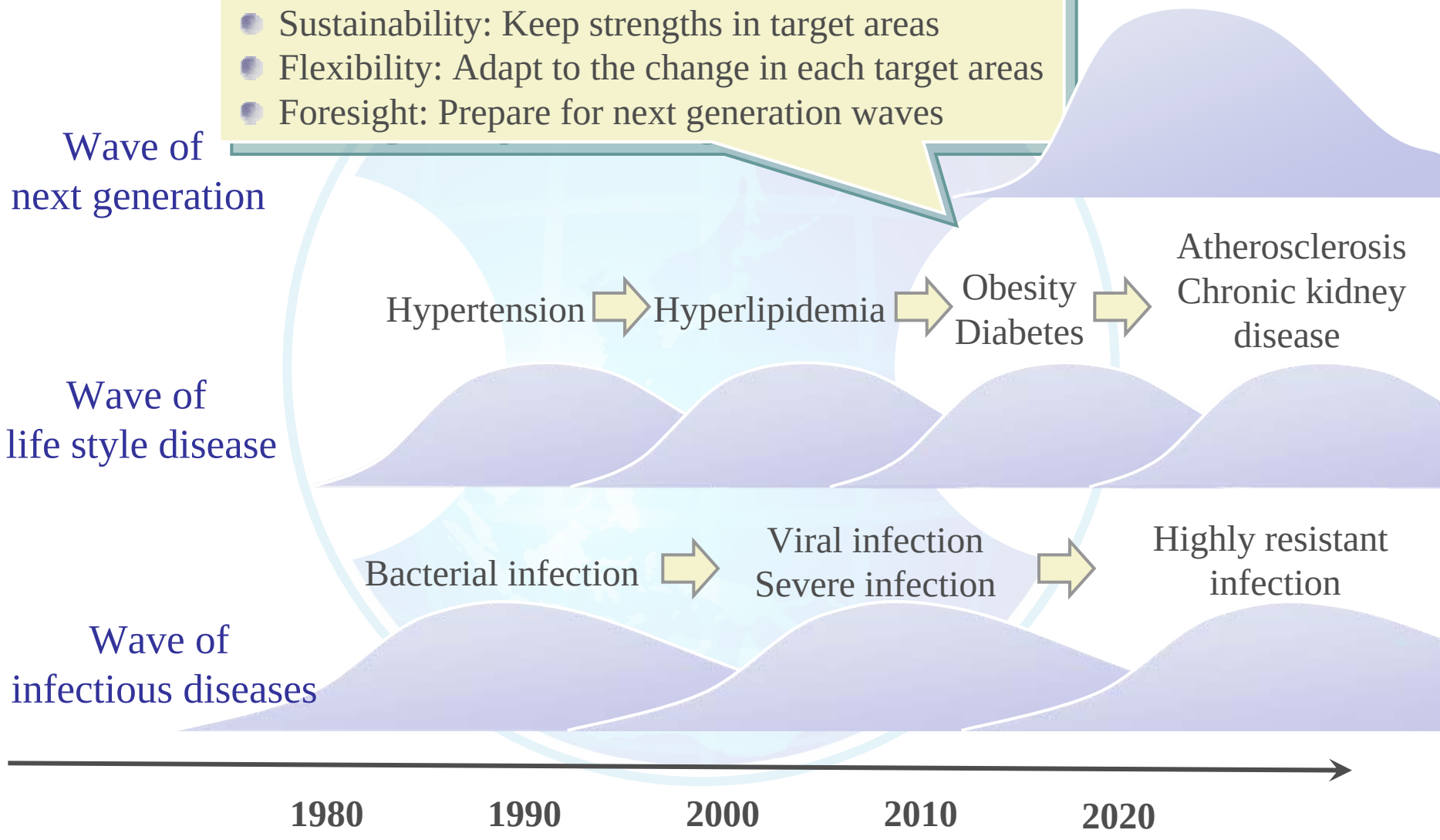


Shionogi Strategy for Targeting Disease Area

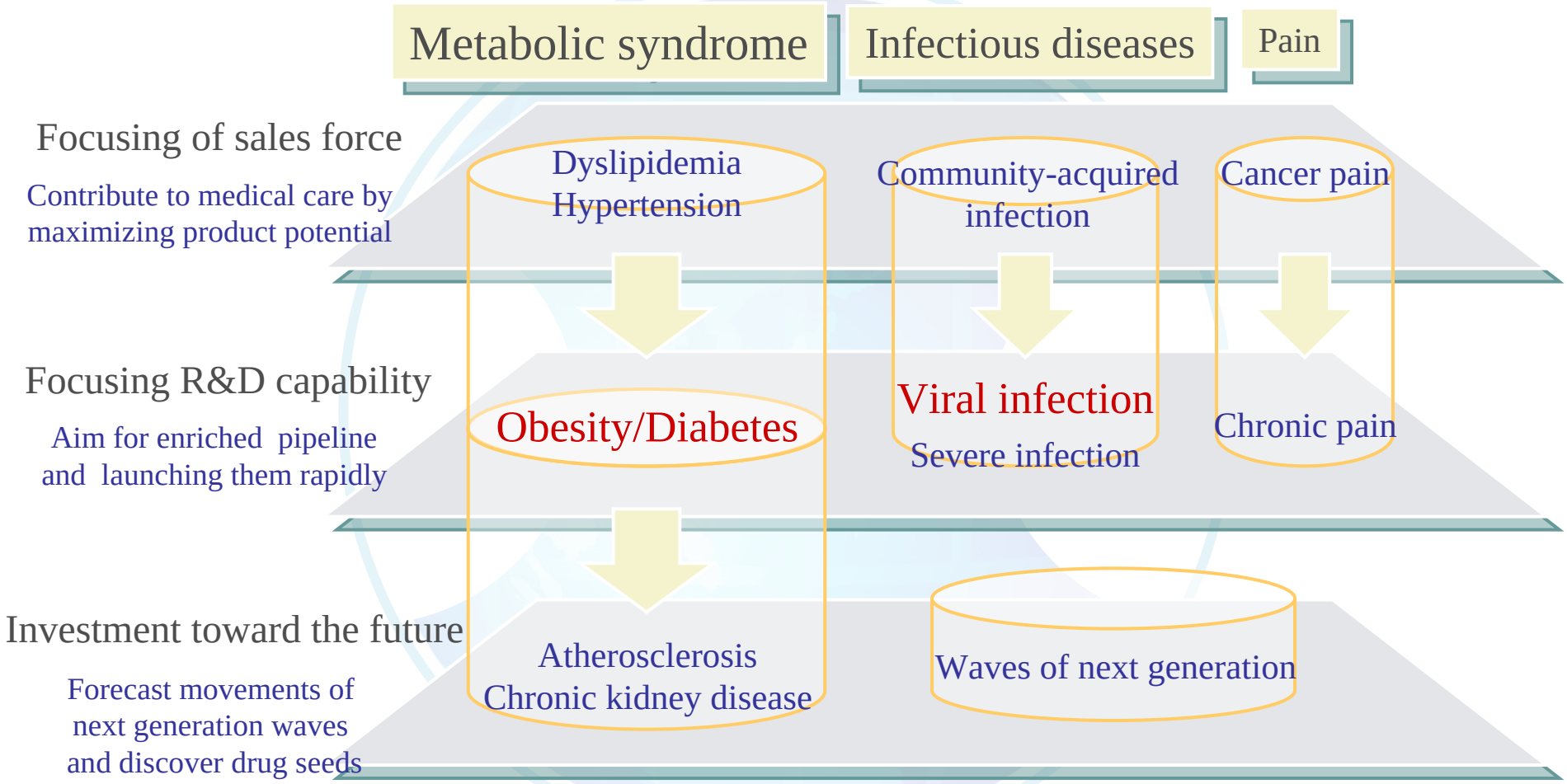
SONG for you!

Embrace multi-layered wave structure

- Sustainability: Keep strengths in target areas
- Flexibility: Adapt to the change in each target areas
- Foresight: Prepare for next generation waves



Therapeutic Areas to Be Focused on



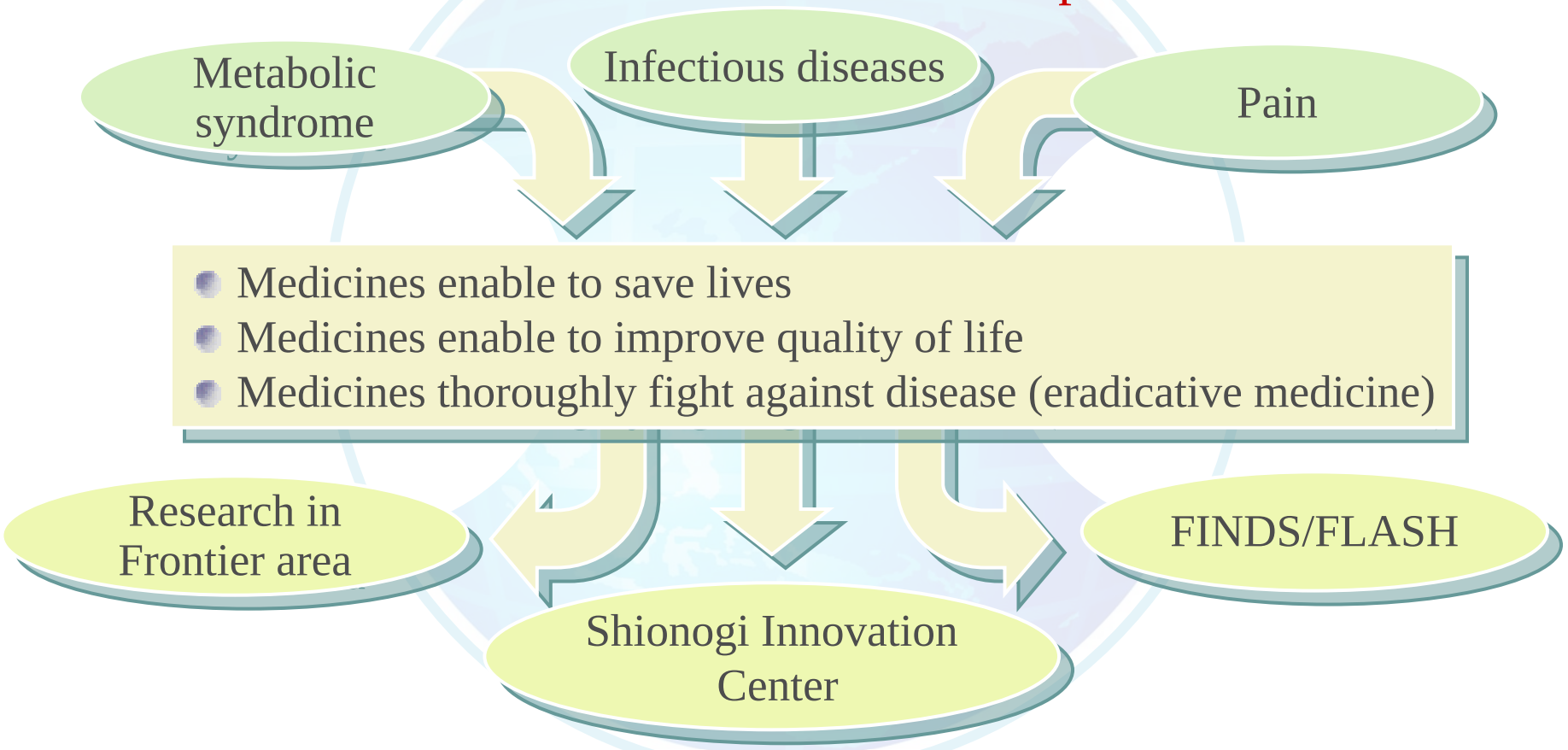
R&D priority areas during the 3rd medium-term business plan are Obesity/Diabetes and Viral infection

Catch the New Wave of Next Generation

SONG for you!

