Research and Development at Shionogi

March 27, 2009

SHIONOGI & CO., LTD.

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- **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

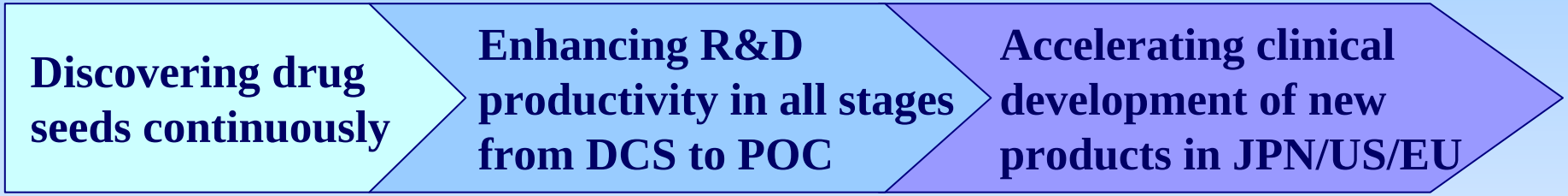
1. **Research : Hirosato Kondo, Ph.D.**
   Executive General Manager, Pharmaceutical Research Division
2. **Development : Takuko Sawada**
   Executive General Manager, Pharmaceutical Development Division
3. **Sciele R&D : Edward J. Schutter**
   President, Chief Operating Officer and Director, Sciele Pharma, Inc.
   : Larry M. Dillaha, M.D.
   Executive Vice President and Chief Medical Officer, Sciele Pharma, Inc.
4. **Summary : Isao Teshirogi, Ph.D.**
   President and Representative Director
5. **Q&A**

The Research and Development Goals in the Second Medium-Term Business Plan

- **Enrich infectious disease product line for and add pain and metabolic syndrome to new target areas**
- **Move at least 5 new chemical entities to Phase II or further by the end of FY2009**
- **Establish an unbroken pipeline stream through strategic development of licensing activities**
- **Increase the R&D efficiency and success rate by forming active alliance with outside resources**
- **Maximize product potential through life cycle management to start in early development stages**

Toward Achieving the Goals of the Second Medium-Term Business Plan and Ensuring Long-Term Growth

Achieve medium to long-term growth by continuously launching new products



DCS: Drug candidate selection, POC: Proof of concept

Research

Continuously discover globally competitive drugs

Ensure FTIH for two or more new in-house drug candidates each year

Development

Simultaneously develop in-house products in the three regions of Japan, the USA and the EU

One to two Phase IIb and one Phase III products or three Phase IIb products

Research

Hirosato Kondo, Ph.D.
Executive General Manager
Pharmaceutical Research Division
Shionogi & Co., Ltd.

Research

The Pharmaceutical Research Division Goals in the Second Medium-Term Business Plan

Goals

- Enrich infectious disease product line for and add pain and metabolic syndrome to new target areas
- Move at least 5 new chemical entities to Phase II or further by the end of FY2009
- Establish an unbroken pipeline stream through strategic deployment of licensing activities
- Increase the R&D efficiency and success rate by forming active alliance with outside resources
- Maximize product potential through life cycle management to start in early development stages

Vision for FY2009

Continuously discover globally competitive drugs

Ensure FTIH for two or more new in-house drug candidates each year

Achieve the highest R&D productivity in the pharmaceutical industry

- ➔ Acting quickly
- ➔ Developing outstanding drug discovery technologies

FTIH: First trial in human

Research

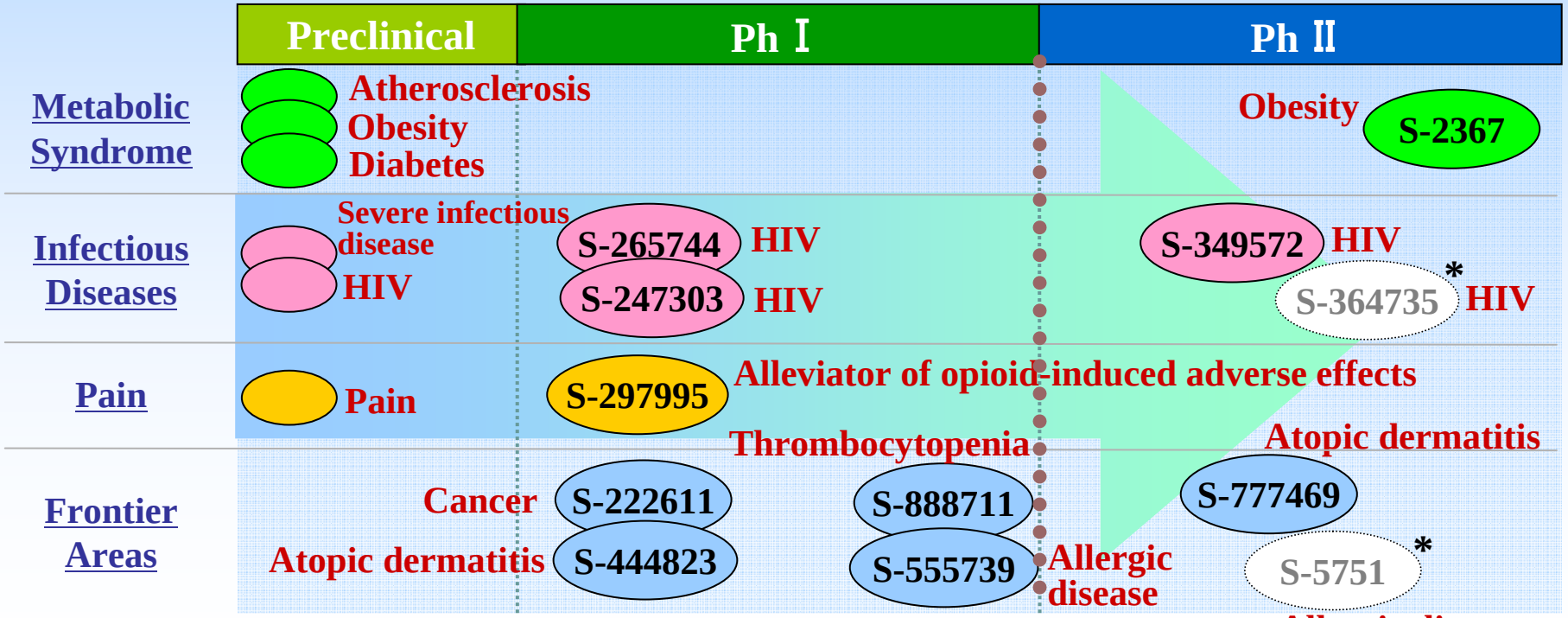
Prospects for Achieving Targets for the Research Division under the Second Medium-Term Business Plan

Target: Add metabolic syndrome and pain to target disease areas alongside infectious diseases

➡ **Forming drug candidate pipelines from in-house drug discovery research in three target disease areas**

Target: Move five or more new compounds to Phase II or further by March 2010

➡ **Move five to Ph2, with several others on the timeline**



* *Dropouts*

Achievements of FY2008 (1)

- **Ensure FTIH for two or more compounds and DCS for four or more compounds**
  - Firmly institute Shionogi's quarterly program management system
    - Ensure developmental risks of drug candidates are communicated and evaluate achievements of targets
    - Prioritize programs in late phase of drug discovery research and reallocate resources

Selected four new compounds for DCS

- Anti-severe infectious disease drug
- Anti-HIV drug
- Anti-obesity drug
- Anti-diabetic drug

Advanced three compounds to FTIH

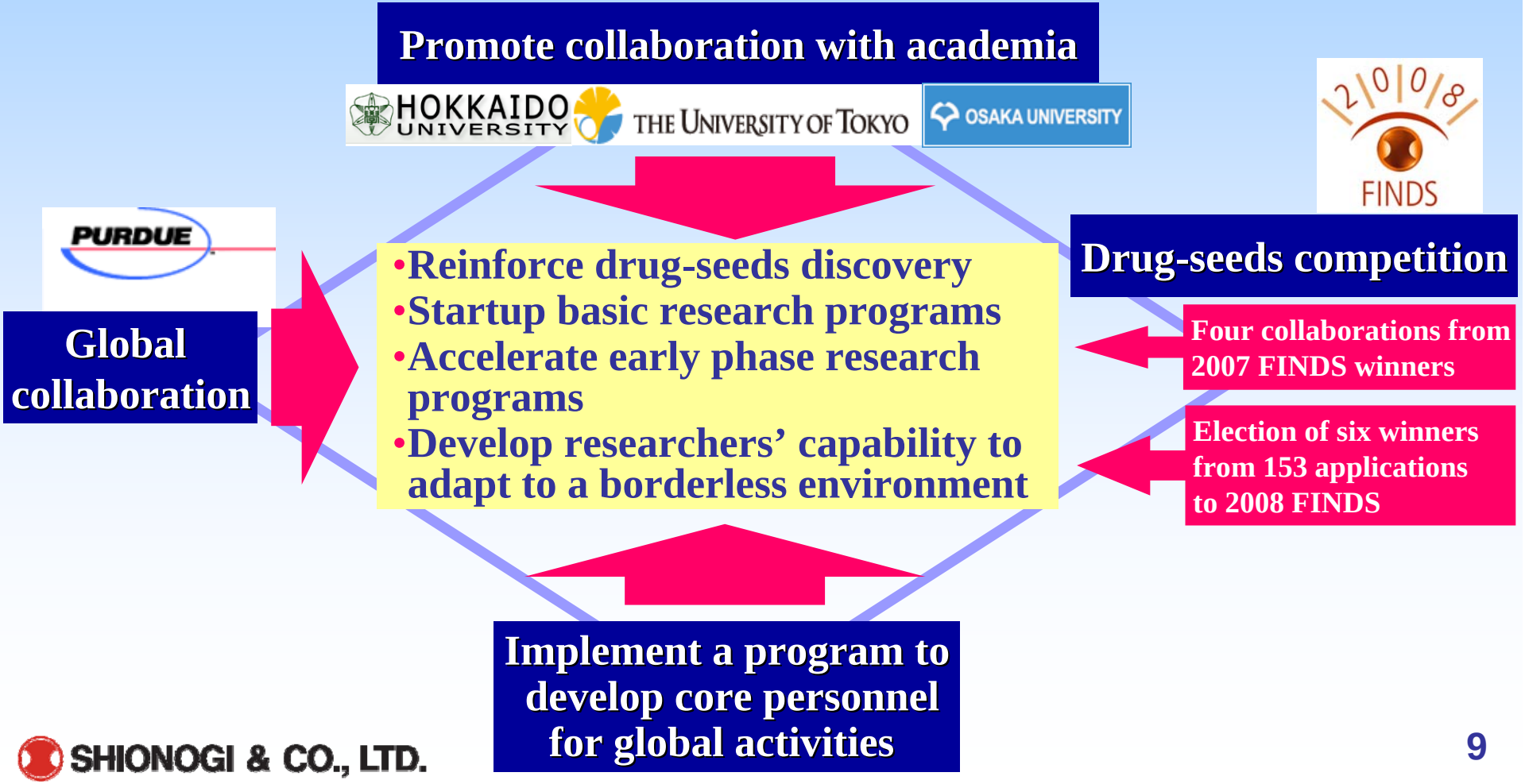
- Molecular-targeted anti-cancer drug: S-222611
- Anti-atopic dermatitis drug: S-444823 (Mar. 2009)
- Alleviator of opioid-induced adverse effects : S-297995

FTIH: First trial in human

Research

Achievements of FY2008 (2)

- Facilitate discovery of drug seeds and move them to research programs
- Develop researchers' capability to drive globalized drug discovery



Key Topics in FY2008

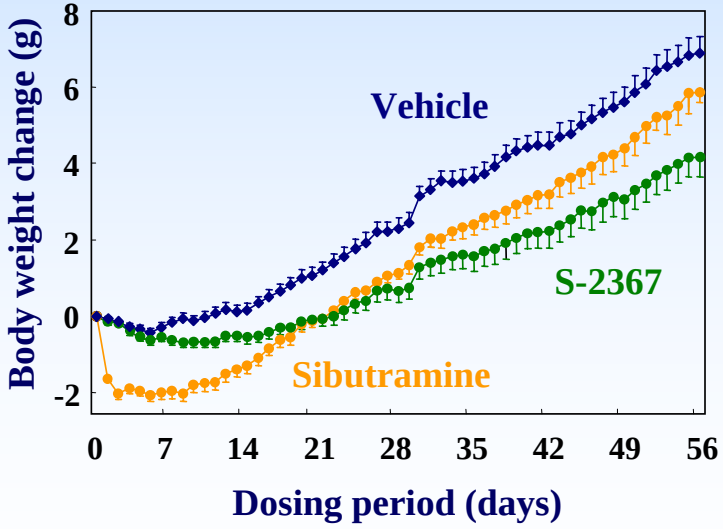
Research (Topics)