Shionogi's Policy

Provide Medicines of the Best Possible Kind Essential for the Protection of the Health of the People



Always deal with unmet medical needs flexibly and also challenge early research on the new therapeutic areas

Enhancement Plans for Each Value Chain Component

【Research】Goals for the 3rd Medium-Term Business Plan

Our Goal：World Top-Level Research Productivity

- Create NMEs with success rate of 50% or more in POC study
- Select four or more NMEs for DCS per year
  (Aim to establish a system to realize 5 or more DCS in 2015)

Enhancement of early phase research-portfolio

Improvement of predictive performance for clinical efficacy

Centralization of functions and strengthening of flexibility

Points to be strengthened during the 3rd Medium-Term Business Plan

Strengths in Shionogi drug discovery research acquired through the 2nd medium-term business plan

"Highly efficient low molecular SAR-engine"

NME: New molecular entity
SAR: Structure-activity relationship

【Research】Enhancement of Early Phase Research-Portfolio

SONG for you!

Target → Lead selection → SAR optimization → Non-clinical → Ph 1 → Ph 2 → POC

Build Shionogi's own alliance network inimitable by other companies

- Acceleration of in-house and collaborative researches mainly through the Shionogi Innovation Center
- Expansion of FINDS and FLASH
- Expansion of collaborations with megapharma and bioventures, etc.

Take every opportunity while balancing internal research and collaborative research

Execution of global academia-industry alliance network with the British government

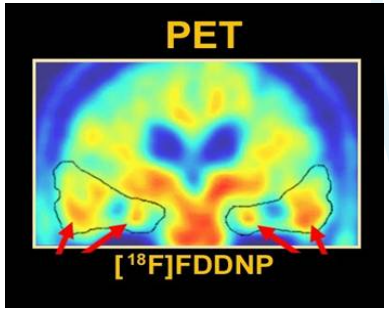
【Research】Improvement of Predictive Performance for Clinical Efficacy

Target → Lead selection → SAR optimization → Non-clinical → Ph 1 → Ph 2 → POC

For the first time in the pharmaceutical industry, make extensive use of the molecular imaging with academia-industry collaboration

Enhancement of collaborative framework with Osaka University on the molecular imaging

- Centralize PET-related researches at Osaka University Medical Molecular Imaging Center
- Accelerate translational research and improve predictive performance for the clinical efficacy



Start up academia-industry joint facility in May 2010

- Set criteria for progressing into clinical stage to achieve world top-level success rate in POC study
- Keep flexibility to revise routinely by updated data-feedback

【Research】Centralize Functions and Strengthen Flexibility

SONG for you!

Target → Lead selection → SAR optimization → Non-clinical → Ph 1 → Ph 2 → POC

Refine drug discovery-engine by enhancing research productivity through centralizing functions

Centralize domestic research facilities at SPRC

- Concentrate research functions into one location
- SPRC has some CMC research functions, and promote seamless development of investigational/commercial manufacturing

SPRC start-up in January 2011

On the other hand, determine not to become “a big fish in a little pond”

- Strengthen accessing capability to the up-dated information
- Develop human resources emphasizing importance to diversity
- Consider establishment of overseas research laboratories

SPRC: Shionogi Pharmaceutical Research Center

【Development】Goals for the 3rd Medium-Term Business Plan

Our Goal: Speed-Up of Global Clinical Development

Decide and carry out quickly---"When, Where, Who, What studies at what cost"

Enhancement of strategic decision making function

Establishment of 3 regional development footholds worldwide

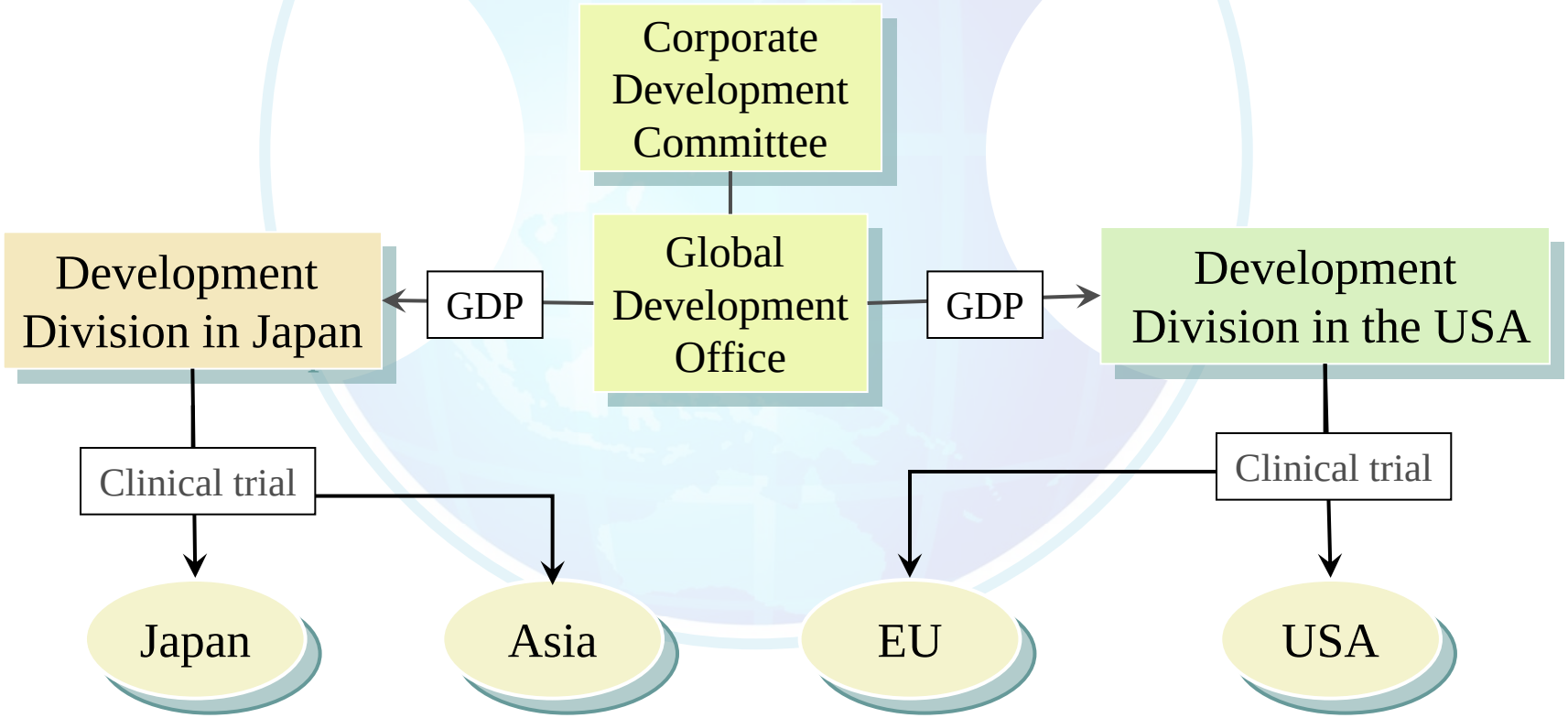
Points to be Strengthened during the 3rd Medium-Term Business Plan

Strengths in Shionogi clinical development capability acquired through the 2nd Medium-Term Business Plan

"High success rate on the domestic clinical development "

【Development】Enhancement of Strategic Decision Making Function

- Establishment of "Global Development Office"
  - Planning of Global Development Plan (GDP) for 3 regions worldwide
  - Include strategic functions such as marketing and medical science
  - Clarify the responsibility by separating strategic planning and operation



【Development】Establishment of 3 Regional Footholds Worldwide

Conduct clinical trials efficiently and quickly by selecting the best region depending on the progress of phase

Early-phase clinical trials
- Regions: Japan, USA, EU
- Objective: Top level efficacy evaluation capability in the pharmaceutical industry (Ability to identify druggability)

Late-phase clinical trials
- Regions: Asia, Eastern EU, South America, South Africa in addition to Japan/USA/EU
- Objective: Speedy drug development

Establish development footholds in EU in addition to Japan and USA, and conduct high-level POM/POC clinical studies, and make a Go/No Go decision in the early stage

Develop large-scale global clinical trials through EU, USA and Asia. Conduct drug clinical development with high-speed and low-cost

【Manufacturing】Guarding Keystone of Shionogi

Centralize β-lactam manufacturing

- Build new drug formulation facility for injectable cephem antibiotics at the Kanegasaki Plant
- Make Settsu Plant β-lactam-free for globalization
- Establish manufacturing system aiming to globally develop the next-generation of cephem antibiotics

Completion of seamless CMC systems

- Go into full-scale operation of D&M formulation facility in Setsu Plant
- Consider to build D&M facility to manufacture late-stage investigational drugs and to set up commercial manufacturing
- Accomplish seamless CMC systems to manufacture API and to develop formulation over from drug discovery to commercial manufacturing

Maintain trust and confidence through Shionogi's product quality

- Set a company policy on the Shionogi products being developed globally
- Improve CMC research level based on the excellent formulation technology
- Maximize the product values through persistent LCM developments

D&M: Development & Manufacturing

【Domestic Sales】Goals for the 3rd Medium-Term Business Plan

SONG for you!

Our Goal：More Than 70% of Total Net Sales from 8 New Products

Achieve total net sales of 100 billion yen with 3 key strategic products
Establish the business foundation by maximizing new products

Persistence with “selection and concentration”

Enhancement of sales productivity

Points to be strengthened during the 3rd medium-term business plan

Strengths in Shionogi sales force acquired through the 2nd medium-term business plan
“Establishment of new franchise area for sales”
(Cardiovascular area)

【Overseas sales】Expansion of Sales Network in the USA

SONG for you!

Our Goal : Convert Business Model of Shionogi Pharma Inc.

Brand-Name Pharma

Specialty Pharma

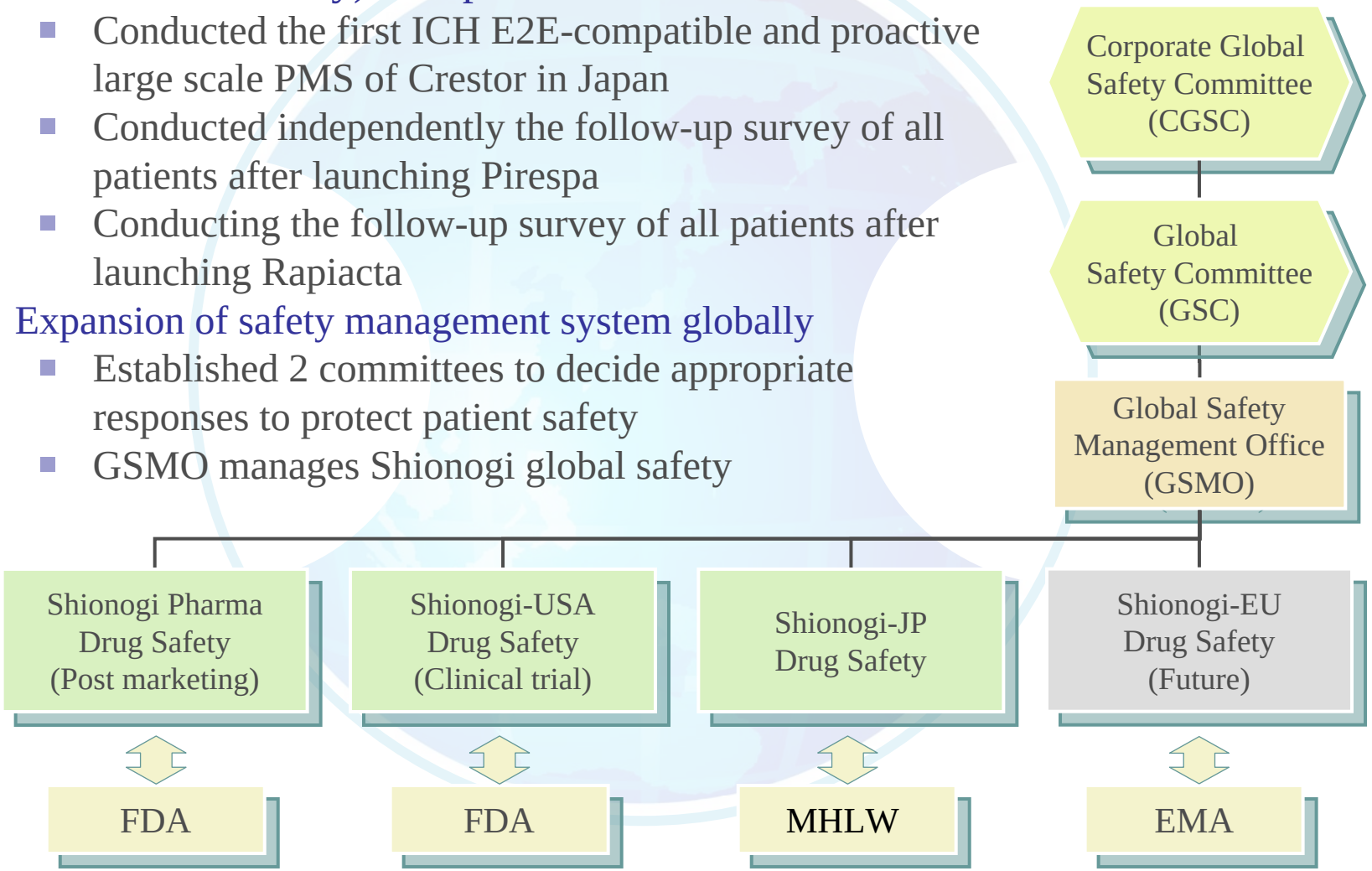
- Company capable of creating new market
- Company capable of maximizing the value of products
- Company capable of fighting in HP market

Goals to be achieved during the 3rd medium-term business plan

- Target 10 to 15% growth per year mainly through marketed products
- Expand sales from PSD502, Ulesfia, Jenloga, Clonicel
- Covert the current business model to sell “Shionogi-brand products”

Establishment of Global Safety Management System

- Achievement of proactive PMS (Post Marketing Surveillance Study) in Japan
  - Conducted the first ICH E2E-compatible and proactive large scale PMS of Crestor in Japan
  - Conducted independently the follow-up survey of all patients after launching Pirespa
  - Conducting the follow-up survey of all patients after launching Rapiacta
- Expansion of safety management system globally
  - Established 2 committees to decide appropriate responses to protect patient safety
  - GSMO manages Shionogi global safety



Corporate Functions Supporting Global Growth

SONG for you!

Corporate functions

- Strengthen global strategic function
- Realize efficient corporate management through promotion of shared service
- Promote small headquarters by cost restructuring

Corporate governance

- Establish a global brand
- Promote high transparency of corporate management by reinforcing disclosure
- Further strengthen speedy operating system

Corporate social responsibility

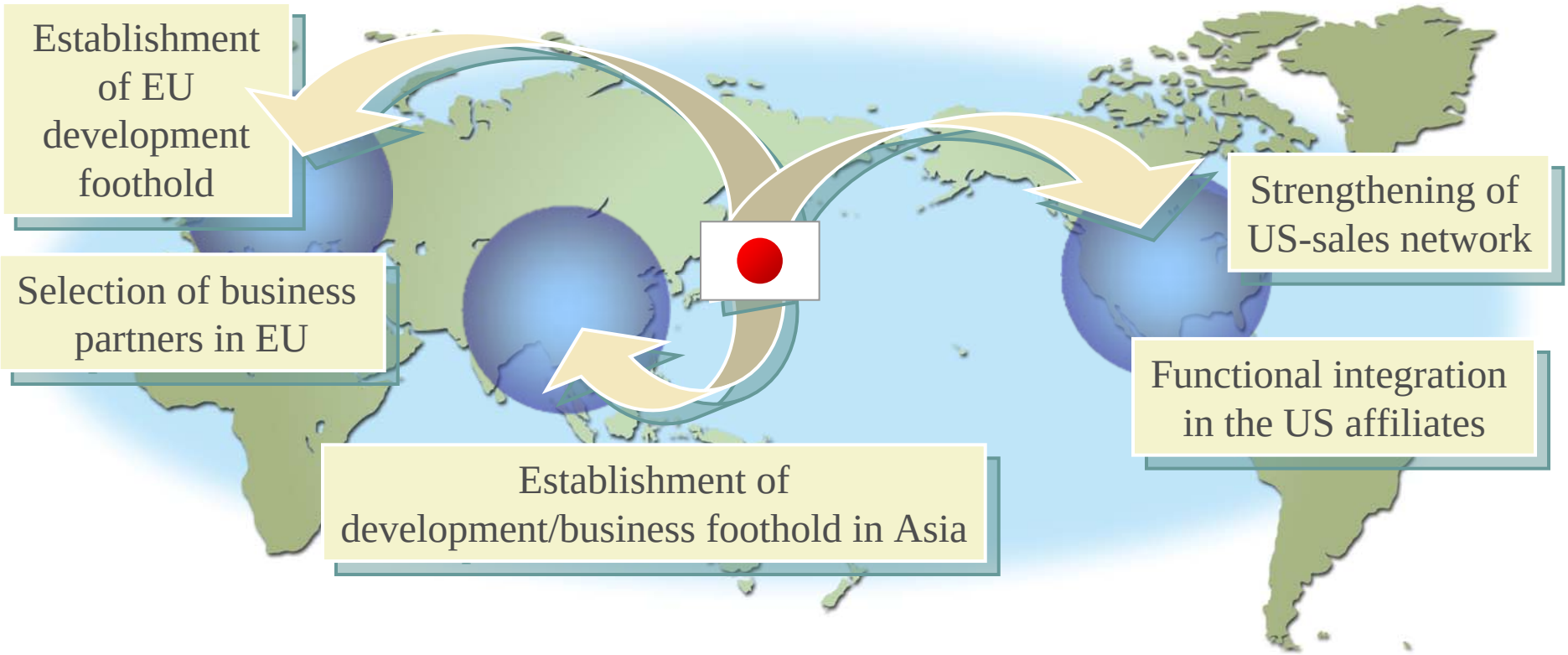
- Promote compliance activities globally
- Promote faithful corporate management for the stakeholders
- Promote EHS activities (Environment/Health/Safety)

Development of human resources capable of supporting globalization of Shionogi's policy

- Development of global leaders through opportunities for overseas assignments
- Development of far-sighted managers through promoting career path rotation
- Systematic development and aggressive recruitment of human resources by visualizing human resource pipeline

Globalization during the 3rd Medium-Term Business Plan

- Establish footholds in EU, USA and Asia for global development of new drugs
- Establish aggressively a business platform in Asia aiming for direct sales
- Select multiple alliance partners in EU for sales



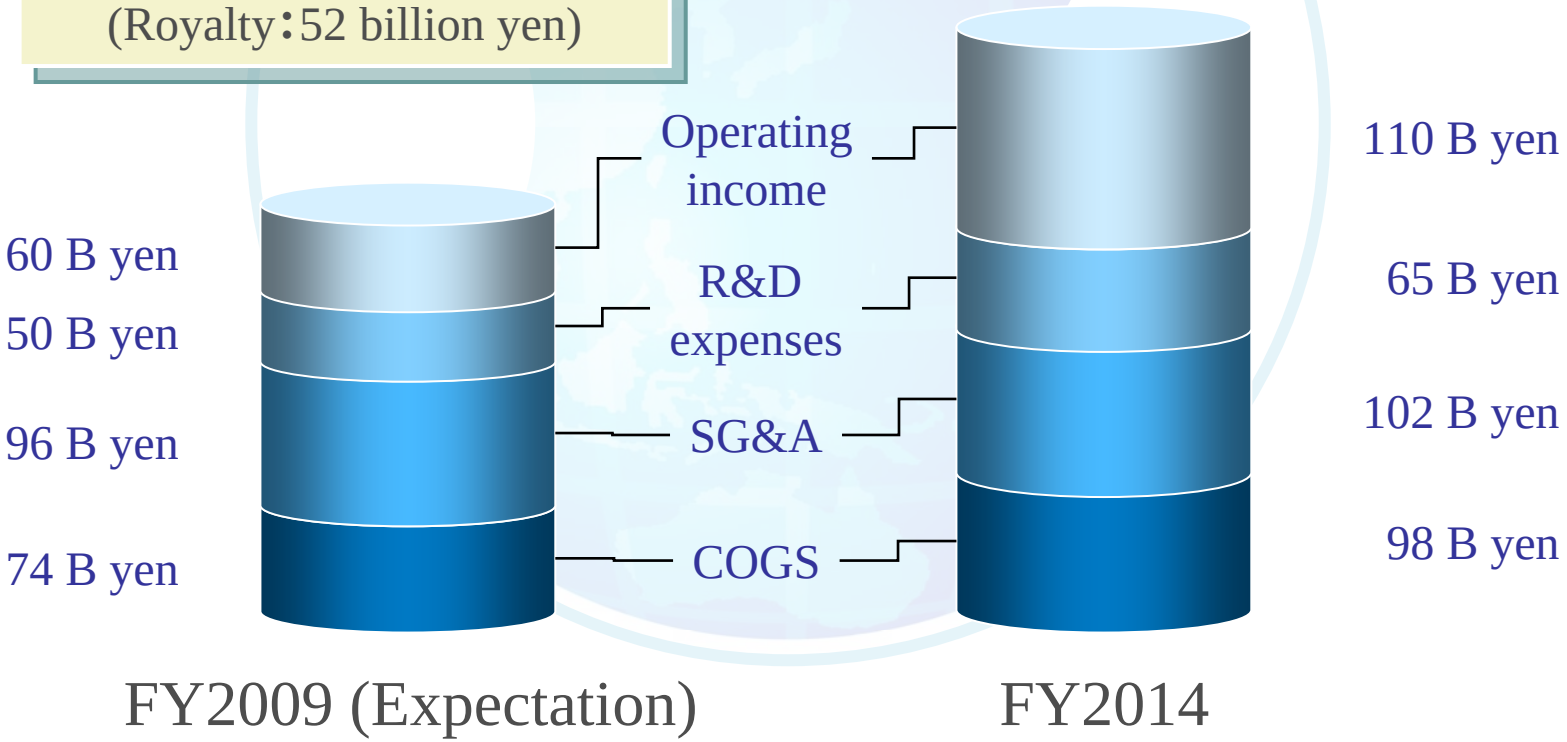

Financial Goals

Financial Target for FY2014（Consolidation）

Exclude additional sales through strategic business development deals

Net sales：280 billion yen
(Royalty：52 billion yen)

Net sales：375 billion yen
(Royalty：75 billion yen)