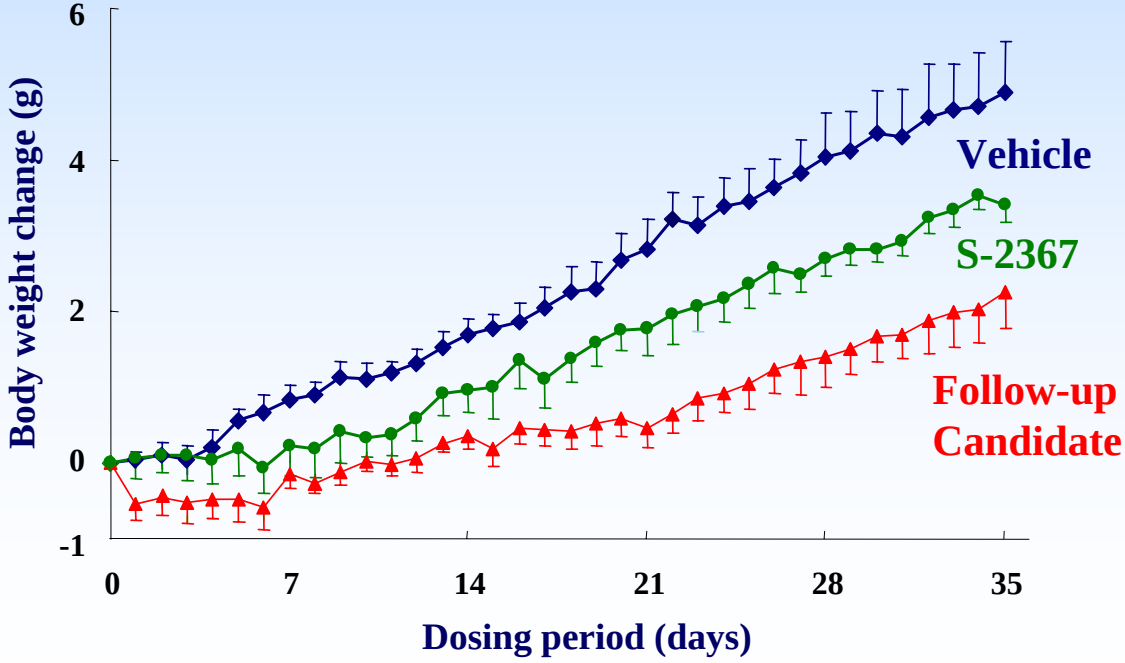
S-2367 Follow-up Program

- **Selected candidate with stronger anti-obesity activity at lower dose than S-2367**
  - **10-fold higher affinity to NPY Y5 receptor than S-2367**
  - **2-fold stronger anti-obesity activity at less than 1/5th the dose of S-2367**

Anti-obesity Activity

(High-fat Diet-induced Obese Mice)





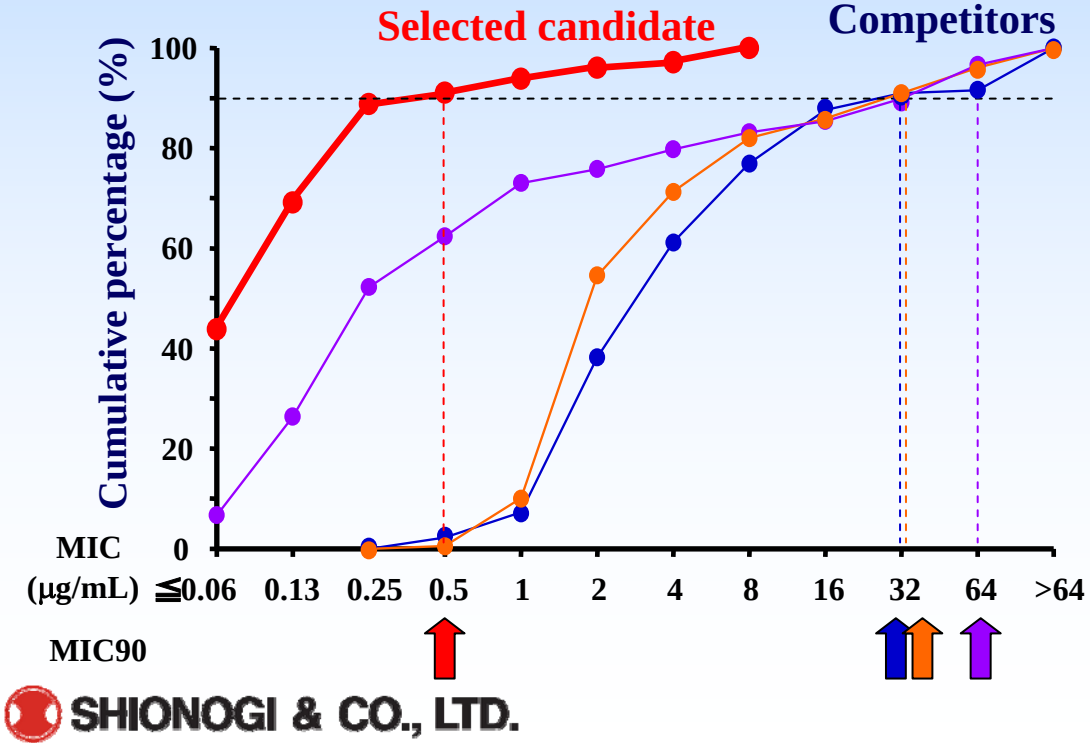
(Presented at Shionogi R&D Meeting 2006)

Research (Topics)

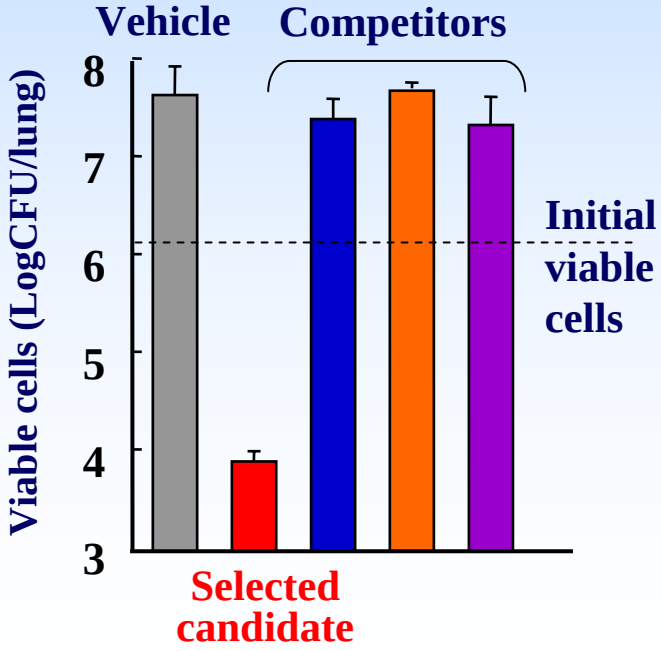
Injectable Cephalosporin against Gram-negative Bacteria

- **Selected candidate with strong antibacterial activity against wide spectrum of gram-negative bacteria**
  - **Strong antibacterial activity against *P. aeruginosa***
  - **High efficacy against multidrug-resistant *P. aeruginosa*, including metallo-β lactamase-producing strains**

Antibacterial Activity against *P. aeruginosa*
(177 strains clinically Isolated)



Murine lung infection model
by multidrug-resistant *P. aeruginosa*



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Research (Topics)

Strengths Acquired through the Second Medium-Term Business Plan and Future Issues

Acquired strengths

- **Research capability to keep on discovering globally competitive drug candidates**
- **Alliance capability to build win-win relationships with partners**
  - ➢ **Discover several drug candidates at the GSK joint venture or from collaborations with Purdue and the Institute of Medical Molecular Design, Inc**

Ongoing plan

- **Facilitate collaboration that harnesses external resources to move basic researches to innovative drug discovery**
  - ➢ **Collaboration based around the Shionogi Innovation Center for Drug Discovery**
  - ➢ **Adopt drug seeds via FINDS (PHarma-INnovation Discovery competition Shionogi)**

Future issues

- **Build up drug discovery technologies to achieve the top-level success rate in proof-of-concept studies**
  - ➢ **Technologies for molecular imaging and biomaker discovery**
  - ➢ **Establish animal models correlated to human diseases**

Research (Topics)

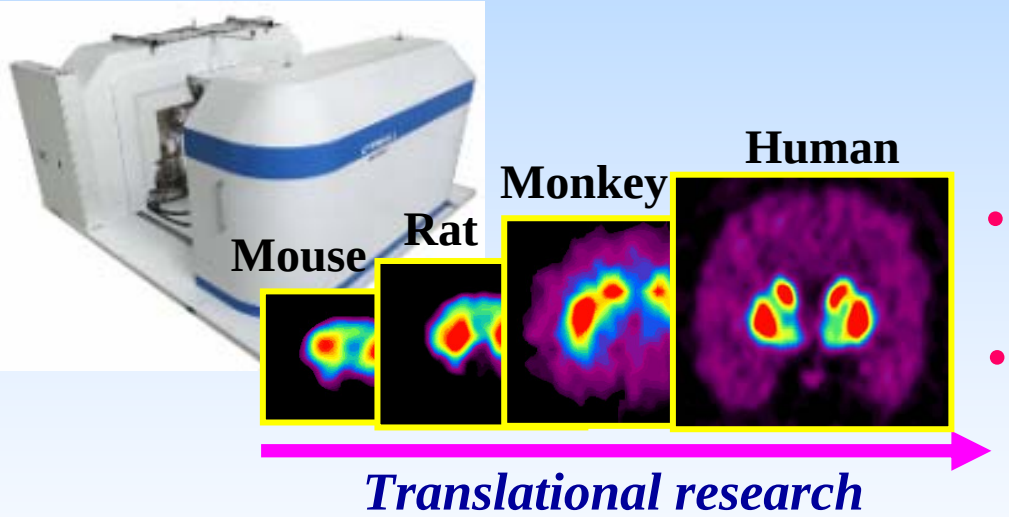
Targets and Measures for FY2009

- **Ensure FTIH for two or more compounds and DCS for four or more compounds**
  - Selecting and focusing on drug discovery research programs in target disease areas
- **Build up drug discovery technologies to achieve the top-level success rate in proof-of-concept studies**
  - Drug discovery technologies to close the gap between preclinical and clinical studies
    - Molecular imaging technology
      - Foundation of Osaka University Molecular Imaging Center and promotion of collaboration based on it
    - Discovery of biomarkers
      - Foundation of Ezose Science, Inc., a jointly owned venture company providing serum glycan analysis services
- **Set forth a grand design for drug discovery research for the Third Medium-Term Business Plan**
  - Plan research strategies and focus on the target therapeutic areas
  - Restructure research activities and plan to develop drug discovery technologies

Research (Topics)

Foundation of Osaka University Medicinal Molecular Imaging Center

- Understand phenomena of life on the molecular level and facilitate bridging studies from preclinical to clinical phases to improve efficiency of drug discovery researches and success rate in clinical studies
- Set up PET-related facilities, including a self-shielded cyclotron



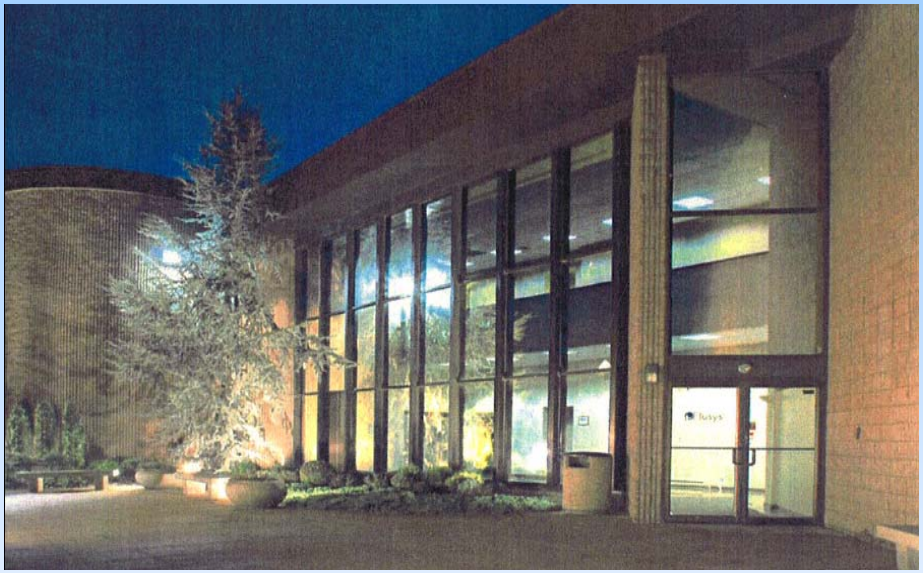
- Date of construction: Start in Sep. 2009
  Complete in Apr. 2010
- Address: Suita Campus, Osaka University

- Promote collaborations with Osaka University's Graduate School of Medicine and Faculty of Medicine
  - Establish contributed chairs
  - Adopt drug seeds via FLASH (PHarma-Link between Academia and SHionogi)

Research (Topics)

Foundation of Ezose Sciences, Inc.