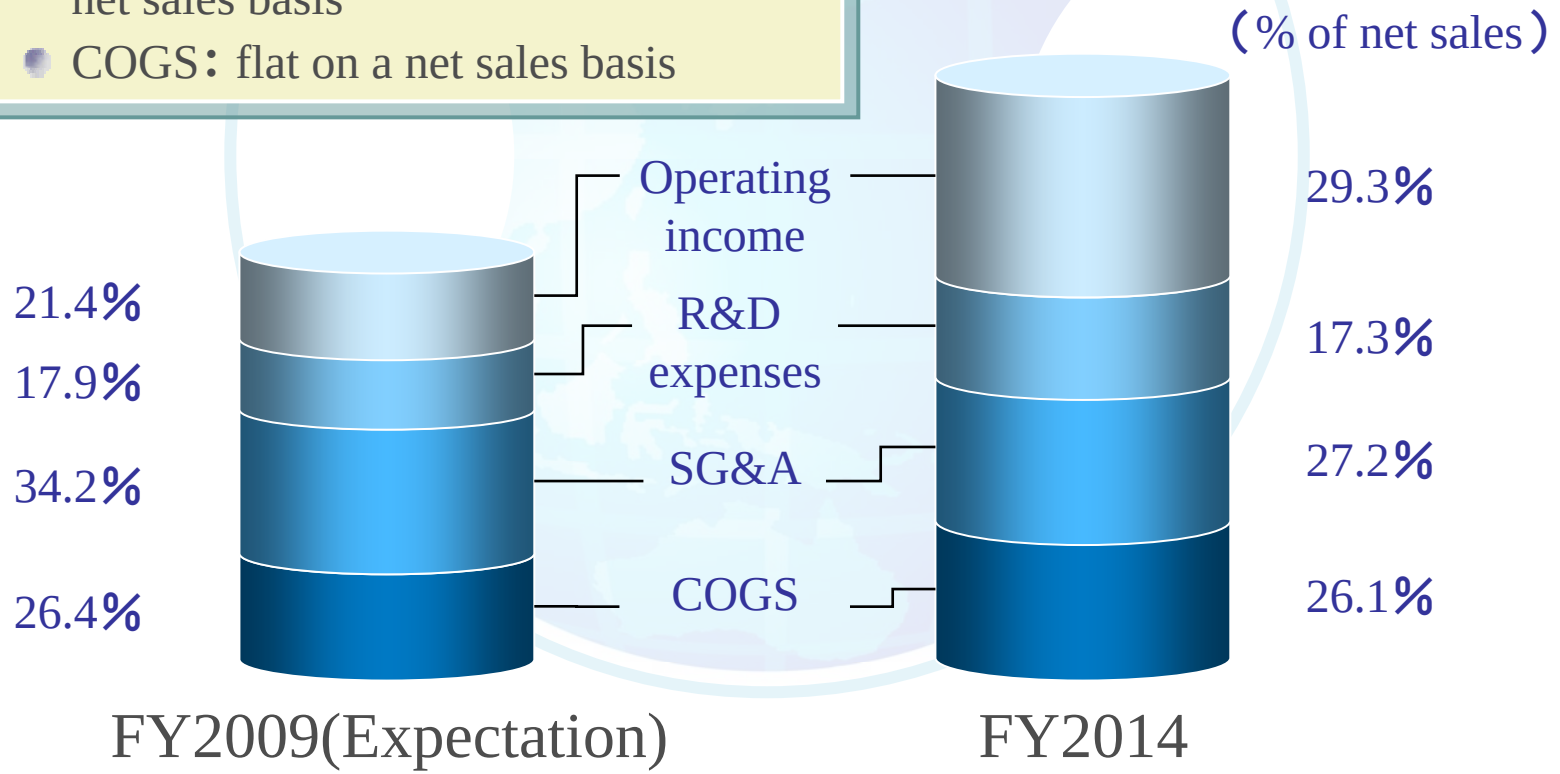
Change in Income/Cost Structure（Consolidation）

Investment for growth

- R&D expenses：30%up on an absolute value basis

Adjustment for cost

- SG&A expenses：7 % reduction on a net sales basis
- COGS：flat on a net sales basis



Strengthening of Operational Fundamentals and Shareholder Return

Put 3 Gears in Motion and Implement Both Strengthening of a Business Foundation and Shareholder Return While Balancing the Two Well

Shareholder return

- Keep 35% of payout ratio
  Expected total dividend amount:94 B yen
- Dividend enable to feel the real growth
  Expected dividend per share:36 ⇒ 78yen

Investment toward the future

- R&D expenses: 305 B yen
- Capital investments: 75 B yen

Improvement of B/S for financial strategy

- Dept refund/bond retirement: 111 B yen
  Term-end balance: 121 ⇒ 10 B yen
- Strategic business development funds: 150 B yen
  Term-end balance:100 ⇒ 250 B yen

Determination for the Real Growth

SONG for you!

Toward the New Stage Where We Can All Feel the Real Growth

The 1st medium-term management plan
"Laying the foundation"

Completion of corporate restructuring to concentrate on pharmaceutical business

The 2nd medium-term management plan
"Accelerating toward significant strides"

Establishment of incessant stream of pipeline through energizing and globalizing R&D

The 3rd medium-term management plan
"SONG for the Real Growth"

Launch of multiple products developed globally and real growth

SHIONOGI & CO., LTD.

Development

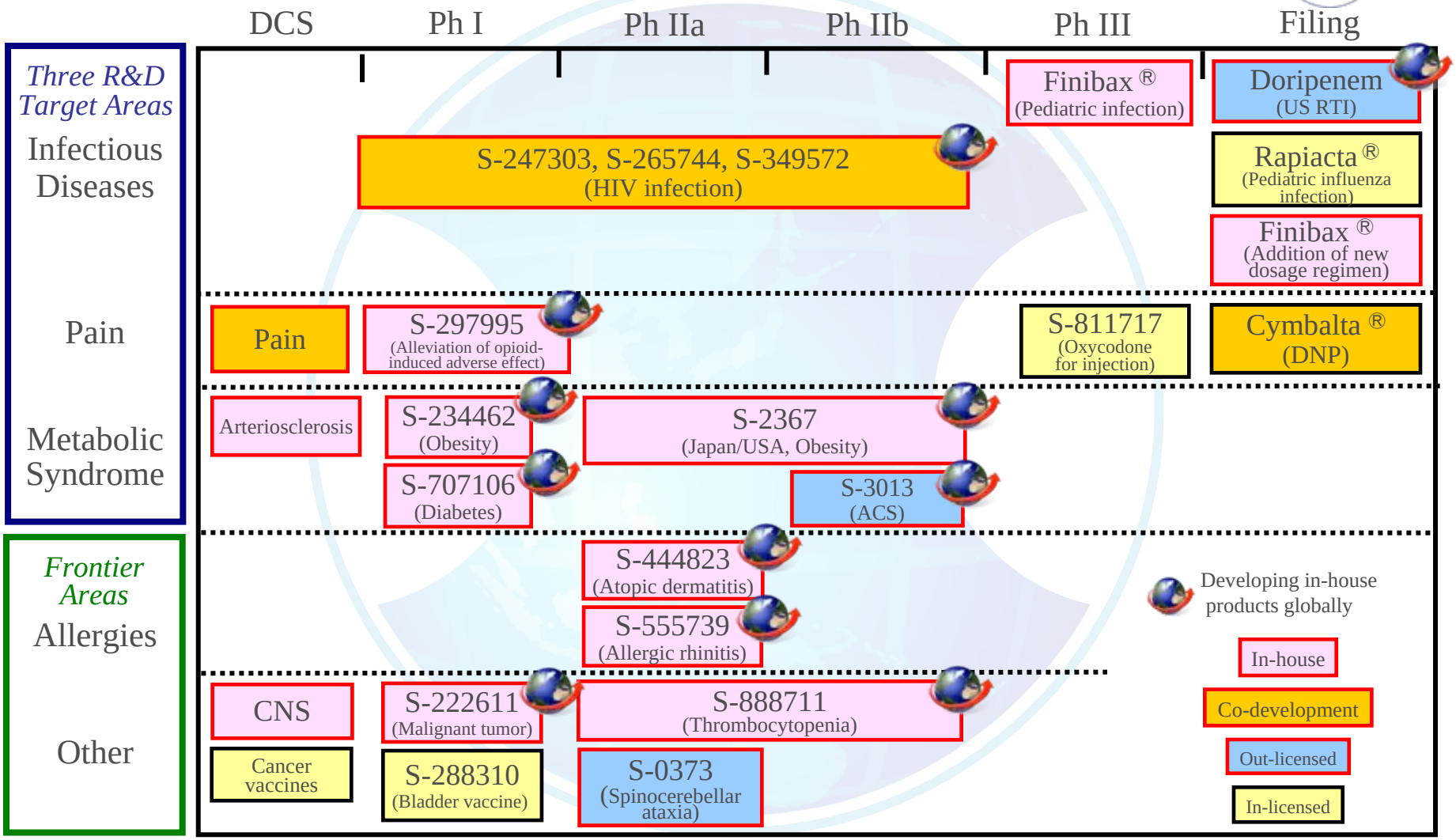
March 16, 2010

SHIONOGI & CO., LTD.
Executive General Manager
Pharmaceutical Development Division

Takuko Sawada

Development Pipeline (As of March 2010)

- Enrichment by In-house Compounds



The reason for discontinued three compounds
S-013420 (Bacterial infection): Marketability
S-0139 (Cerebrovascular diseases): Success probability and marketability etc.
NS75B (Benign prostatic hypertrophy): Efficacy in the overseas Phase III studies

RTI: Respiratory tract infection, ACS: Acute coronary syndromes
DNP: Diabetic neuropathic pain, DCS: Drug candidate selection

Core Development Products
Infectious Diseases Area

▪HIV integrase inhibitor

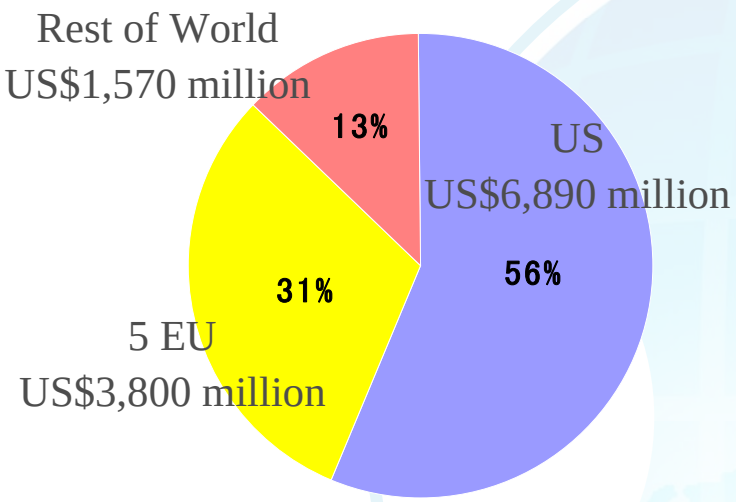
- Current state of market
- Product characteristics
- Non-clinical and clinical data, etc.

HIV Market (1)

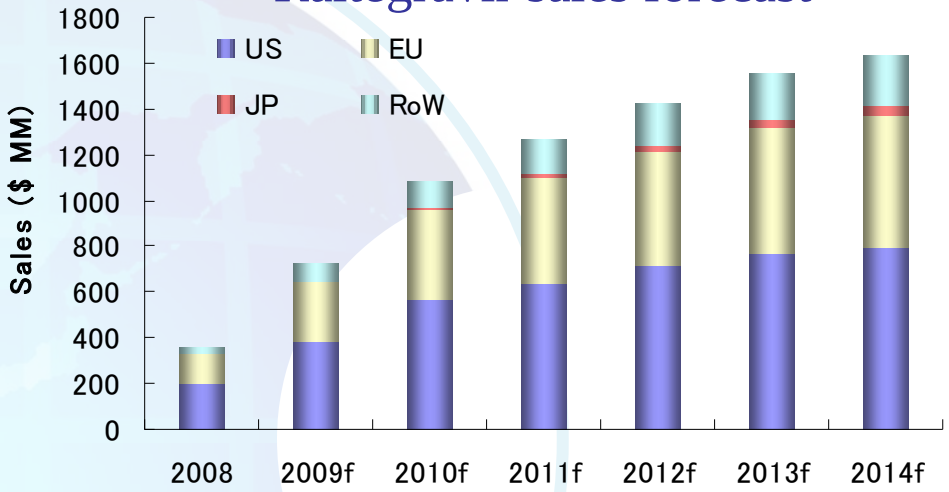
- Number of Patients:
  - HIV patients (worldwide): about 33.4 M
- Market Situation in 2008:
  - Global value sales: US$12,000 million
  - US: US$6,890 million, 5 EU: US$3,800 million,
    Rest of world: US$1,570 million
  - African market is growing rapidly
- Trend of anti-HIV drug sales:
  - The sales of NRTIs and Protease inhibitors are flat
  - First Integrase inhibitor, Isentress (Raltegravir), was launched at the end of 2007. Sales in 2008 was US$361 million and US$752 million in 2009, and currently growing

HIV Market (2)

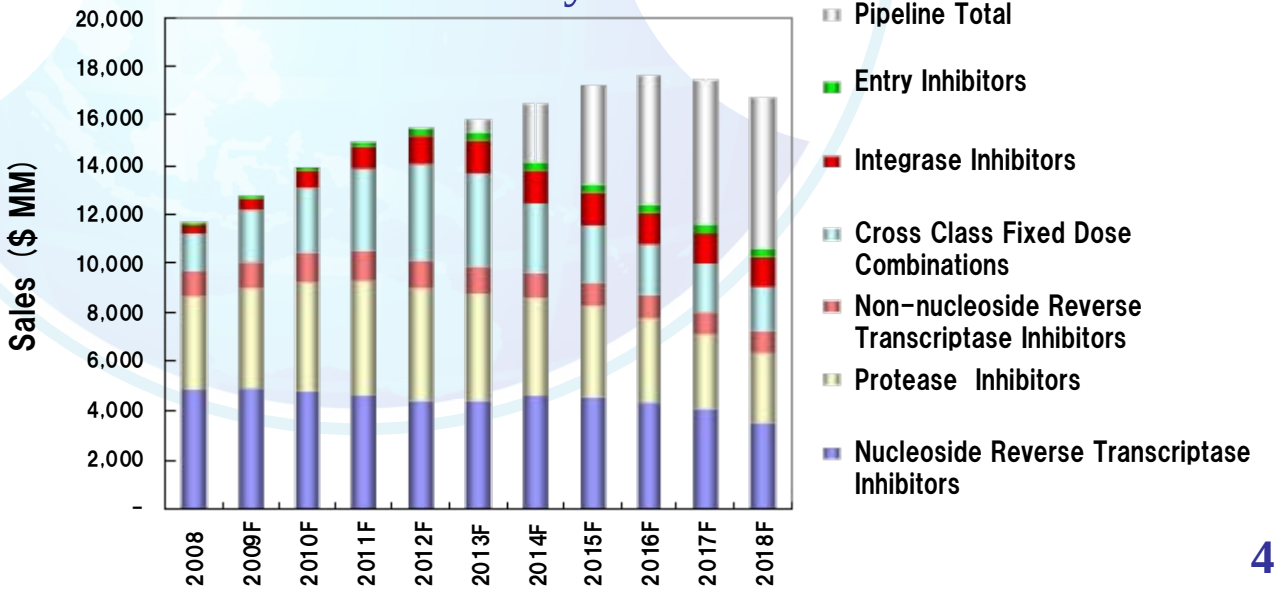
Sales by region (2008)



Raltegravir sales forecast



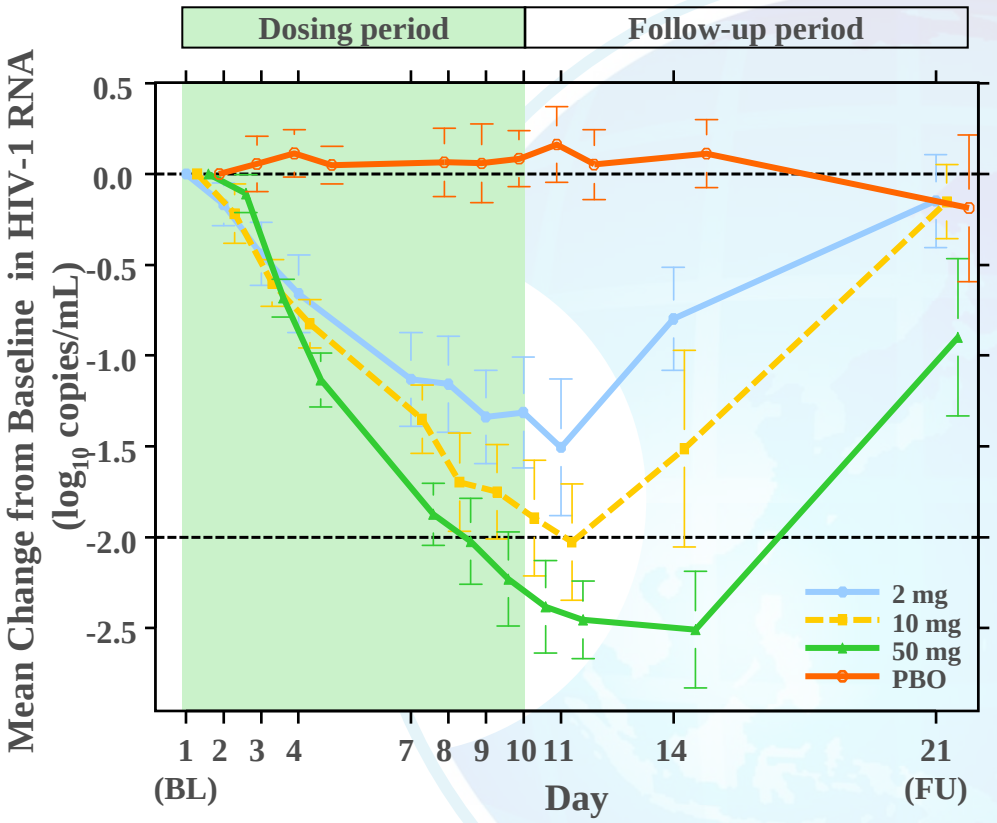
Sales forecast by class



Profile

- Developed by Shionogi-GlaxoSmithKline Pharmaceuticals, LLC (Shionogi and ViiV Healthcare)
- HIV integrase inhibitor (oral)
- Characteristics:
  - Strong anti-HIV activity
  - Good *in vitro* resistance profile
  - Good pharmacokinetic profile
  - Low risk of drug-drug interactions
- S-349572: Phase IIb in the USA and the EU ongoing
- S-265744: Phase IIa in the USA completed
- S-247303: FTIH in the USA

S-349572: Attributes of a Next Generation INI

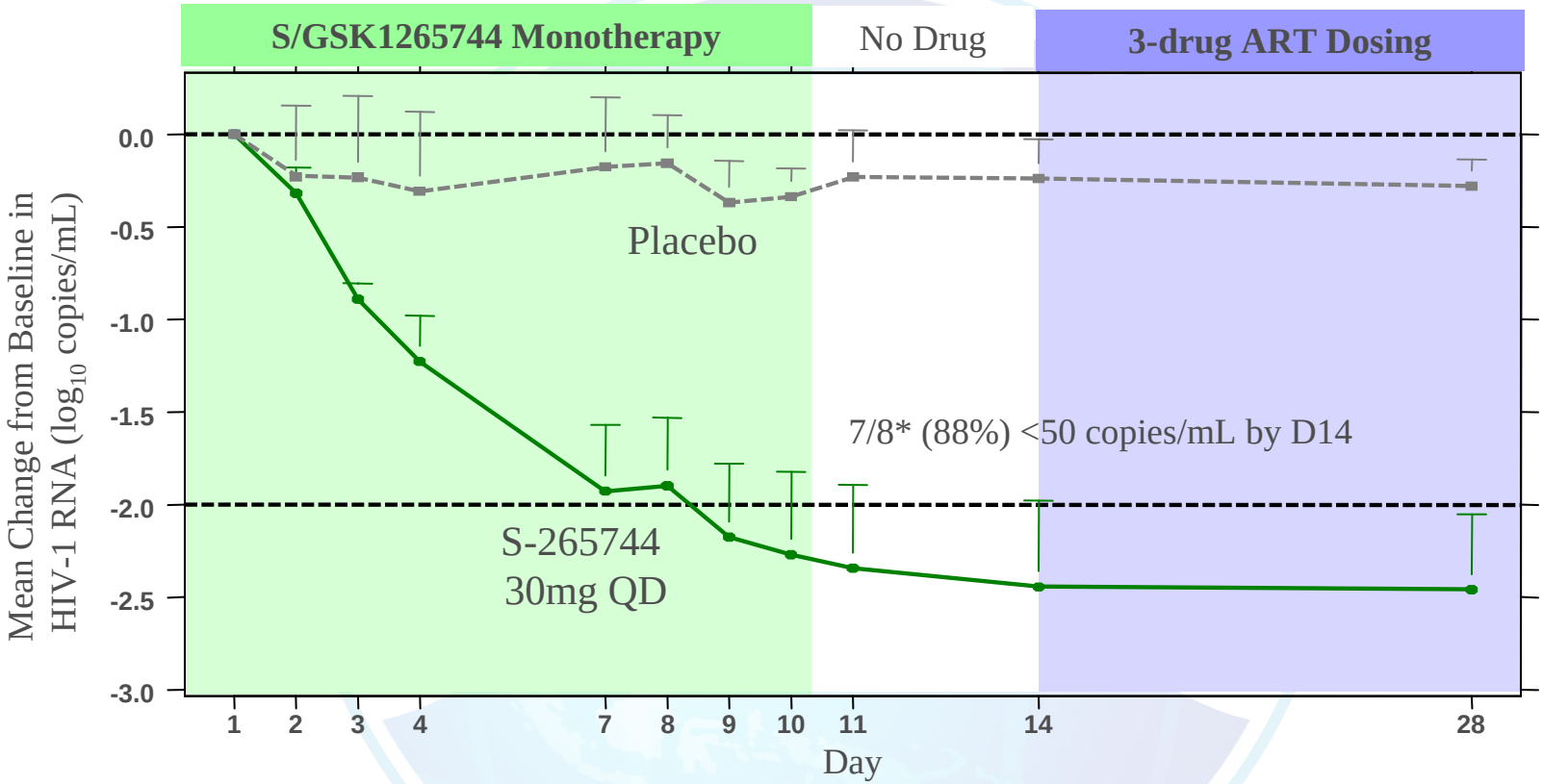


- Only once daily, unboosted INI in clinical development[1]
- Low PK variability and predictable exposure-response relationship with a low mg dose[2,3]
- Unprecedented antiviral activity in a Phase 2a study[1]
- Superior in vitro resistance profile with potential for higher genetic barrier to resistance[4,5,6]

1. Lalezari J. et al. IAS 2009, Cape Town, abstract TUAB105.
2. Min S, et al. IAS 2009, Cape Town, abstract WEPEA099.
3. Song I, et al. IAS 2009, Cape Town, abstract WEPEB250.
4. Sato A, et al. IAS 2009, Cape Town, abstract WEPEA097.
5. Underwood M, et al. IAS 2009, Cape Town, abstract WEPEA098.
6. Seki T, et al. CROI 2010, Poster abstract 555.