- Company name: Ezose Sciences, Inc.
- Main business: Novel glycan analysis services
- Date of establishment: Mar. 2009
- Address: New Jersey, U.S.A.
- Initial capitalization: Shionogi 87%, Sumitomo Bakelite 13%



Unmet needs

Drug companion test
Personalized therapy
Disease biomarkers
Discovery of drug targets

Services to provide

1. High-throughput direct quantitation of glycans in sera
   - Glycan profiling marker
   - Single glycan marker
2. Identification of parent proteins by reverse-glycomics
   - Glycoprotein marker

From business experience to biomarker researches and development of novel technologies

Development

Takuko Sawada
Executive General Manager
Pharmaceutical Development Division
Shionogi & Co., Ltd.

Development

The Pharmaceutical Development Division Goals in the Second Medium-Term Business Plan

Goals

- Enrich infectious disease product line for and add pain and metabolic syndrome to new target areas
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Vision for FY2009

Simultaneously develop in-house products in the three regions of Japan, the USA and the EU

One to two Phase IIb and one Phase III products or three Phase IIb products

Establish a development base and start operations in the EU in addition to the USA

File NDAs both in the USA and the EU alone or through partnering

FTIH: First trial in human

Achievements in FY2008 (1): Post-NDA Filing Products

Approval/Launch	
Irbetan®	Launched in July 2008 (hypertension)
Differin® Gel	Launched in Oct 2008 (acne vulgaris)
Pirespa®	Launched in Dec 2008 (idiopathic pulmonary fibrosis)
Flomox® Fine Granules for Children	Approved in Nov 2008 (additional indication for adults)
Post-NDA Filing	
Duloxetine	Depression; post-NDA regulatory activities on-going

Development

Achievements in FY2008 (2): Phase I - III

Progress in development status	
S-2367	Phase IIb completed; the next clinical study in preparation
S-349572*	Phase IIa POC acquired; Phase IIb in preparation
S-021812	Phase II POC acquired; Asian multinational Phase III in progress
NS75B	Pivotal study in preparation
S-777469	Phase IIa completed in Japan; US POC study in progress
S-555739	Phase I multi-dosing study in the EU completed; POM study in progress
S-888711	Phase I multi-dosing study in Japan completed and in the USA initiated
FTIH Achievements	
S-297995	Initiated in Feb 2009
S-222611	Initiated in Mar 2009
S-444823	Initiating at the end of March 2009

FTIH: First trial in human
* Developed by Shionogi–GSK (JV)

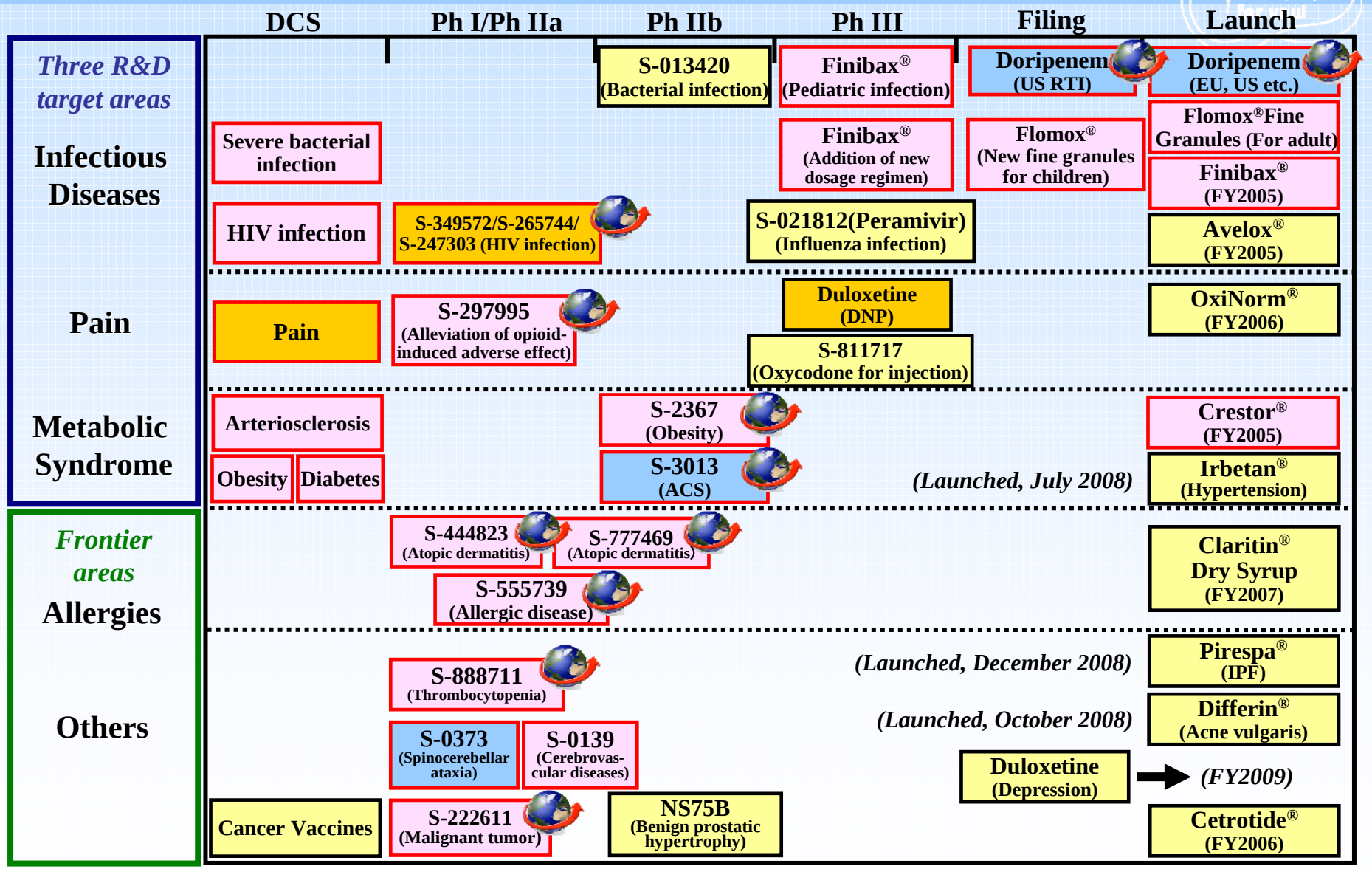
Development

Achievements in FY2008 (3): Progression of Life Cycle Management

Addition of new indication	
Duloxetine	**Diabetic neuropathic pain; Phase III in progress**
Post-marketing clinical studies	
Crestor®	**Efficacy on plaque regression in coronary arteries (COSMOS trial)** **Achievements: Analysis of IVUS; plaque regression confirmed; presentation at the scientific meeting of the Japanese Circulation Society (March 22, 2009)**
Imunace®	**Pharmacogenomics study with renal cell carcinoma patients** **Achievements: CRF locked; under data analysis**
Claritin®	**Examination on PPK* in pediatric and adult patients** **Achievements: Patient enrolment completed; under data analysis**
Development for new dosing route	
Oxycodone for injection	**Clinical study by intravenous injection** **Achievements: patient accrual started**

PPK: Population Pharmacokinetics

Pipeline Enrichment by In-house Compounds (As of March 2009)



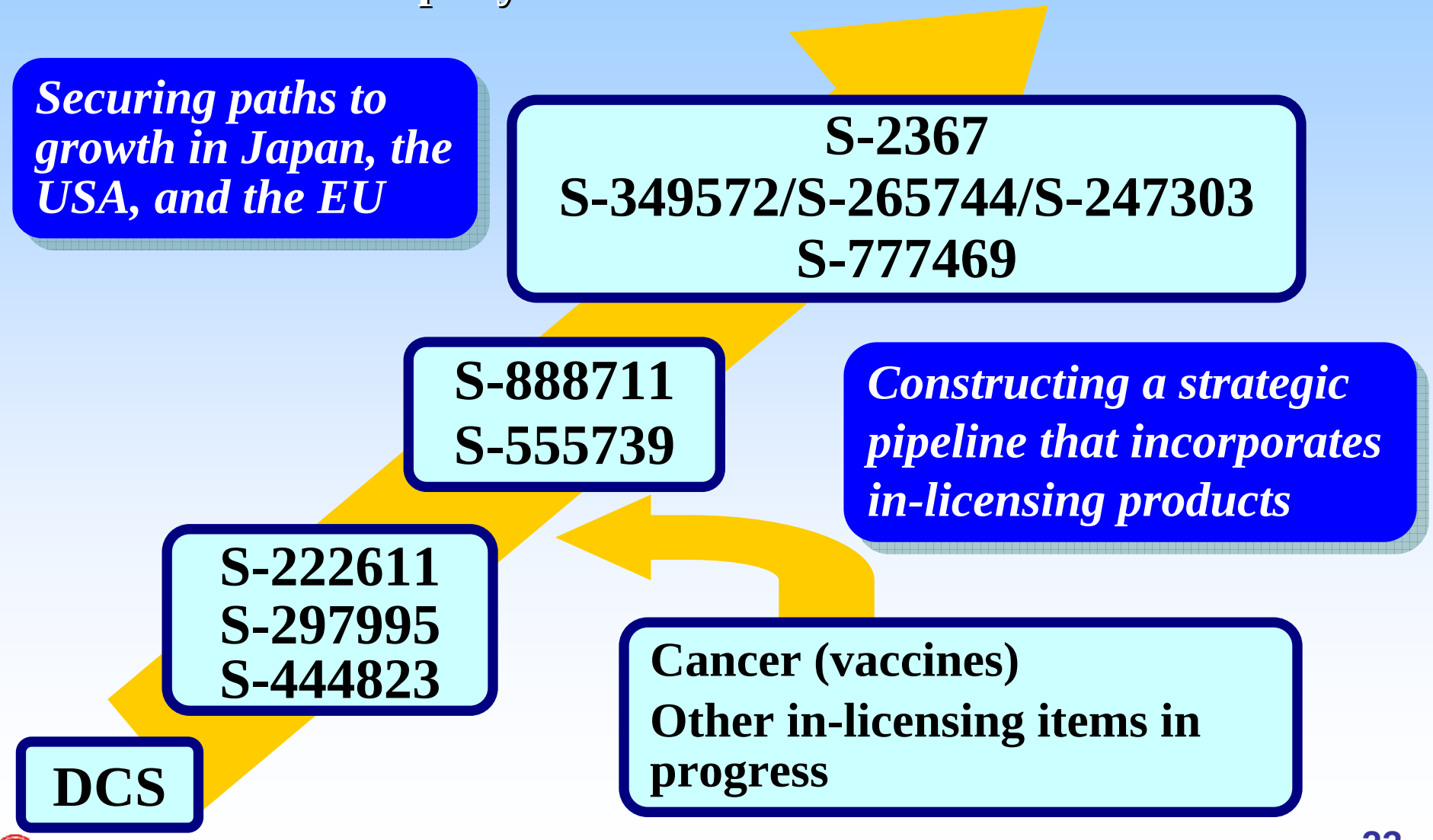
IPF: Idiopathic pulmonary fibrosis, DNP: Diabetic Neuropathic Pain, RTI: Respiratory Tract Infection, ACS: Acute coronary syndromes

In-house | Co-development | Out-licensed | In-licensed

Developing in-house products globally

Development

Steadily Advance the Development of Global Compounds and Create the Company's New Growth Drivers



Development

Target Milestone for FY 2009 (1):
NDA Filing, Launch and LCM of Domestic Strategic Products

Approval/Launch	
Duloxetine	Depression
Flomox®	New fine granules for children
NDA filing	
S-021812	Influenza virus infection
Duloxetine	Diabetic neuropathic pain (DNP)
Doripenem	Additional indication for adults; Dose of 1g t.i.d.

Target Milestones for FY2009 (2): Phase I - III

Make appropriate Go/No-Go decisions	
S-2367	Consult FDA; initiate additional Phase IIb
S-349572* and S-777469	Go/No-Go decision on Phase IIb
S-555739, S-888711, S-297995 and S-444823	Go/No-Go decision on Phase IIa
S-222611	Initiate dosing in Phase Ib; negotiate out-licensing
Progress to FTIH	
2 products	

FTIH: First trial in human
* Developed by Shionogi–GSK (JV)

Core Development Products

- **Product characteristics**
- **Indications**
- **Non-clinical and clinical data, etc.**

Infectious Disease Area

S-349572/S-265744/S-247303: Profile

- Developed by Shionogi-GlaxoSmithKline Pharmaceuticals, LLC
- HIV integrase inhibitor (oral)
- Characteristics
  - Strong anti-HIV activity in inhibiting virus replication in vitro
  - Good in vitro resistance profile
  - Good pharmacokinetic profile
  - Low risk of drug-drug interactions

- S-349572: FTIH in the USA completed; Phase IIa under data analysis; Phase IIb in preparation
- S-265744/S-247303: FTIH in the USA

S-349572: Summary of First-Time-in-Human Study

- **Pharmacokinetics**
  - The PK profile suggests once-daily, low dose will achieve a therapeutic concentration
  - The tablet had a reasonable relative bioavailability vs suspension
  - Food did not impact exposure
  - No impact on CYP3A probe
- **Safety**
  - Single and multiple doses well tolerated by healthy subjects

Development (Core development products: Infectious disease area)

S-349572: Phase IIa

- Phase IIa, POC study using once-daily, 10-day monotherapy in HIV-infected subjects
  - Dosing completed and data under analysis
- Proof of concept has been achieved
- Results will be presented at a relevant scientific conference in the near future
- Phase IIb study in preparation

S-021812 (Peramivir): Profile

- Licensed from BioCryst Pharmaceuticals, Inc. (USA)
- Anti-influenza virus drug (neuraminidase inhibitor; injection)
- Characteristics
  - ➢ Highly active against influenza A and B viruses
    - ➔ More potent against influenza B virus than Tamiflu®
  - ➢ Strong activity against highly pathogenic avian influenza virus (H5N1)
    - ➔ Strong affinity to influenza neuraminidase and slow off-rate
      Possibly effective with a single-dose administration
  - ➢ Potentially potent even if dosing is delayed (administration later than 48 hours after onset of infection)
  - ➢ Broad indications from ordinary seasonal influenza to influenza in patients with high risks

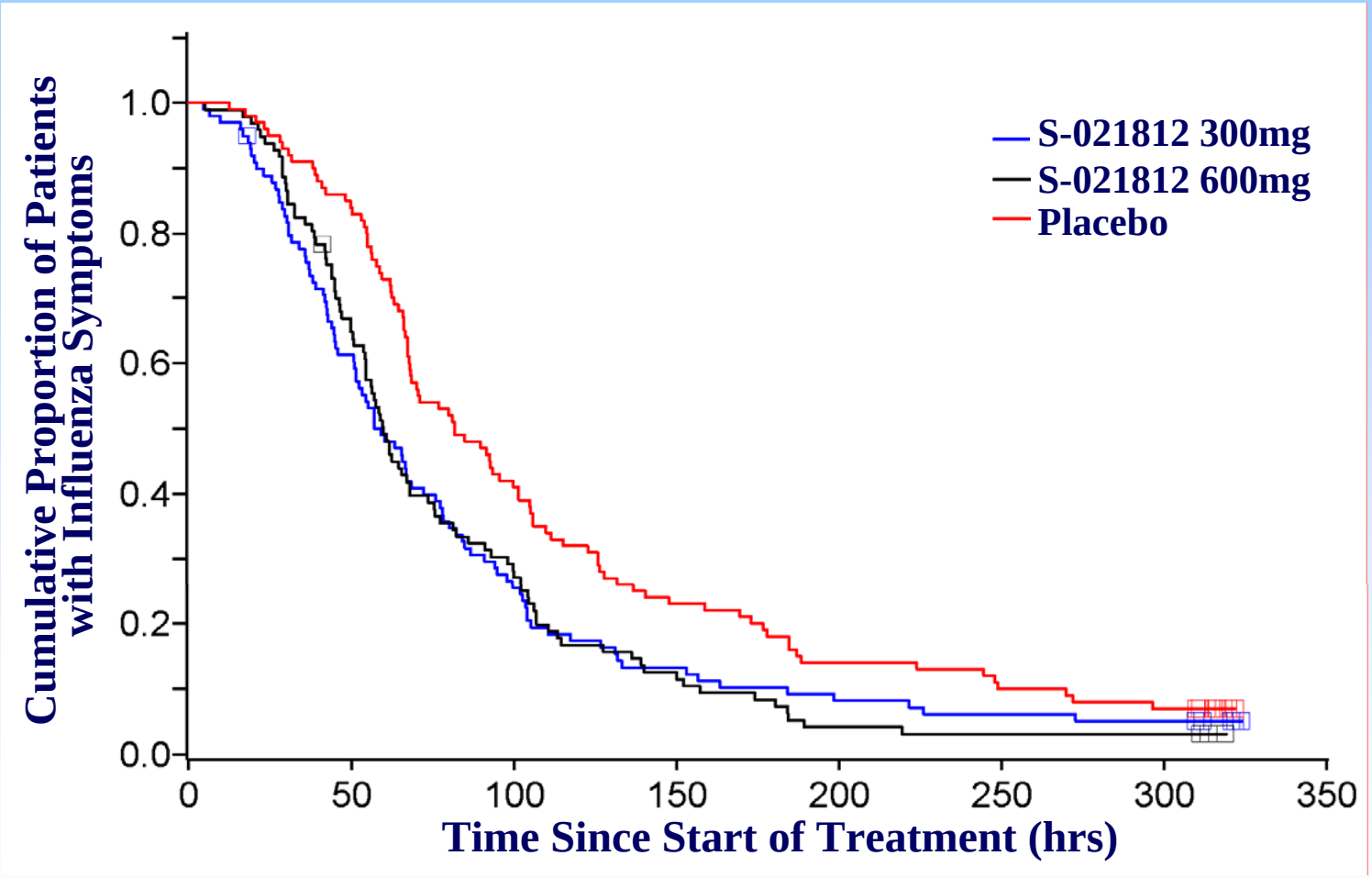
S-021812: Results of Phase II Study

- **Indication**
  - Influenza virus infection
- **Study design**
  - Double-blind, placebo-controlled, multicenter study
- **Administration route**
  - Single intravenous injection
- **Efficacy**
  - Times to alleviation of symptoms and to resolution of fever significantly reduced compared to placebo
- **Safety**
  - No serious adverse events reported
  - Well tolerated, with a similar adverse event profile to that of placebo

High efficacy and good safety profile were demonstrated
Asian multinational Phase III study in progress

Development (Core development products: Infectious disease area)

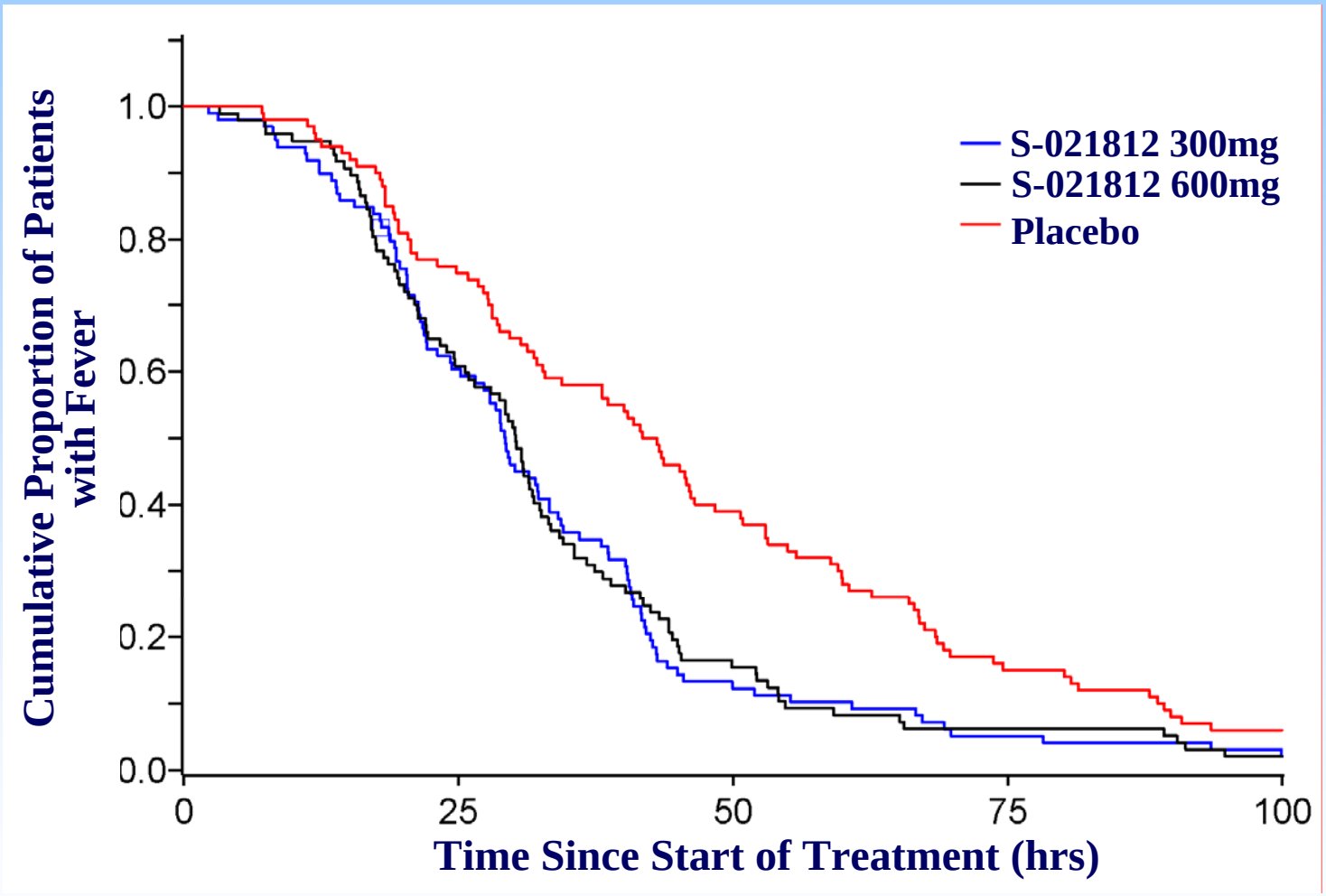
S-021812: Time to Alleviation of Symptoms in Phase II



Time to alleviation of symptoms significantly reduced compared to placebo

Development (Core development products: Infectious disease area)

S-021812: Time to Resolution of Fever in Phase II



Time to resolution of fever significantly reduced compared to placebo

S-021812: Outline of Phase III Studies

- **Single-dose study**
  - ➢ **Indication**
    - Influenza virus infection
  - ➢ **Study design**
    - Double-blind, oseltamivir phosphate-controlled, multinational study (Japan, Korea, and Taiwan)
- **Study in patients with high risks**
  - ➢ **Indication**
    - Influenza virus infection in patients with high risks
  - ➢ **Study design**
    - Double-blind, non-controlled, multicenter study

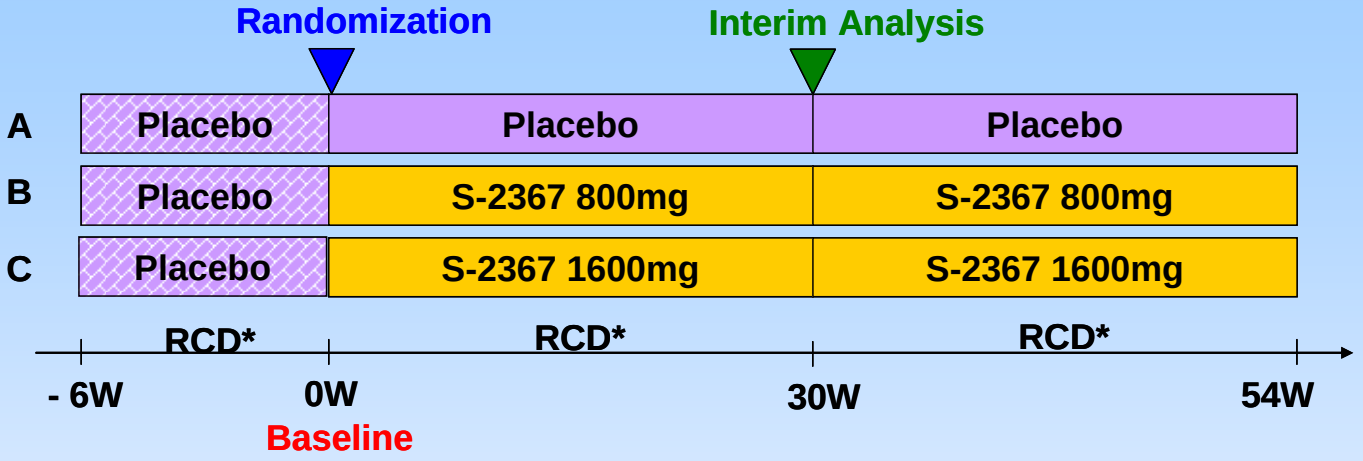
Plan to complete the studies within this influenza season (2008–2009)