S-265744: Antiviral Activity

Mean (95% CI) Change from Baseline in HIV-1 RNA (log_{10} copies/mL)

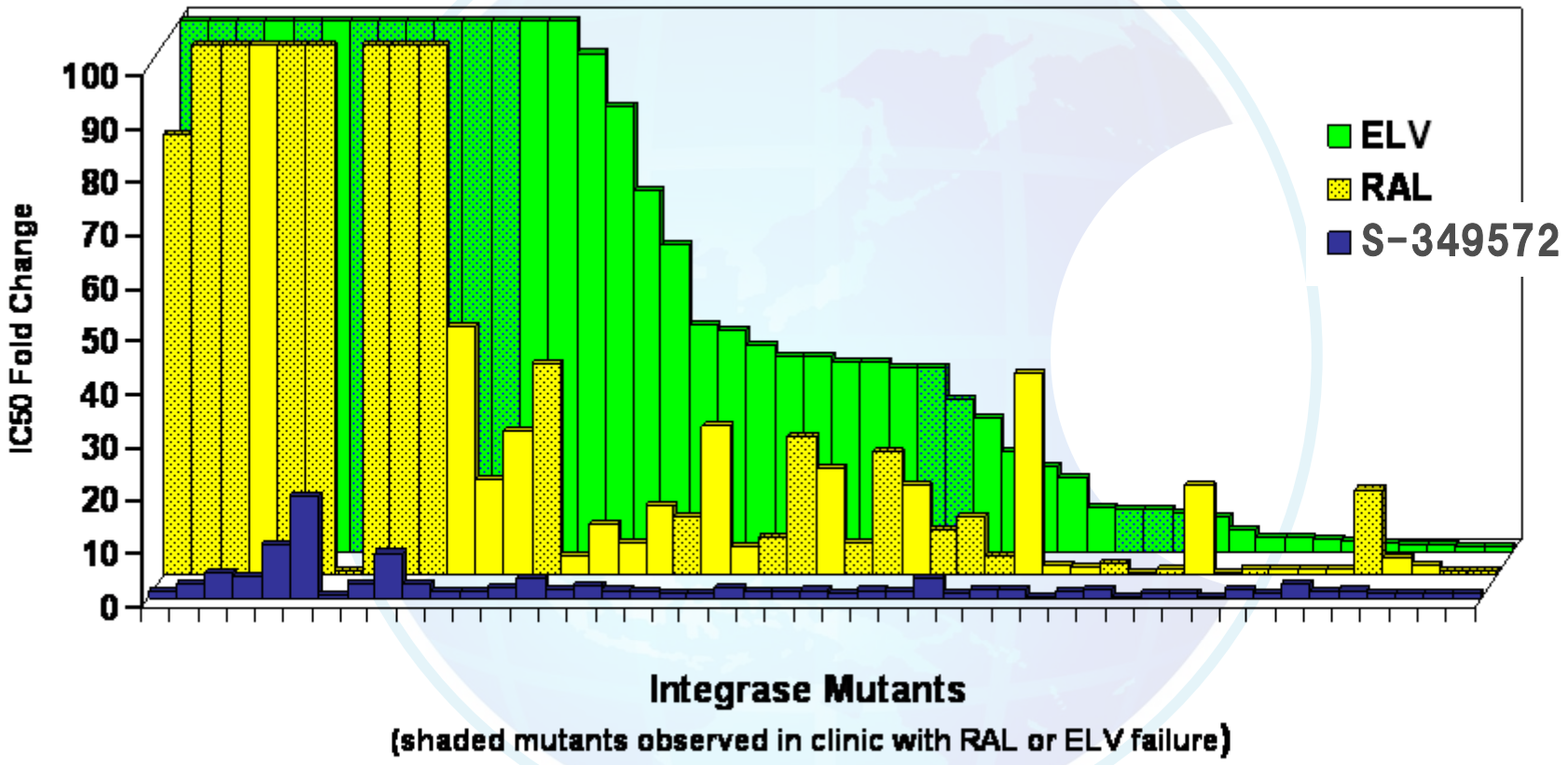


Median HIV-1 RNA Decline Baseline to Day 11		Range	CD4
S/GSK1265744	-2.6 log_{10} copies/mL	(-3.0, -1.0)	+15 (-100, +100)
Placebo	-0.27 log_{10} copies/mL	(-0.4, 0.0)	-90 (-190, -20)

Min, et al. 49th ICAAC, 12–15 September 2009, San Francisco, CA, USA. Abstract #H1228.

*: One subject with screening VL of 8410 copies/mL had HIV-1 RNA of 474 copies/mL at Day 1

Most Raltegravir (RAL)- and Elvitegravir (ELV)-resistant Mutants are Susceptible to S-349572



Seki T, et al. CROI 2010, Friday poster abstract 555.

Core Development Products
Metabolic Syndrome Area

- Anti-obesity drug
- Anti-diabetes drug

- Current state of market
- Product characteristics
- Future plan

S-2367: Anti-obesity Market

- Market in the USA
  - The United States is the biggest market for anti-obesity treatment
  - The prevalence of obesity in the USA continues to be high:
    In 2007-2008, the prevalence of obesity (BMI≧30) was 33.8%, and that of overweight (30＞BMI≧25) were 34.2% among USA adults *JAMA*.2010;303 (3):235-241
- Anti-obesity agent that meets the following unmet needs is desired by physicians
  - Efficacy: Greater weight loss in volume and % weight loss from baseline
    Agents without showing decreased body weight regain
    Effects on CVD risk factors such as glucose or lipids
  - Safety: Long-term safety
    Agents without CNS or cardiovascular side effects
- Market potential
  - The global anti-obesity market valued at US$1,400 million in 2009 is estimated to grow over US$3,000 million by 2016 by introduction of agents having greater efficacy and safety

S-2367: Profile

- Anti-obesity
- NeuropeptideY Y5 receptor antagonist (oral)
- Key findings from non-clinical studies:
  - Increased energy consumption
  - Suppressed visceral fat accumulation and improved blood glucose and serum lipid levels
  - Expected product profile: sustainable weight suppression without rebound
  - Confirmed excellent safety
- Key findings from clinical studies to date:
  - Completed one year Phase IIb study in the USA
    - Met the criteria in the FDA's draft guidance by year-long treatment*

      Confirmed attractive potential of S-2367 as anti-obesity drug
    - Minor change in parameters related to red blood cells
  - Completed total two-year treatment of Phase IIb study including open label extension period
  - Completed Phase I PK study in combination with Orlistat in the USA
    - Preliminary report revealed co-administration of S-2367 with Orlistat had no appreciable effect on PK of S-2367
  - Completed multiple oral ascending dose study in Japan

*: Draft Guidance for Industry, Developing Products for Weight Management, Feb. 2007

S-2367

Phase II Study of Combined Use with Orlistat in the USA

- **Objective:**

  To evaluate the weight loss effect and the safety of S-2367 and Orlistat administered individually and combined

- **Study population:**

  Patients with a BMI of 30.0 to 45.0 kg/m^2 inclusive

- **Study Design:**

  24 weeks treatment after 4 weeks placebo lead-in period while consuming a reduced calorie diet (800 kcal deficit diet per day)

- **Four-treatment parallel-groups:**
  - Placebo
  - S-2367
  - Orlistat
  - S-2367 + Orlistat

Phase II Studies in Japan

- **Objective:**

  To evaluate the weight loss effect and the safety of S-2367

  in obese patients who have more than 2 complications out of diabetes, dyslipidemia and hypertension

- **Subject Population:**
  - BMI $\geqq$ 25 kg/m^2
  - Visceral fat area $\geqq$ 100 cm^2
- **Two Studies in Progress:**
  - Obesity with Diabetes and Dyslipidemia
  - Obesity with Hypertension and Dyslipidemia

Future Plan

- Phase II study of combined use with Orlistat in the USA
  - Initiated in FY2010 1Q, dosing to be completed in FY2010 4Q
- Phase II study in Japan:
  - Obesity with Diabetes and Dyslipidemia
    - Initiated in FY2009 3Q, dosing to be completed in FY2010 3Q
  - Obesity with Hypertension and Dyslipidemia
    - To be initiated in FY2010 1Q, dosing to be completed in FY2010 4Q

S-234462: Profile

- Anti-obesity
- NeuropeptideY Y5 receptor antagonist (oral)
- Key findings from non-clinical studies:
  - 10 times higher affinity for human type NPY Y5 receptor than that of S-2367
  - Approximately 2-fold more suppression of body weight gain at a dose of one-fifth or less than that of S-2367
  - Decrease in food intake and increase in energy expenditure
  - Decreases in mesenteric fat weights and hepatic triglyceride content and improvement of insulin resistance
  - Confirmed excellent safety
- Key findings from clinical studies to date:
  - Phase I single ascending dose study in the USA in progress
  - No concern about safety data
  - Plasma drug profile suggested once-daily dosing
- Future plan:
  - Phase II study to be started in 2010

S-707106: Anti-diabetics market

- The characteristics of diabetes in western countries:
  - Almost 80% of type 2 diabetes patients are obese or overweight and supposed to be insulin resistant
- Unmet needs for treatment of type 2 diabetes in the USA
  - Ideal new agent would be disease modifier, reducing onset and/or duration of type 2 diabetes
  - Improvements in type 2 diabetes comorbidities
    - Beneficial effect on lipids
    - Body weight reduction
  - Improvements in safety/tolerability issues associated with approved agents
- USA anti-diabetics market in 2008:
  - Total anti-diabetics market amounts to US$13,000 million, including US$5,700 million of intravascular insulin and US$6,700 million of oral
  - Insulin sensitizers has garnered sales of US$4,600 million out of oral drugs
  - It is forecasted that type 2 diabetes market will almost double in 2018

S-707106: Profile

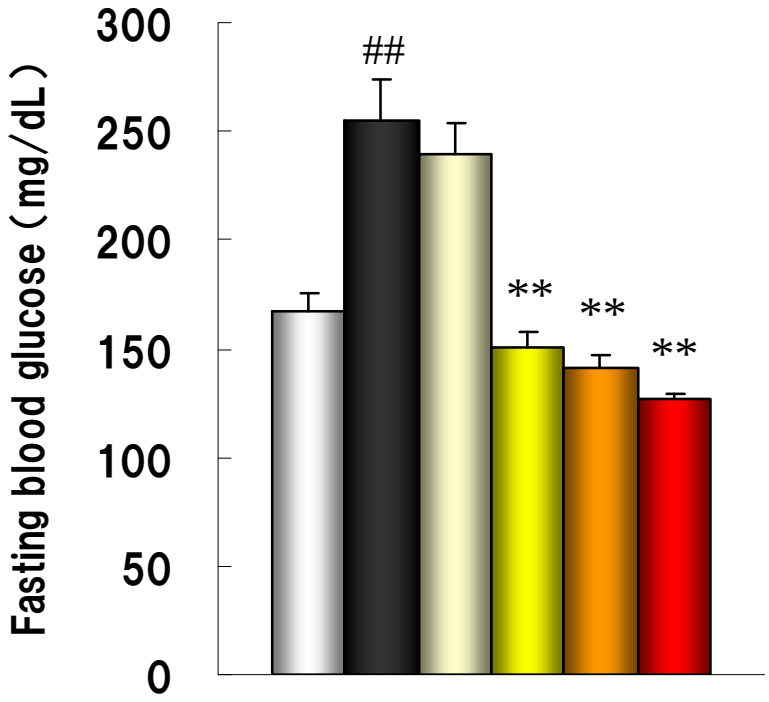
- Indication: Type 2 diabetes
- Mechanism: Insulin sensitizer (oral)
- Key findings from non-clinical studies:
  - Improvement of insulin resistance and reduction of blood sugar with lowering of plasma lipids
  - No concern of increase in body weight, induction edema, bone metabolism, lactic acidosis or hypoglycemia
  - DDI would be unlikely through CYP inhibition
  - Once a day
- Development stage: FTIH in Mar 2010 in the USA
- Development plan: Phase I and POC studies to be scheduled in the USA

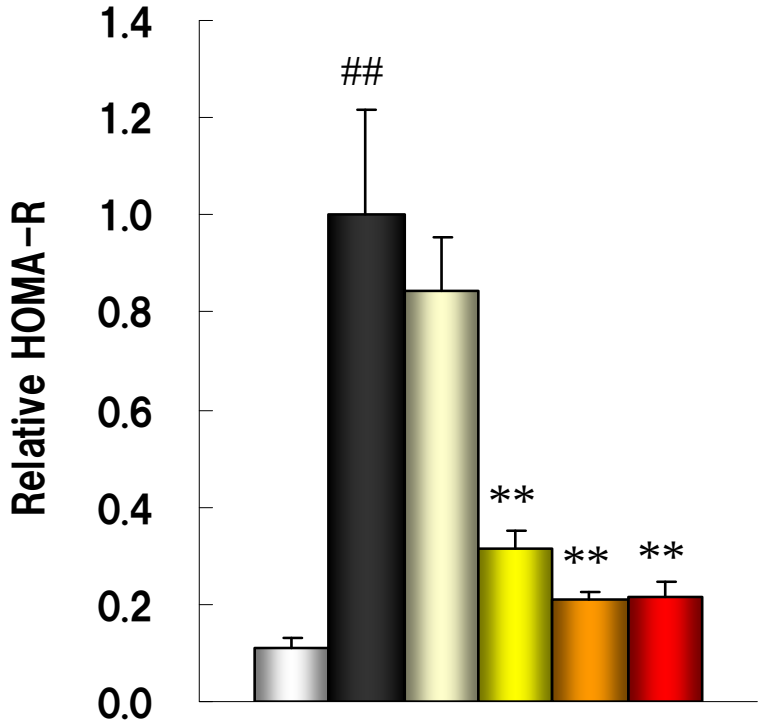
DDI: Drug-drug interaction, CYP: cytochrome P-450, FTIH : First time in humans, POC: Proof of concept

Effects on Fasting Blood Glucose and Insulin Resistance in Diabetic Mice

Vehicle（Control mice）
Vehicle（Diabetic mice）
S-707106 low dose （Diabetic mice）
S-707106 （Diabetic mice）
S-707106 （Diabetic mice）
S-707106 high dose （Diabetic mice）

##: P<0.01 vs Vehicle, Control mice (Student's)
**: P<0.01 vs Vehicle, Diabetic mice (Dunnett's)





Core Development Products
Pain, Allergies and Other Areas

- Alleviator of opioid-induced GI side effects
- Anti-atopic dermatitis
- Thrombopoietin mimetics

  - Product characteristics
  - Positioning
  - Non-clinical and clinical data, etc.