Metabolic Syndrome Area

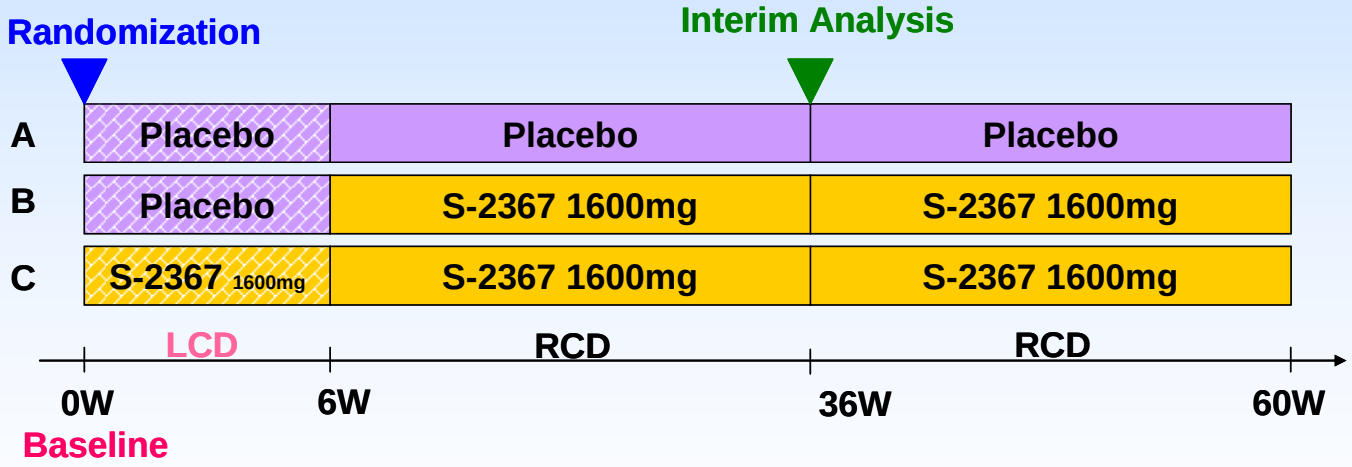
Development (Core development products: Metabolic syndrome area)

S-2367: Phase IIb Study Design

Reduced-Calorie Diet (RCD) Study
BMI 30-45
MITT 656 subjects



Low-Calorie Diet (LCD) Study
BMI 30-45
MITT 771 subjects



LCD: Low-Calorie Diet; restricted to 900-950 kcal daily
RCD: Reduced-Calorie Diet; recommended daily calorie intake for individual subject reduced by 800 kcal
MITT: Subjects who received at least one dose of randomized study drug and had at least one scheduled body weight measurement data collected after receiving the drug

Development (Core development products: Metabolic syndrome area)

S-2367: Phase IIb Study Results (Efficacy)

- **Reduced-Calorie Diet (RCD) Study**

Body weight reduction (reduction rate) from baseline (at randomization)		
Placebo	0.8 kg (0.9%)	
Strongest performing group 800 mg	3.8 kg (3.9%)	p<0.0001
Subjects who lost ≥5% from baseline		
Placebo	12%	
800 mg	35%	p<0.0001

(Met FDA's the criteria*)

- **Low-Calorie Diet (LCD) Study**

Body weight reduction (reduction rate) from baseline (at randomization)		
Placebo/Placebo	4.3kg (4.4%)	
Strongest performing Placebo/1600 mg	7.1 kg (6.9%)	p<0.0001
Subjects who lost ≥5% from baseline		
Placebo/Placebo	35%	
Placebo/1600 mg	52%	p<0.0001

All numerical values indicate MITT
LOCF: Last scheduled body weight measurement projected forward for missing data
* Draft Guidance for Industry, Developing Products for Weight Management, Feb. 2007

Development (Core development products: Metabolic syndrome area)

S-2367: Phase IIb Study Results (Safety)

- S-2367 was well tolerated in all treatment groups

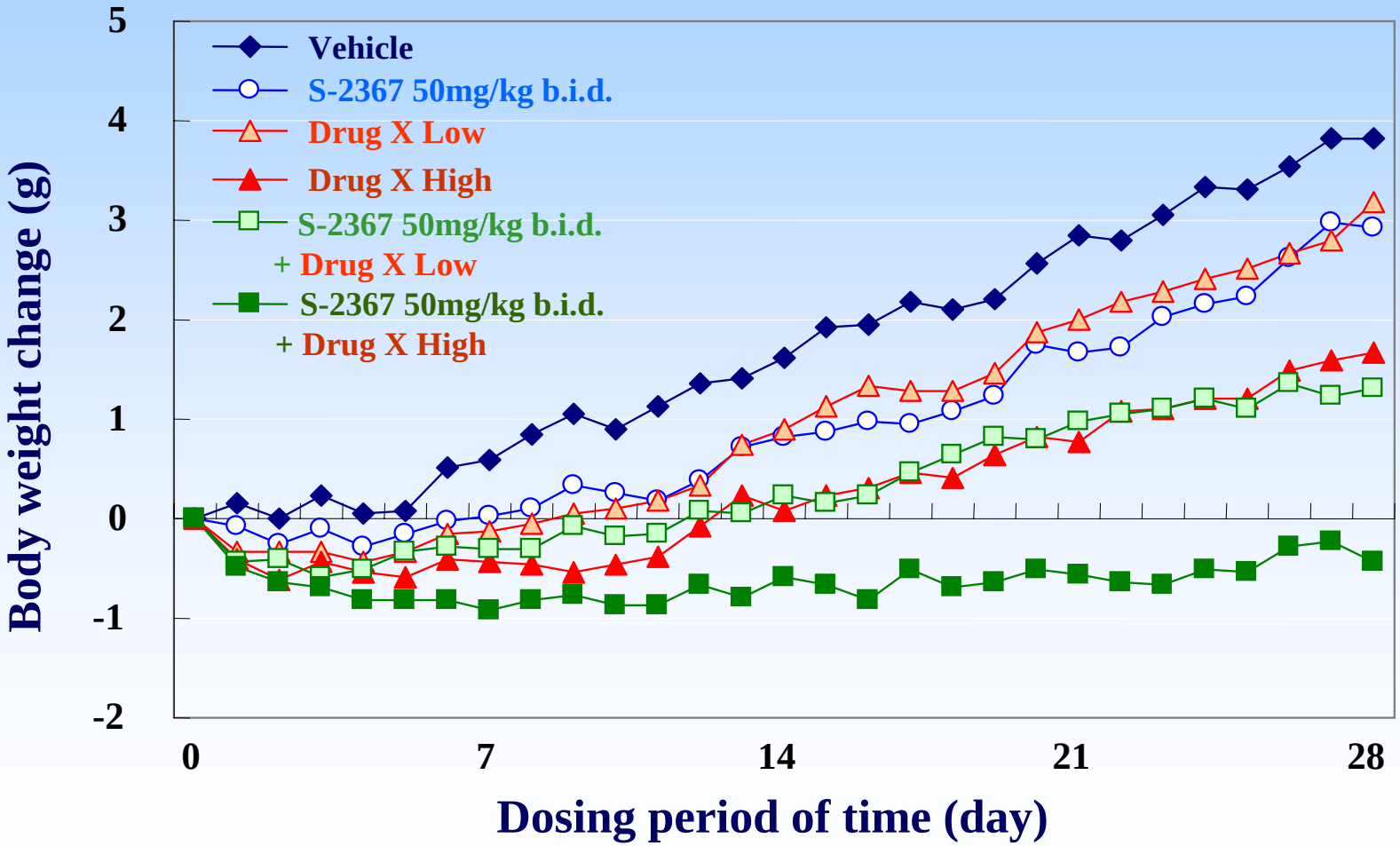
Withdrawal due to adverse events (AEs)			
RCD Study	Placebo: 7%	800 mg: 7%	1600 mg: 7%
LCD Study	Placebo: 5%	Placebo/1600 mg: 7%	1600 mg/1600 mg: 10%

- Most frequent AEs: nasopharyngitis, upper respiratory infection, sinusitis, headache
  → No significant difference in incidence of AEs between S-2367 and placebo groups
- Psychological assessment → No psychiatric effect
- Mild decrease in hematocrit, hemoglobin and red blood cell count, and mild increase in reticulocytes → Minor magnitude and within normal range

Met the criteria in the FDA's draft guidance by year-long treatment
Confirmed attractive potential of S-2367 as NPY Y5 receptor antagonist

S-2367: Combination of S-2367 and Drug X

Diet-Induced Obese (DIO) Mouse Study



S-2367: Future Plan

- Focus on partnering (FY2009, 1Q)
- Planning FDA meeting (FY2009, 1Q)
  - Discuss combination therapy
- Planning development in Japan (FY2009, 2Q)
- Publish Phase IIb results at a relevant scientific conference in the near future

Crestor®: IVUS Trial (COSMOS Study)

- **Construction of evidence for efficacy and safety of Crestor**
  - **Patients with high-risk cardiovascular events targeted**
  - **Plaque regression on coronary artery observed**
  - **Safety during long-period treatment confirmed**
  - **Conducted in conjunction with AstraZeneca**
- **Presentation at the 73rd Japanese Circulation Society (Osaka, March 22, 2009)**

Crestor®: IVUS Trial (COSMOS Study)

- **Efficacy**
  - The first achievement of coronary plaque regression in Japanese patients with stable coronary artery disease
  - Primary endpoint: plaque volume regression was -5.07% (mean, p<0.0001 vs. baseline)
  - In spite of over 70% patients were prior to use lipid lowering drugs before treatment, rosuvastatin
    - Reduced significantly LDL-C to 82.9mg/dL (38.6% reduction, p<0.0001 vs. baseline)
    - Increased significantly HDL-C to 55.2mg/dL (19.8% elevation, p<0.0001 vs. baseline)
    - Improved significantly LDL-C/HDL-C ratio to 1.56 (47.5% reduction, p<0.001 vs. baseline)
- **Safety**
  - Well tolerated in 2.5 mg through 20 mg

Allergies, Cancer and Pain Areas

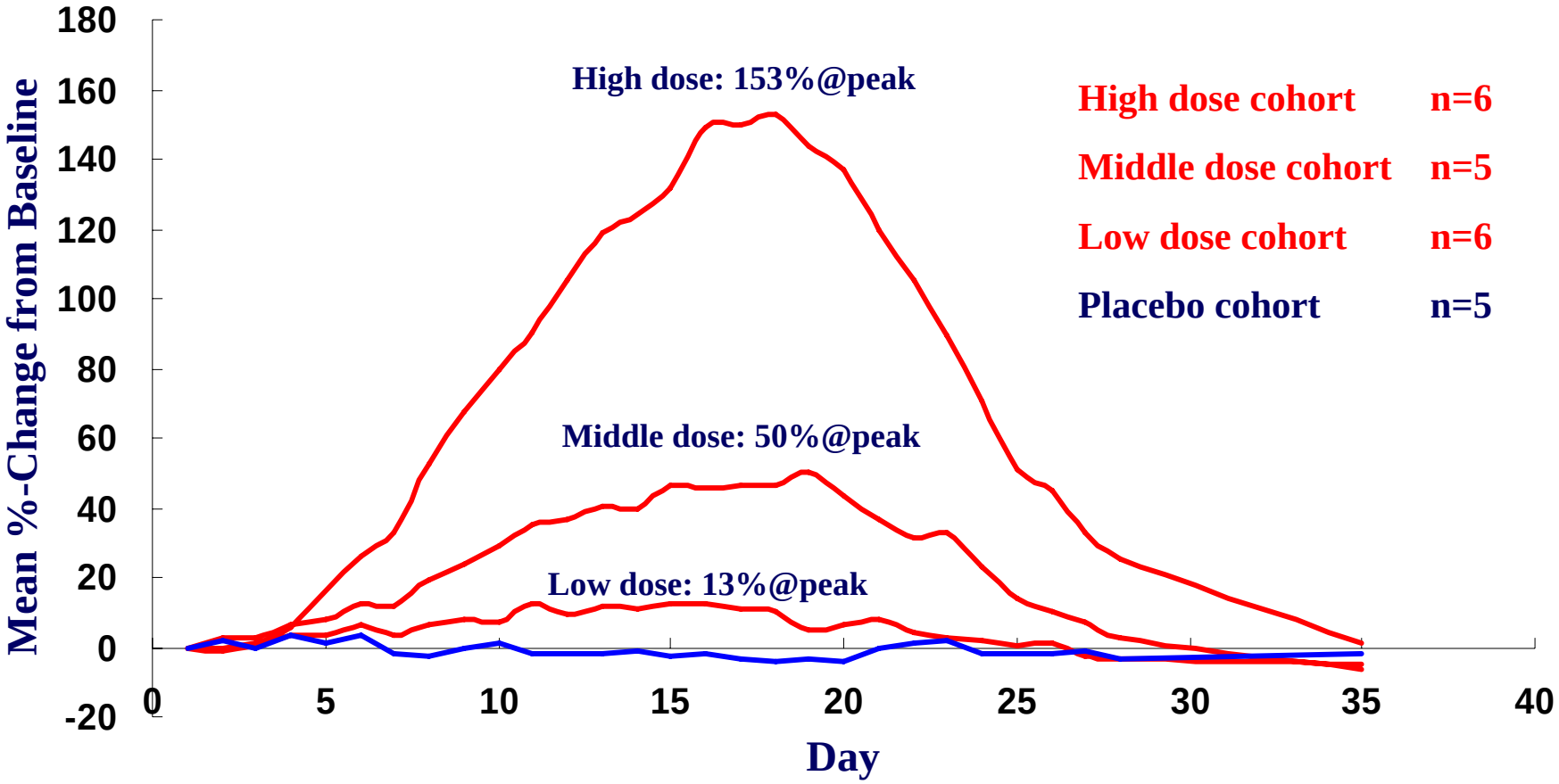
S-888711: Profile

- **Indications: Various diseases with thrombocytopenia**
- **Thrombopoietin receptor agonist (oral)**
- **Developmental stage**
  - **Japan: Phase I multiple dose study completed**
  - **USA: Phase I multiple dose study in progress**
- **Pharmacological properties from clinical studies in Japan**
  - **Good pharmacokinetic profiles**
    - **Increases Cmax and AUC dose-dependently**
    - **Little food effects on PK profiles**
    - **Little ethnic differences on PK profiles (Japanese vs. Caucasian)**
  - **Fast onset of platelet increase by q.d. dosing schedule**
    - **Increases in platelet counts are correlated with Cmax and AUC**
  - **Good tolerability and safety profiles up to the maximum testing dose**
    - **No characteristic profile of adverse events due to S-888711**
- **Upcoming clinical studies**
  - **Phase II POC study (global)**

Development (Core development products: Allergies, Cancer and Pain areas)

S-888711: Change in Platelet Counts

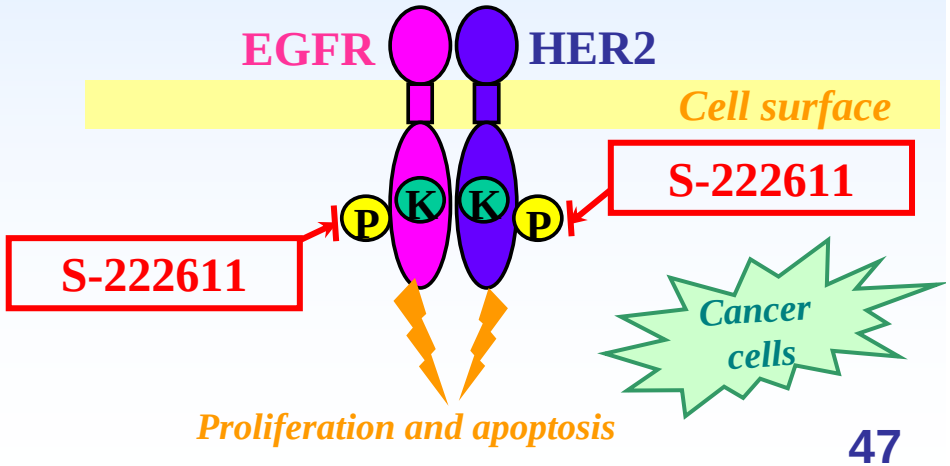
Multiple dosing for 14 consecutive days (q.d.) in healthy Japanese males



q.d.: once a day

S-222611: Profile

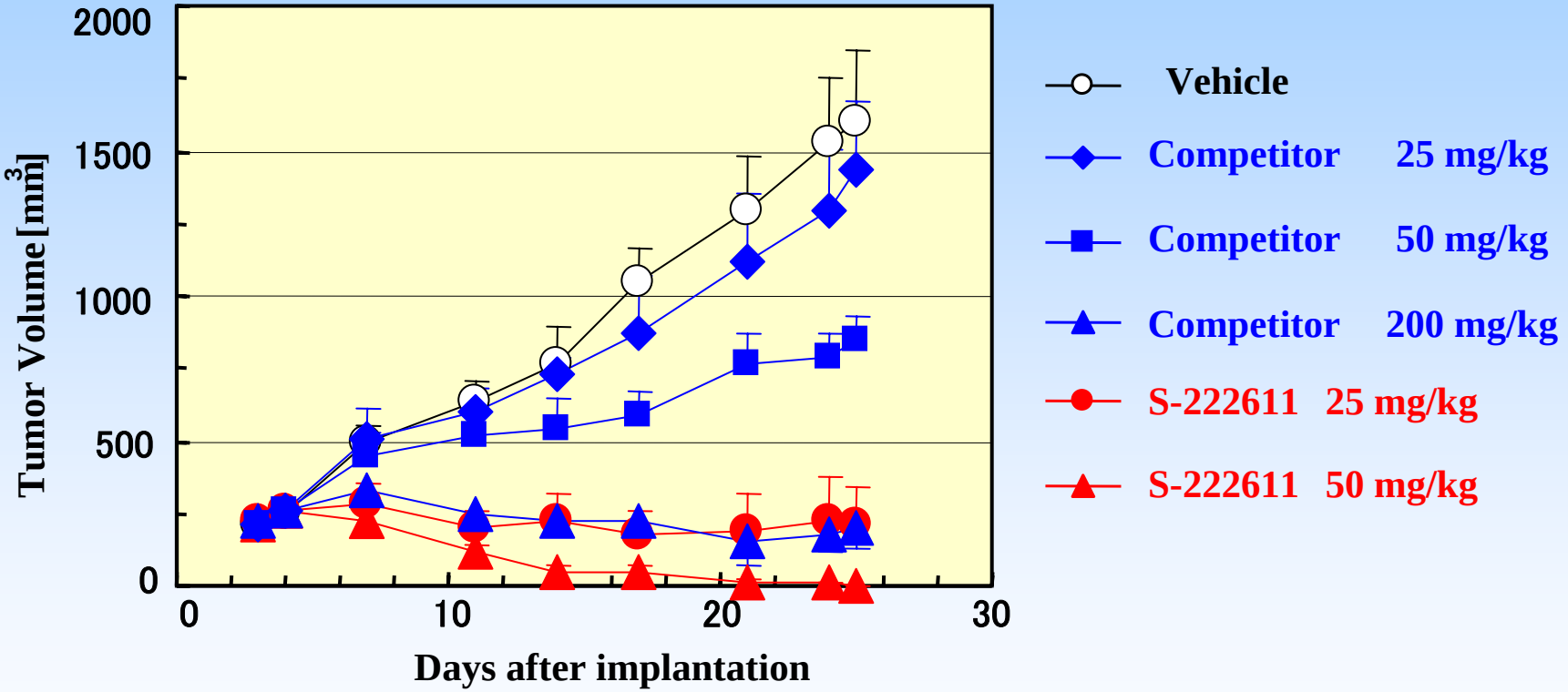
- **Indication: Cancers over-expressing HER2 and/or EGFR**
- **Mechanism: Orally active, reversible dual tyrosine kinase inhibitor of HER2 and EGFR (oral)**
- **Pharmacological properties from non-clinical studies**
  - **Specific and strong inhibitor against HER2 and EGFR**
  - **Superior anti-tumor activities with q.d. dosing versus a competitor with the same mechanism of action in several antitumor models (in vivo)**
  - **Superior anti-tumor activities versus the competitor in bone metastasis and brain metastasis of breast cancer models**
- **Development stage**
  - **Phase I single dose study (EU)**
- **Upcoming clinical studies**
  - **Phase I multiple dose study (EU)**



Development (Core development products: Allergies, Cancer and Pain areas)

S-222611: Anti-tumor Activities

Administered once daily for 21 days from day 4 post-implantation to immuno-deficient mice implanted subcutaneously with human gastric carcinoma cells



- Much superior activity in suppressing tumor growth versus the competitor
- Remarkable tumor regression at a half of MTD (50 mg/kg) of S-222611, which was superior to that observed at MTD (200 mg/kg) of the competitor

MTD: Maximum Tolerated Dose

Development (Core development products: Allergies, Cancer and Pain areas)

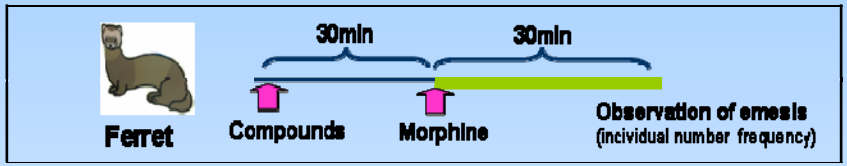
S-297995: Profile

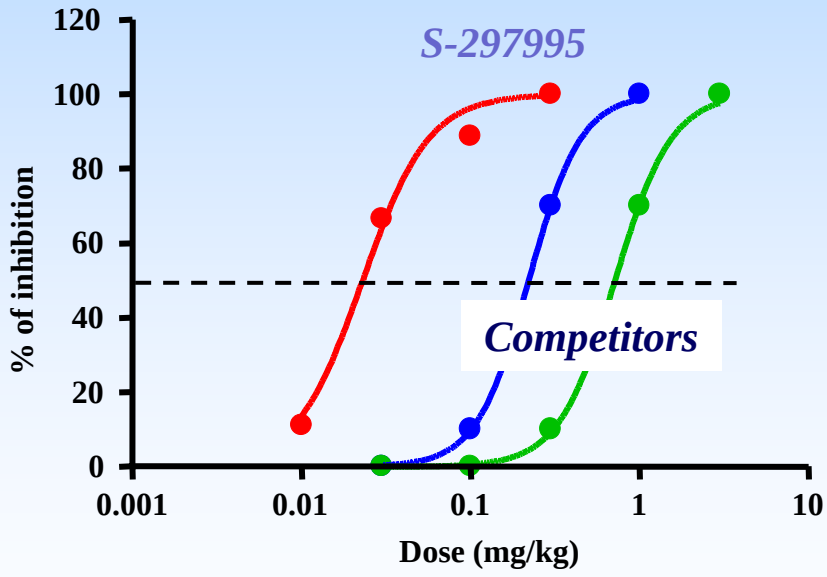
- **Indication: Relief of opioid-induced gastrointestinal symptoms such as nausea, vomiting and constipation**
- **Mechanism: Orally active peripheral opioid receptor antagonist**
- **Pharmacological characteristics (non-clinical)**
  - **Suppressed morphine-induced nausea and vomiting in ferret model**
  - **Suppressed morphine-induced small intestinal hypomotility in rat model**
  - **Showed anti-emetic and anti-constipation effects 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 single dose study in Japan in progress**
- **Future plan**
  - **Phase I multiple dose study in the USA**

Development (Core development products: Allergies, Cancer and Pain areas)

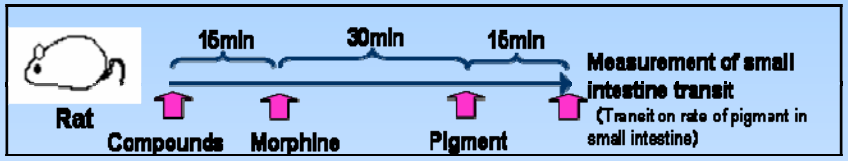
S-297995: Profile

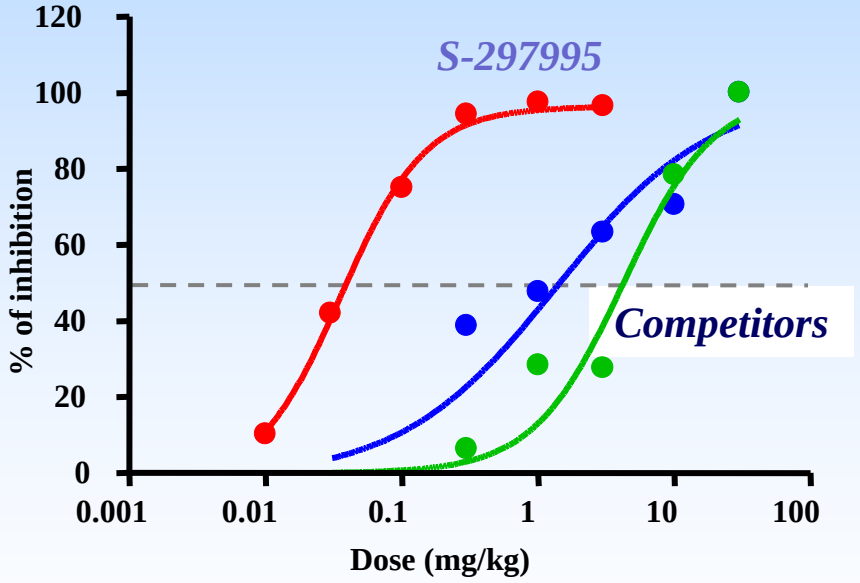
Anti-emesis





Anti-constipation





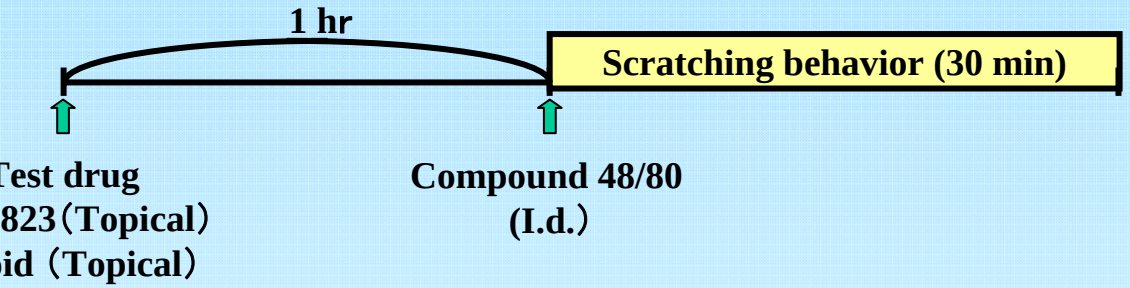
S-297995 suppressed morphine-induced nausea, vomiting and small intestinal hypomotility with lower doses versus competitors