S-297995: Profile

- Indication:

  Relief of opioid-induced gastrointestinal symptoms such as nausea, vomiting and constipation

- Mechanism: Orally active peripheral opioid receptor antagonist
- Pharmacological characteristics (non-clinical):
  - Suppressed morphine-induced nausea and vomiting in ferret model
  - Suppressed morphine-induced small intestinal hypomotility in rat model
  - Showed anti-emetic and anti-constipation effect at a similar exposure level
  - No effect on the analgesic effect of morphine due to low propensity to permeate the blood-brain barrier
- Development Stage: Phase I study completed (Japan)
- Future plan: Phase IIa study to be conducted in the USA

S-297995: Antagonist Activity for Opioid Receptors

SONG for you!

Antagonist activity of S-297995 and competitor for mu, delta and kappa receptors

Substrates	Antagonist activity (Functional Kb, nmol/L)		
	Mu (human)	Delta (human)	Kappa (guinea pig)
S-297995	◎	◎	◎
Competitor	○	×	×

◎ ≦ 10 nmol/L; ○ ≦ 100 nmol/L; × > 100 nmol/L

S-297995 is a pan-opioid receptor antagonist with extremely low functional Kb values for mu, delta and kappa receptors, although competitor is a selective mu antagonist. Therefore, S-297995 can be anticipated to alleviate GI side effects caused by various opioid agonists which possess different selectivity for mu, delta and kappa

GI: Gastrointestinal

S-297995: Progress of Clinical Studies and Future Plan

Japan:

- Phase I single dose study completed
- Phase I BA comparison (solution/tablet) study completed
- Phase I multiple dose study completed

- Tolerability and safety in healthy subjects were confirmed
- Good PK profile was observed

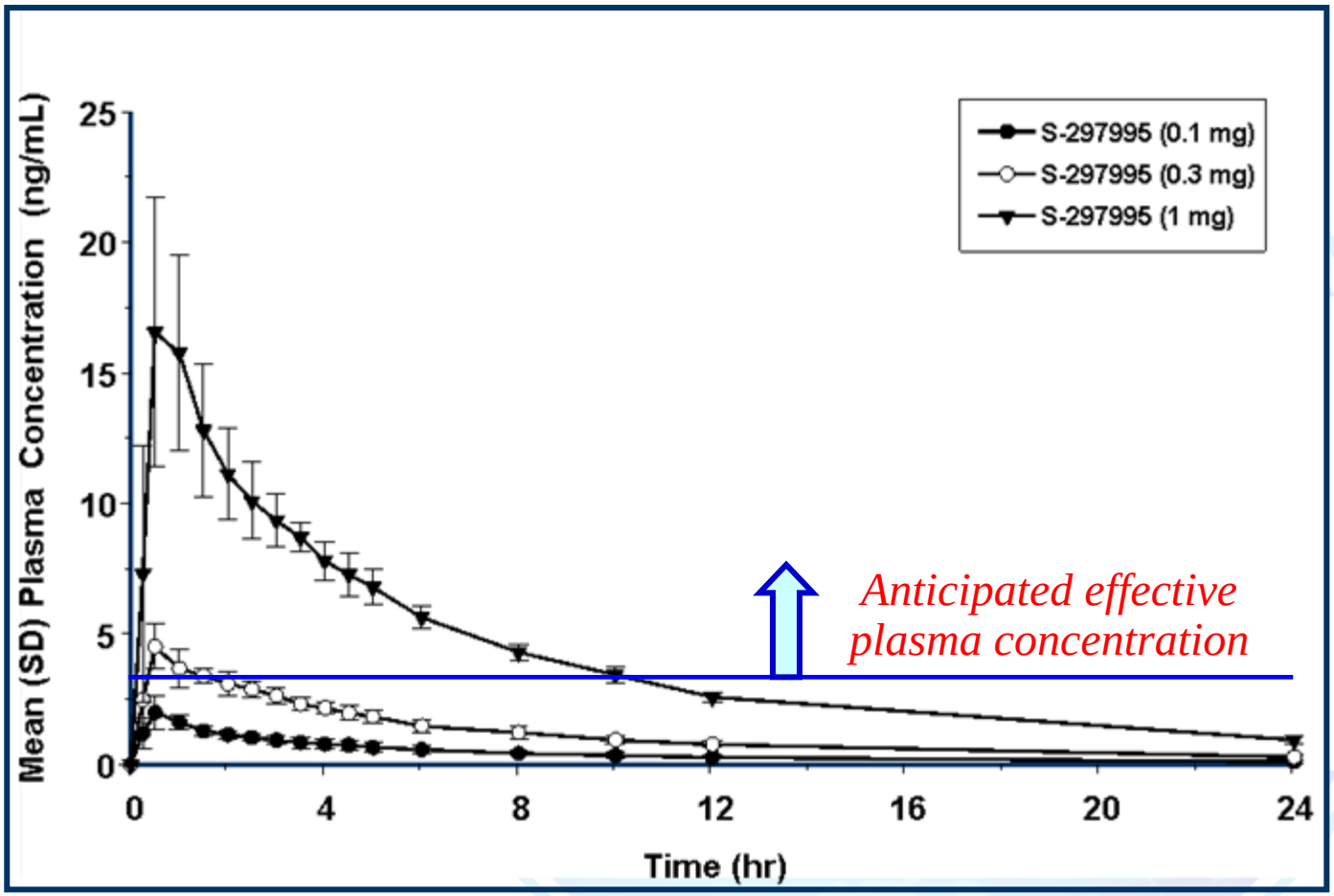
Abroad:

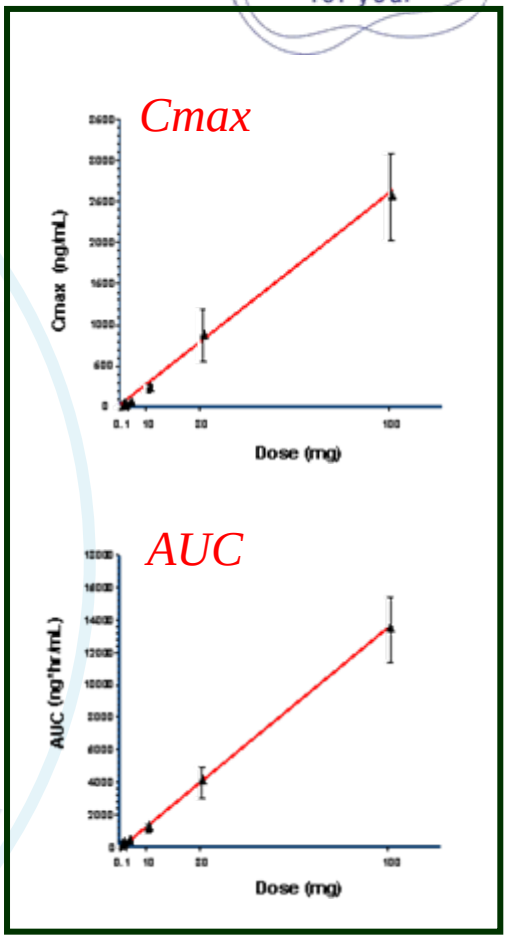
- Phase IIa study in preparation (USA)

  To investigate safety and efficacy profile in chronically opioid-treated patients

BA: Bioavailability, PK: Pharmacokinetic

S-297995: PK Profile in Phase I Single Dose Study





- Inter-individual variations were relatively small and increment of exposure in a dose-dependent manner was observed
- Cmax value after administration of 0.3 mg and more exceeded lower limit of anticipated effective plasma concentration

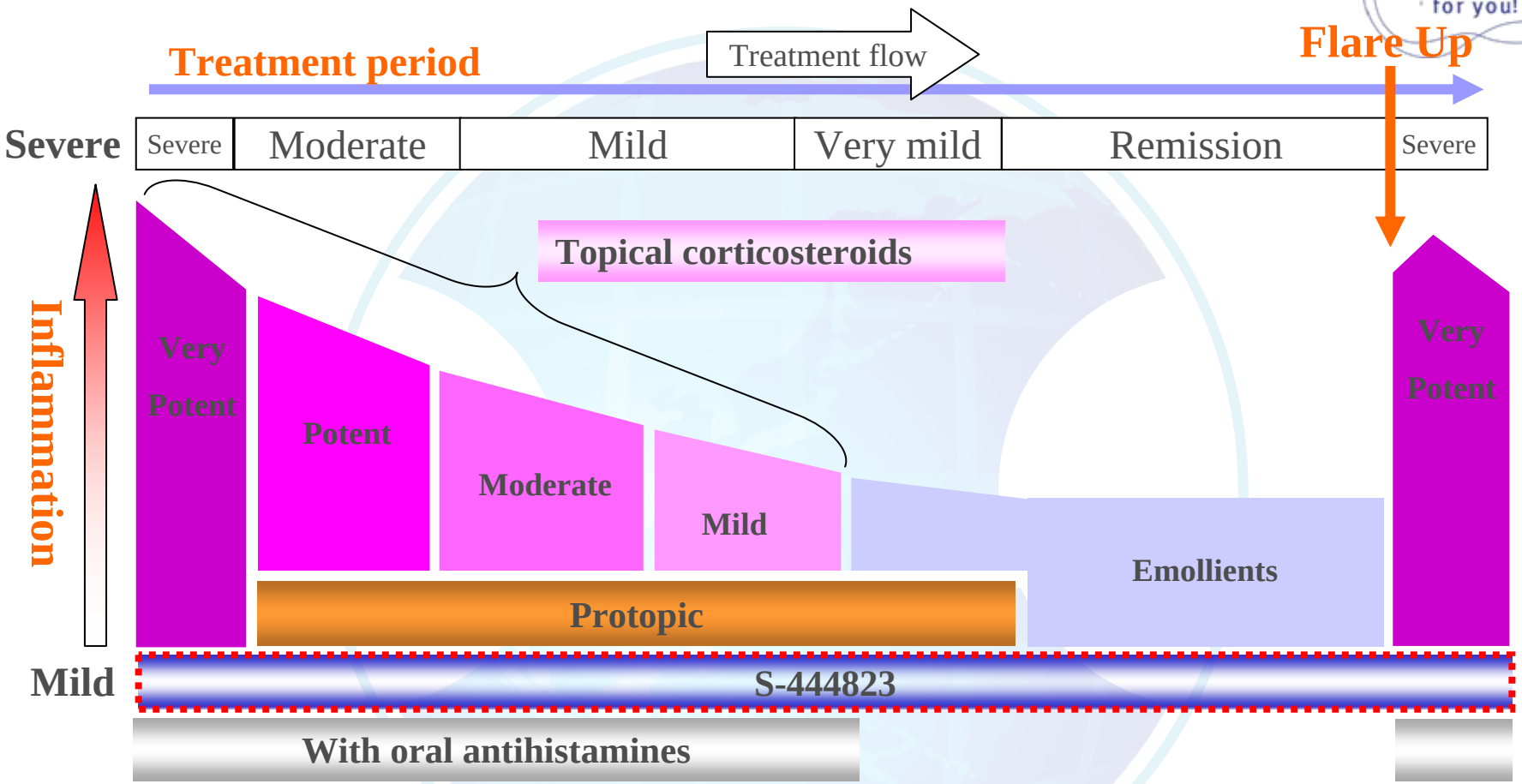
S-444823: Profile

- Indication:

Atopic dermatitis, eczema/dermatitis with pruritus

- Mechanism: Cannabinoid receptor agonist (topical)
- Characteristics:
  - Potently alleviate pruritus through a peripheral action
  - Improve skin inflammation
  - Good safety profile
- Developmental status: Phase IIa study in progress (Japan)
- Result will be available in 2010

S-444823: The Positioning in Atopic Dermatitis



- Atopic dermatitis
  - Atopic dermatitis symptoms gets worse via itch-scratch cycle
- Unmet needs for current treatment
  - High unmet needs for the treatment of pruritus
  - Unmet needs for non-steroidal anti-inflammatory agents

S-444823: Progress in Clinical Studies

- Phase I study in healthy adults (May-July 2009)
  - Good safety and tolerability
  - Good skin permeability
- Phase I study in patients with atopic dermatitis (July-August 2009)
  - Good safety and tolerability
  - Good skin permeability
- Phase IIa study in patients with atopic dermatitis
  (Started in December 2009, to be completed in 2010)

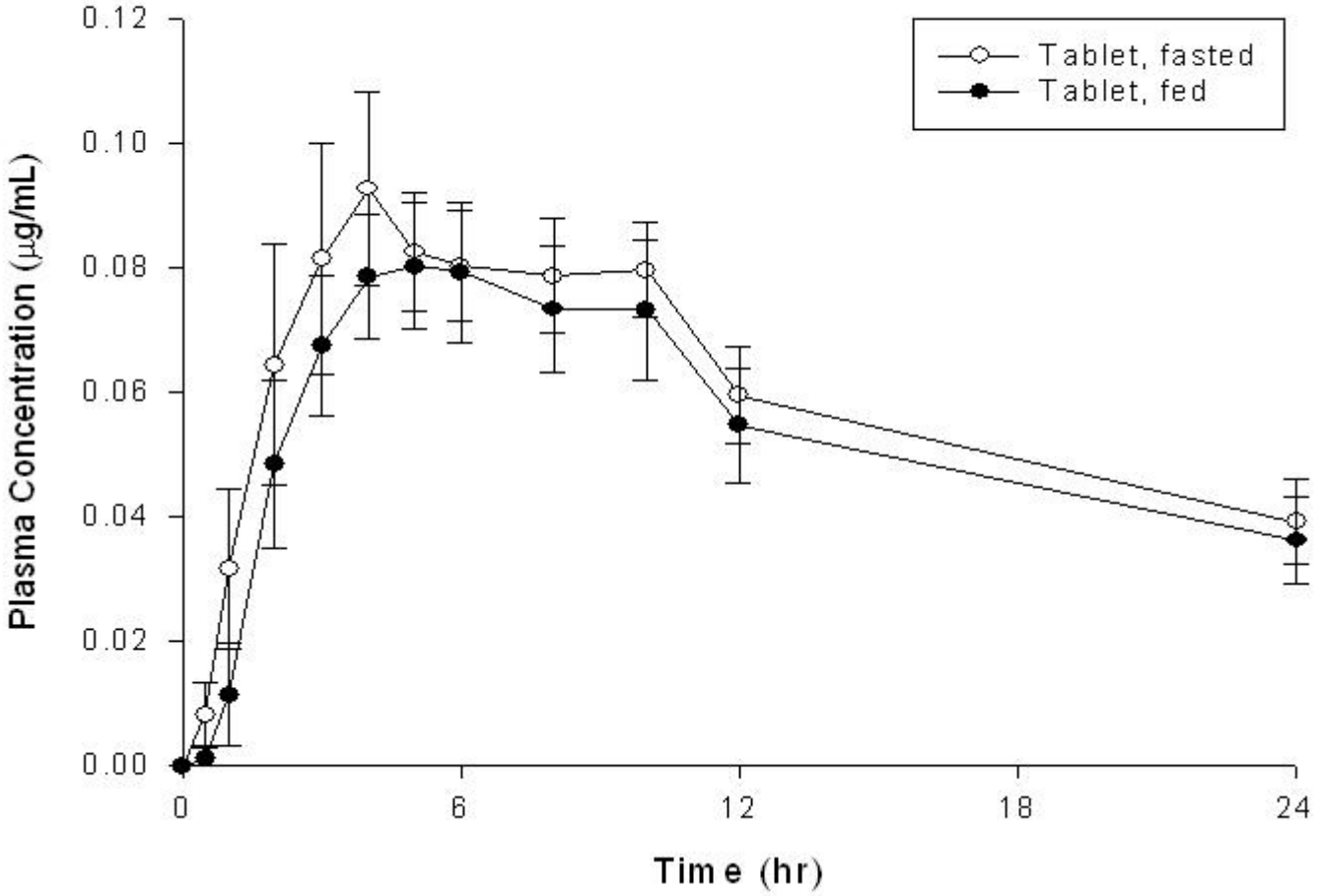
S-888711: Profile

- Indications: Various diseases with thrombocytopenia
- Mechanism: Thrombopoietin receptor agonist (oral)
- Developmental stage:
  - Global: Phase II dose-finding study in patients with immune thrombocytopenia
    - Countries (including intended locations): USA, UK, France, Italy, Hungary, Russia
- Pharmacological properties from clinical studies:
  - Good pharmacokinetic profiles:
    - Increases Cmax and AUC dose-dependently
    - Minimal food effect on PK profiles
    - Minimal race effect on PK profiles (Japanese vs. Caucasian)
    - Minimal risk of drug-drug interaction (CYP 3A4 substrate)
  - Fast onset of platelet increase with QD dosing schedule
  - Good tolerability and safety profiles up to the maximum testing dose
- Upcoming clinical studies:
  - Globally expand further clinical investigations to other thrombocytopenic disorders

PK: Pharmacokinetic, CYP: cytochrome P-450

S-888711: Food Effect

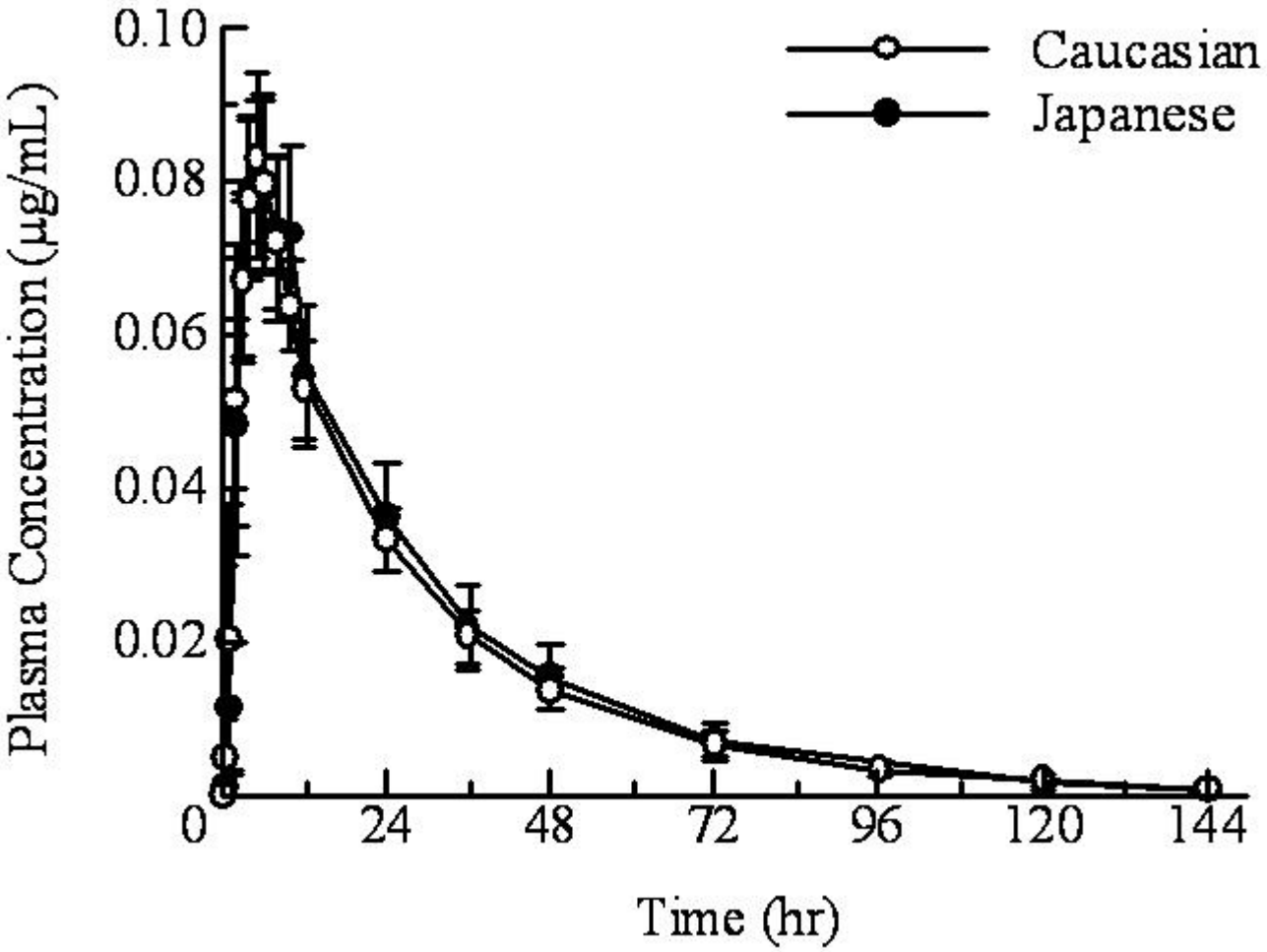
– Single Administration of 2 mg in Fasted and Fed Condition



No clinically significant food effect observed

S-888711: Race Effect

– Single Administration of 2 mg in Caucasian and Japanese



No PK difference between Caucasian and Japanese observed

Increase in Platelet Count in Phase I Multiple Dose Study in the USA

Maximum % increase in platelet count from baseline after 14 day treatments

Dose	Placebo	0.25mg	0.5mg	0.75mg	1mg
% increase in platelet count	0%	8%	35%	48%	67%

Dose-dependent increase in platelet count observed

S-888711: TPO mimetics

Differentiation from the launched competitors

TPO mimetics	Route	Pharmacokinetics		Safety*	
		Food effect	Ethnic Difference	Hepato-toxicity	Other concerns
S-888711	PO	No	No	No concern (Non-clinical studies)	
Nplate (romiplostim)	SC	-	No	No	Production of neutralizing Abs
Promacta (eltrombopag)	PO	Yes Given on empty stomach	Yes Adjustment of dose for each ethnics	Yes Black box warning	Cataract

*：Mechanism-independent toxicity

TPO: Thrombopoietin, Ab: Antibody

Target Milestones for FY 2010

Progress in global development products	
S-2367	Dosing in Phase II (used in combination with Orlistat) completed (USA) Dosing in two Phase II studies completed (Japan)
S-349572*	Phase IIb completed, Phase III initiated (USA, EU etc.)
S-555739	Additional therapeutic exploratory study to be planned
S-444823	Phase IIa completed (Japan)
S-888711	Phase II to be initiated (except immune thrombocytopenia)
S-234462	Phase I completed, Phase II to be initiated (USA)
S-297995	Phase IIa completed (USA)
S-707106	Phase I completed, Phase IIa study to be initiated (USA)
S-288310	Phase I/II completed (Japan)

*: Developed by Shionogi–GSK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