S-444823: Profile

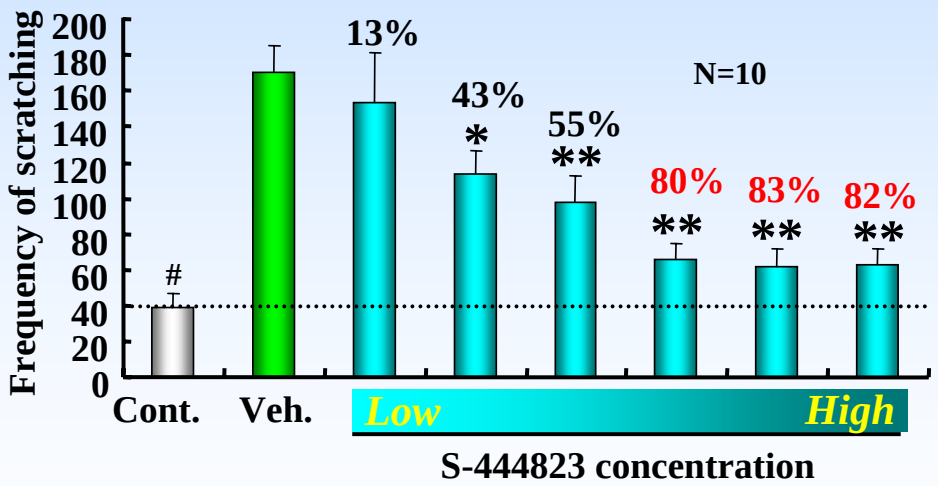
- Indication: Atopic dermatitis, eczema/dermatitis with pruritus
- Mechanism: Cannabinoid receptor agonist (topical)
  Follow-up compound of S-777469
- Characteristics (non-clinical)
  - Strongly reduced scratching behavior induced by various pruritic agents in mouse model
  - Strongly improved dermatitis score in mouse AD model
  - Good safety profile
- Developmental status: Phase I study in progress in Japan
- Upcoming clinical studies: Phase IIa study (to begin in FY2009)

S-444823: Profile

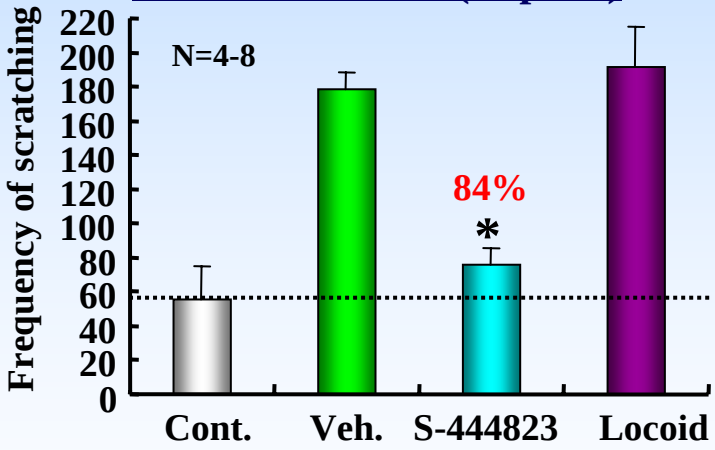
Compound 48/80-induced scratching behavior



S-444823 (Topical)



S-444823, Locoid (Topical)

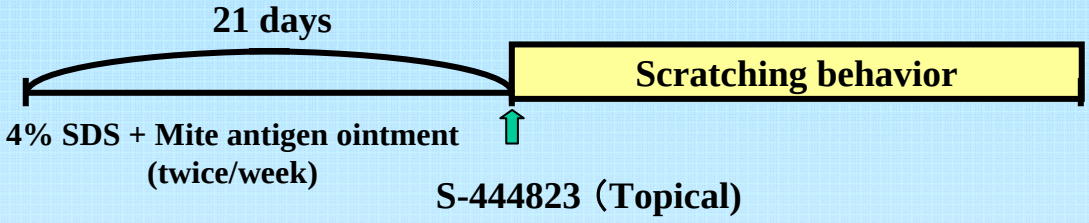


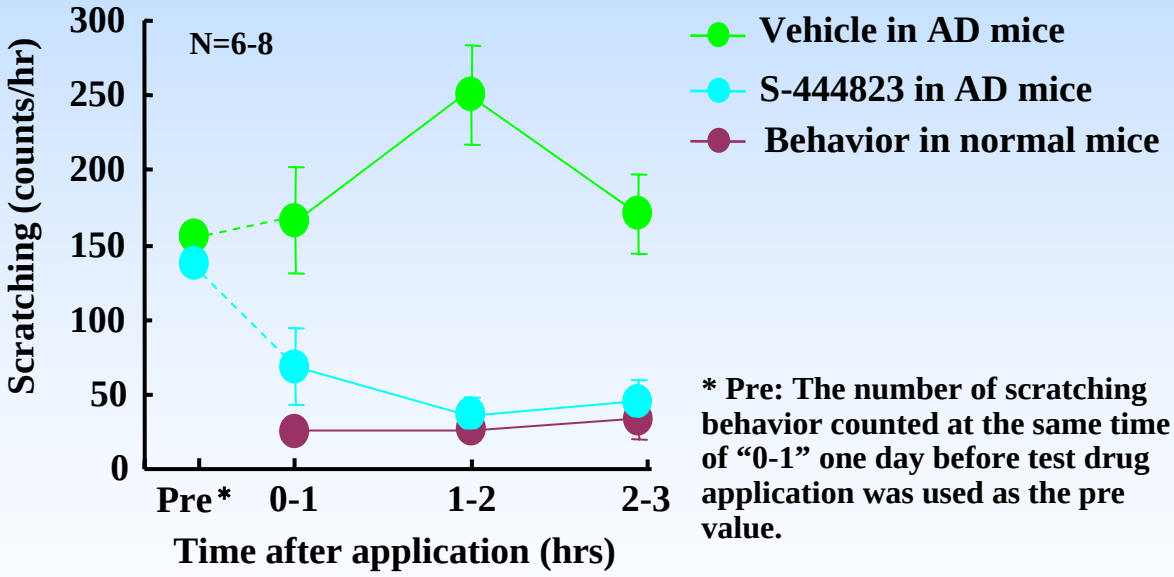
S-444823 significantly inhibited scratching behavior induced by intradermal injection of mast cell activator (compound 48/80) in mice

Development (Core development products: Allergies, Cancer and Pain areas)

S-444823: Profile

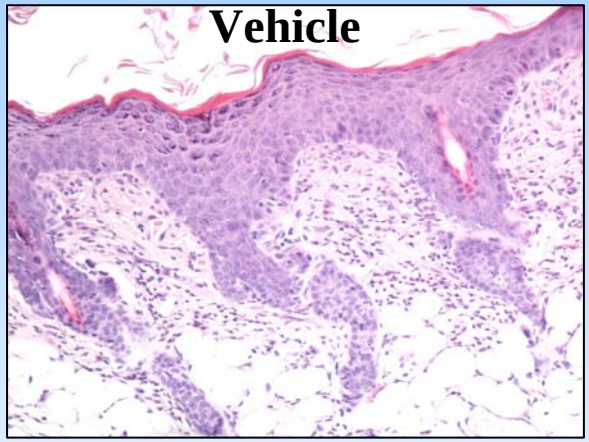
Scratching behavior in atopic dermatitis model

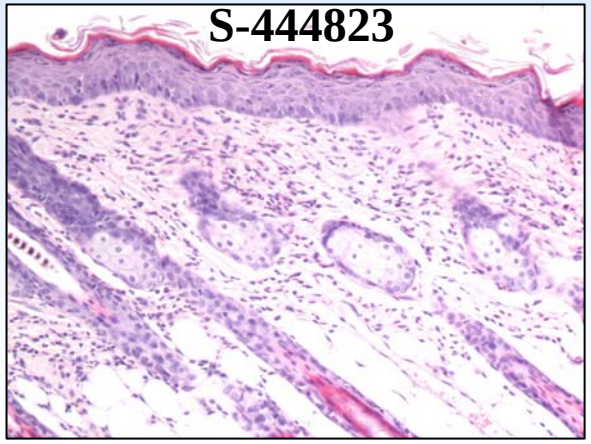




* Pre: The number of scratching behavior counted at the same time of "0-1" one day before test drug application was used as the pre value.

Epidermal tissue after 13-day treatment





- Suppression of scratching behavior was observed immediately after topical application of S-444823 in chronic dermatitis model
- Dermatitis symptoms and thickened epidermis were also improved after 13-day treatment

Development (Core development products: Allergies, Cancer and Pain areas)

Cancer Vaccines: Profile

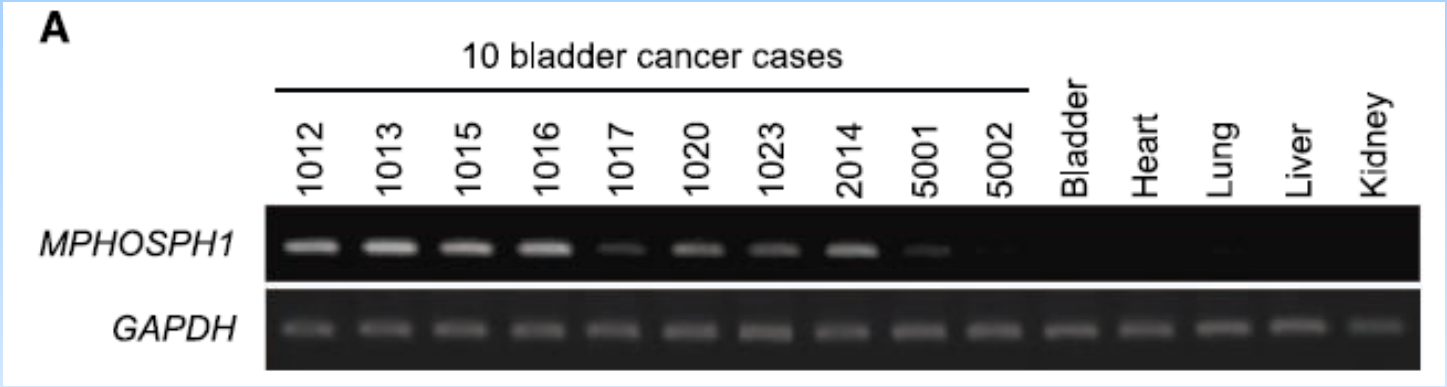
- **Licensed from OncoTherapy Science, Inc. (Japan)**
- **Indications**
  - **Bladder cancer**
  - **Esophageal cancer and squamous cell carcinoma of the lung; bronchial and head and neck cancers**
- **Mechanism**
  - **Peptide cancer vaccine**
- **Characteristics**
  - **Pepetides derived from proteins selectively over-expressed in cancer cells**
  - **Target proteins that are critical for cancer cell growth**
  - **CTL induction confirmed in translational research in bladder and esophageal cancers, and some patients who had failed standard therapy had response to the vaccines**
- **Development stage**
  - **Non-clinical**
- **Future plan**
  - **Phase Ib studies in Japan**

CTL：Cytotoxic T Lymphocyte

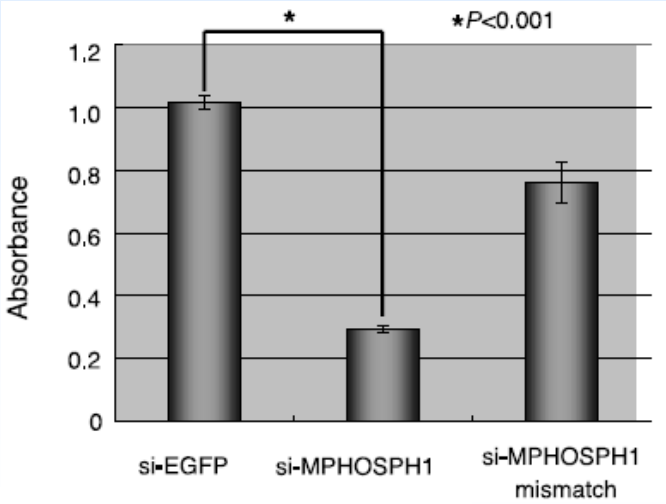
Development (Core development products: Allergies, Cancer and Pain areas)

Cancer Vaccines: Profile

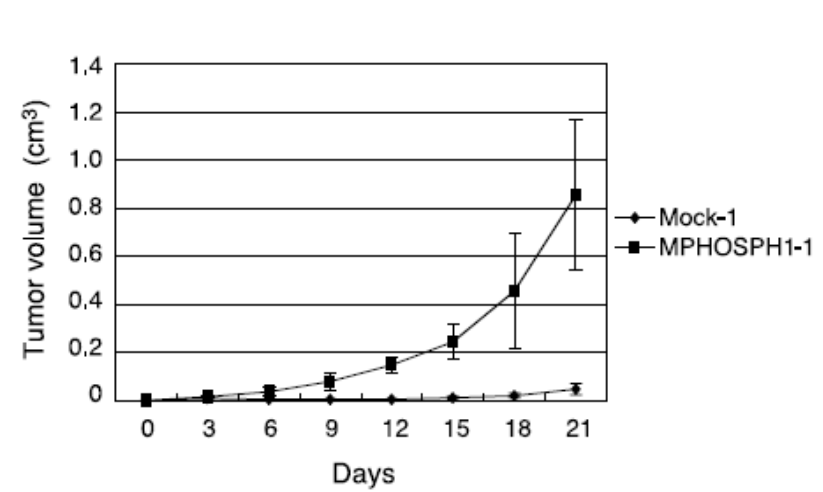
1. A target protein, MPHOSPH1, is selectively over-expressed in bladder cancer



2. Suppression of bladder cancer growth by siRNA



3. Enhanced tumor growth in mice transplanted with NIH3T3 cells transfected with target gene



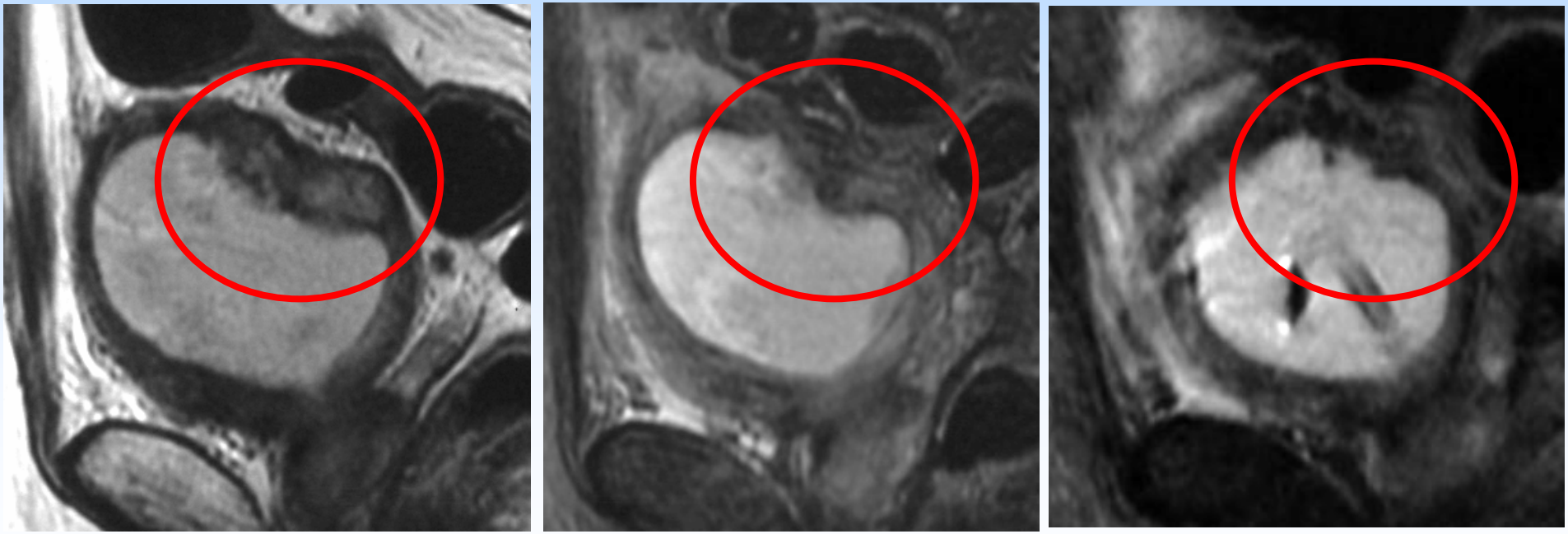
Kanehira et al., Cancer Res 2007; 67 3276-3285

Development (Core development products: Allergies, Cancer and Pain areas)

Bladder Vaccine: Translational Research in Patients

Pelvic MRI

Before	After 1 course	After 2 courses
11Jul07	17Aug07	21Sep07



(These data were provided by Prof. Fujioka, Iwate Medical University)

Sciele R&D

Edward J. Schutter

President, Chief Operating Officer and Director

Sciele Pharma, Inc.

Sciele's Focused Therapeutic Areas

Sciele Pharma, Inc. is a pharmaceutical company specializing in sales, marketing and development of branded prescription products focused on Cardiovascular, Diabetes, Women's Health and Pediatrics.

- **Cardiovascular and Diabetes Products: treat patients with high cholesterol, hypertension, high triglycerides, unstable angina and Type 2 diabetes**
  - **Sular Geomatrix, Nitrolingual® Pumpspray, Prandin®, Prandimet®, Fortamet®, Fenoglide™**

Sciele's Focused Therapeutic Areas

- **Women's Health Products: designed to improve the health and well-being of women and mothers and their babies**
  - **Prenate DHA®, Prenate Elite®, Ponstel®**

- **Pediatrics Products: treat allergies, asthma, anaphylaxis, and attention deficit/hyperactivity disorder (ADHD).**
  - **Allegra OS/ODT, Orapred ODT®, Twinject® Auto Injector, Furadantin®, Methylin® CT/OS**

Sciele's Growth Strategy

1. **Cardiovascular:**
   Grow Nitrolingual Pumpspray (Angina) and maintain Sular sales. Strengthen position in hypertension through launch of Sympres XR (Hypertension)
2. **Diabetes:**
   Expand the market share of Prandin together with the launch of Prandimet (Type2 diabetes), while sustaining sales of Fenoglide/Triglide
3. **Women's Healthcare & Sexual Dysfunction:**
   Expand the market share of Prenate Family through launches of new formulations, and Launch PSD502 (Premature Ejaculation)
4. **Pediatrics:**
   Expand the sales of Allegra OS/ODT (Allergies), Orapred ODT (Asthma) and Twinject, and successfully launch VIQ (Head Lice), Adrenamate (Anaphylaxis), and Clonicel (ADHD)

Four NDA submissions to the FDA are planned in 2009

- **Glycopyrrolate**
  - Chronic moderate-to-severe drooling in pediatric patients
- **Clonicel**
  - Attention Deficit and Hyperactivity Disorder in children
- **Sympres XR**
  - Hypertension
- **Duochol**
  - Lowering no-HDL cholesterol and triglycerides

Sciele R&D

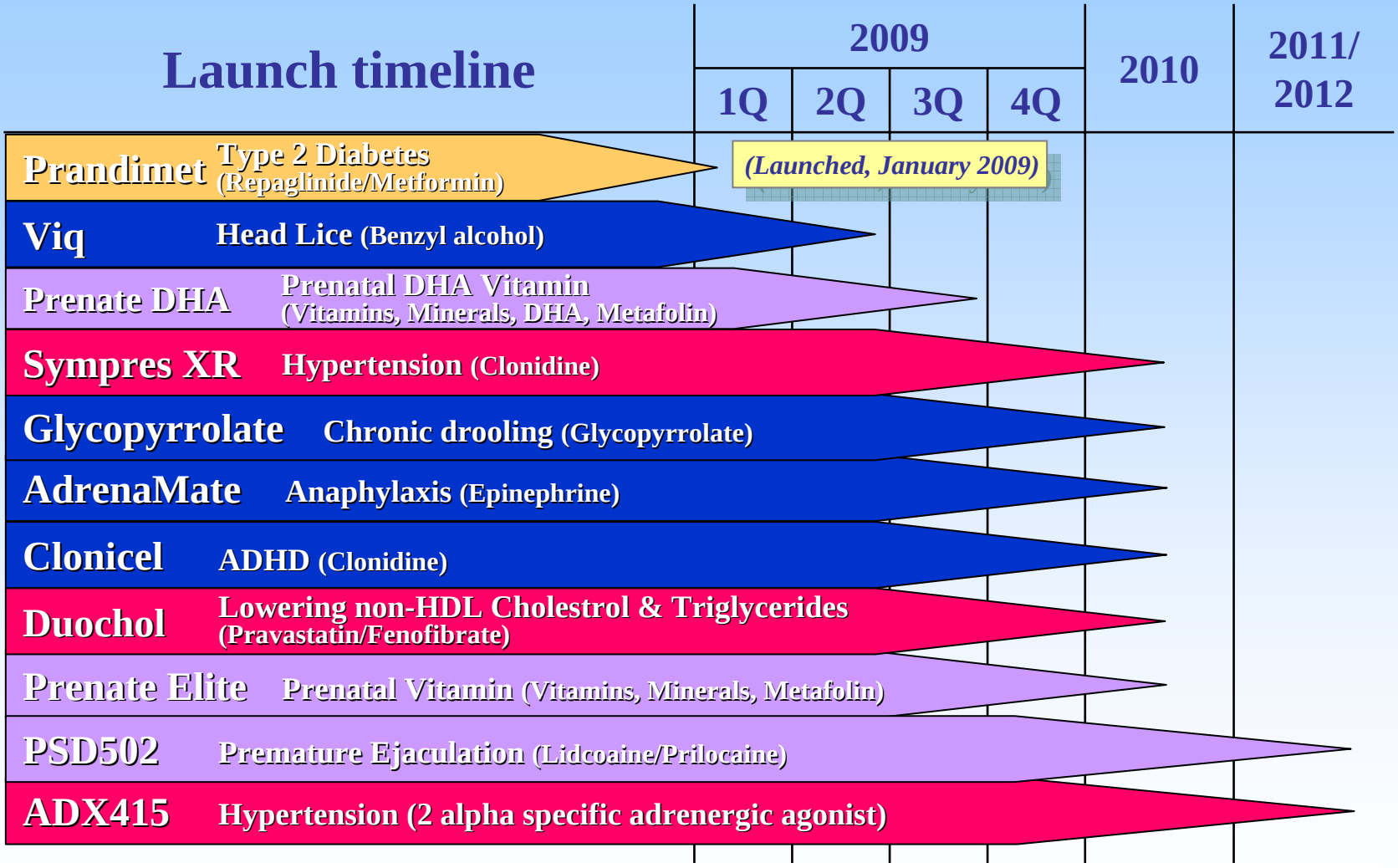
Larry M. Dillaha, M.D.

Executive Vice President and Chief Medical Officer

Sciele Pharma, Inc.

Sciele R&D

Pipeline Leading Sciele's Growth



Cardiovascular Diabetes Women's Health Pediatrics

Sympres XR – Hypertension (Clonidine hydrochloride)

- **Once-a-day sustained release formulation**
  - **Designed to reduce peak concentrations compared to the current immediate release formulation**
- **Current formulation has side effects concern associated with immediate release – 12 million total prescriptions written annually for Clonidine tablets and patches**
- **NDA filing: Second half of 2009**

Glycopyrrolate Liquid
– chronic, moderate-to-severe drooling in pediatrics

- Cerebral Palsy effects 800,000 patients in the U.S.
- Completed Phase III program in the U.S.
- 24 week study to assess safety of oral glycopyrrolate
  - Positive results – well tolerated, no unexpected safety issues
- 8 week efficacy study reached primary end point – modified teacher drooling scale
- Additional pre-clinical studies requested by the FDA
- NDA filing: Second half of 2009

Clonicel – Attention Deficit Hyperactivity Disorder (ADHD)

- **Sustained release formulation of Clonidine**
- **540 patients in Phase III study**
  - **240 in monotherapy trial**
  - **200 in combination therapy trial with Clonicel and stimulants**
  - **Study enrolled children between the ages of 6 and 17**
- **Study design**
  - **8 weeks efficacy study**
  - **6 month follow-up open label safety study**

Clonicel – Positive Phase III results in Monotherapy Trial

- **Statistical significance on primary end point based on ADHD rating scale of 18 symptoms**
- **ADHD-RS-IV score changes were**
  - **Clonicel 0.2 mg : -15.6 ($p<0.0001$)**
  - **Clonicel 0.4 mg : -16.6 ($p<0.0001$)**
  - **Placebo : -7.5**
- **Patient enrollment combination trial was completed in December 2008**
- **NDA filing: Second half of 2009 – including data from both studies**

PSD502 – Premature Ejaculation (PE)

- Lidocaine/prilocaine (metered dose aerosol spray)
- Premature Ejaculation affects 20% to 30% of men
- Phase III study include 540 patients (300 in Europe, 240 in U.S.) – 12 week efficacy study followed by open label study for up to 9 months
- European study results announced in December 2008
  - 268 patients entered into the open label study
  - Achieved statistically significant improvement in all three co-primary and all four secondary end points
- U.S. study to be completed in second half of 2009
- NDA filing: First half of 2010

ADX415 – Hypertension

- **Sciele's first early stage development product**
  - Novel centrally acting 2 alpha specific adrenergic agonist
- **Phase II trial initiated in October 2008**
  - 80 patient multi-center, double-blind random Placebo-controlled dose ranging study
- **Phase IIb with extended release formulation trial to begin in second half of 2009**
- **Phase III extended release program to begin in first half of 2010**
- **Sciele has worldwide marketing rights for ADX415**

Summary

Isao Teshirogi, Ph.D.
President and Representative Director
Shionogi & Co., Ltd.