Research and Development at Shionogi

SHIONOGI & CO., LTD.

March 9, 2006

Speakers

Overview: **IsaoTeshirogi, Ph.D.**

Member of the Board, Executive Corporate Officer

Executive General Manager, Pharmaceutical Research & Development Division

Research: **Hirosato Kondo, Ph.D.**

Corporate Officer

General Manager, Discovery Research Laboratories

Development: **Takuko Sawada**

General Manager, Strategic Development Department

Licensing: **Masaharu Mori**

General Manager, License Department

Achievements in the 1st Year, 2nd Medium-Term Management Plan

♦Organization

- April/05: Reformed research organization based on 3 targeted therapeutic areas (TAs)
  Established a decision-making system integrating Discovery and Development Research Laboratories
- July/05: Introduced TA system in development divisions
  Initiated a new management system integrating Strategic Development and Clinical Research

♦Strategies

- Introduced strategic discussion system through MPDR (Marketing, Production, Development, Research)
  - TA conference :Develop strategies for each TA
  - Pipeline meeting : Review product portfolio

♦Policy

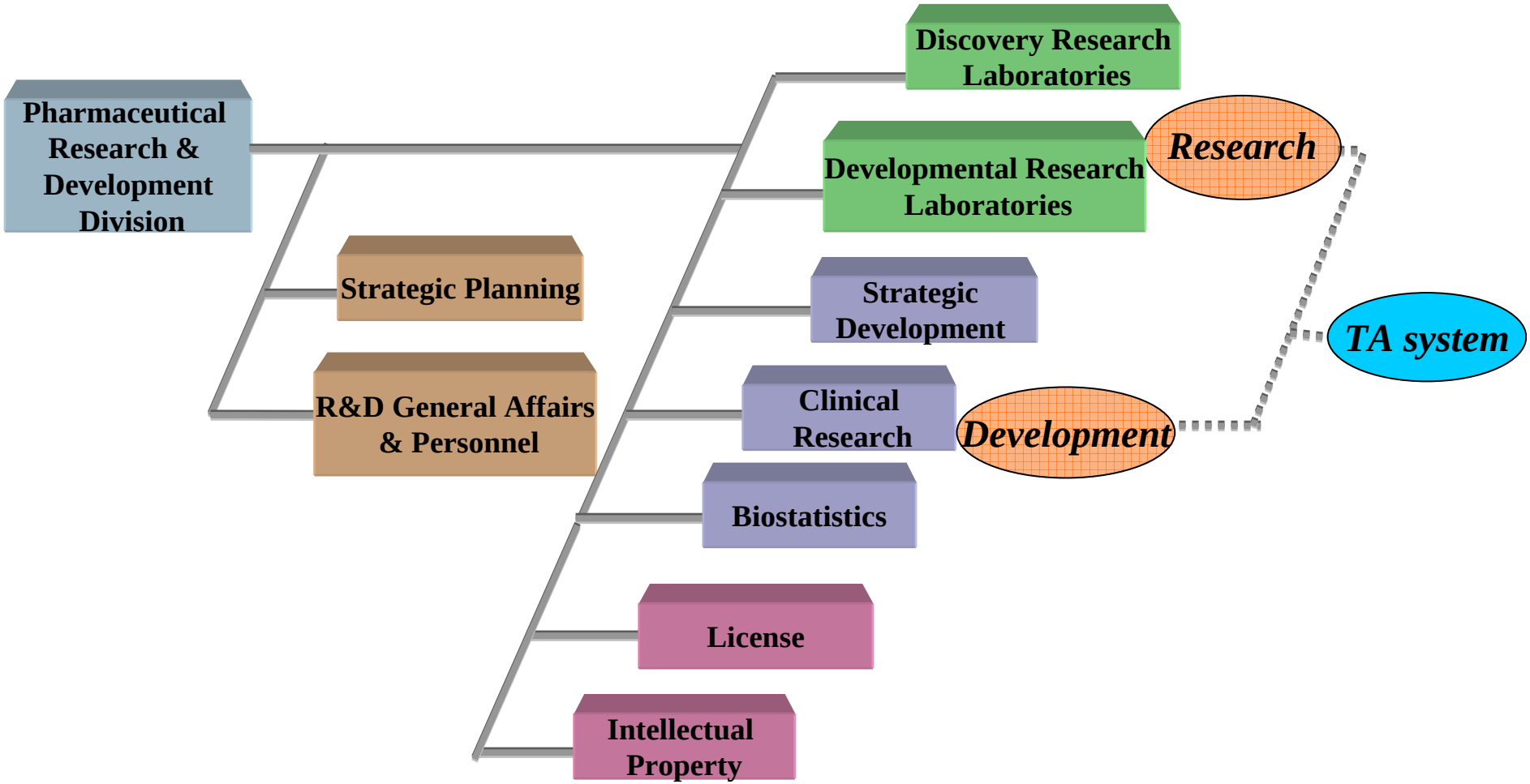
- Established the Frontier TA for future potential

♦R&D Process

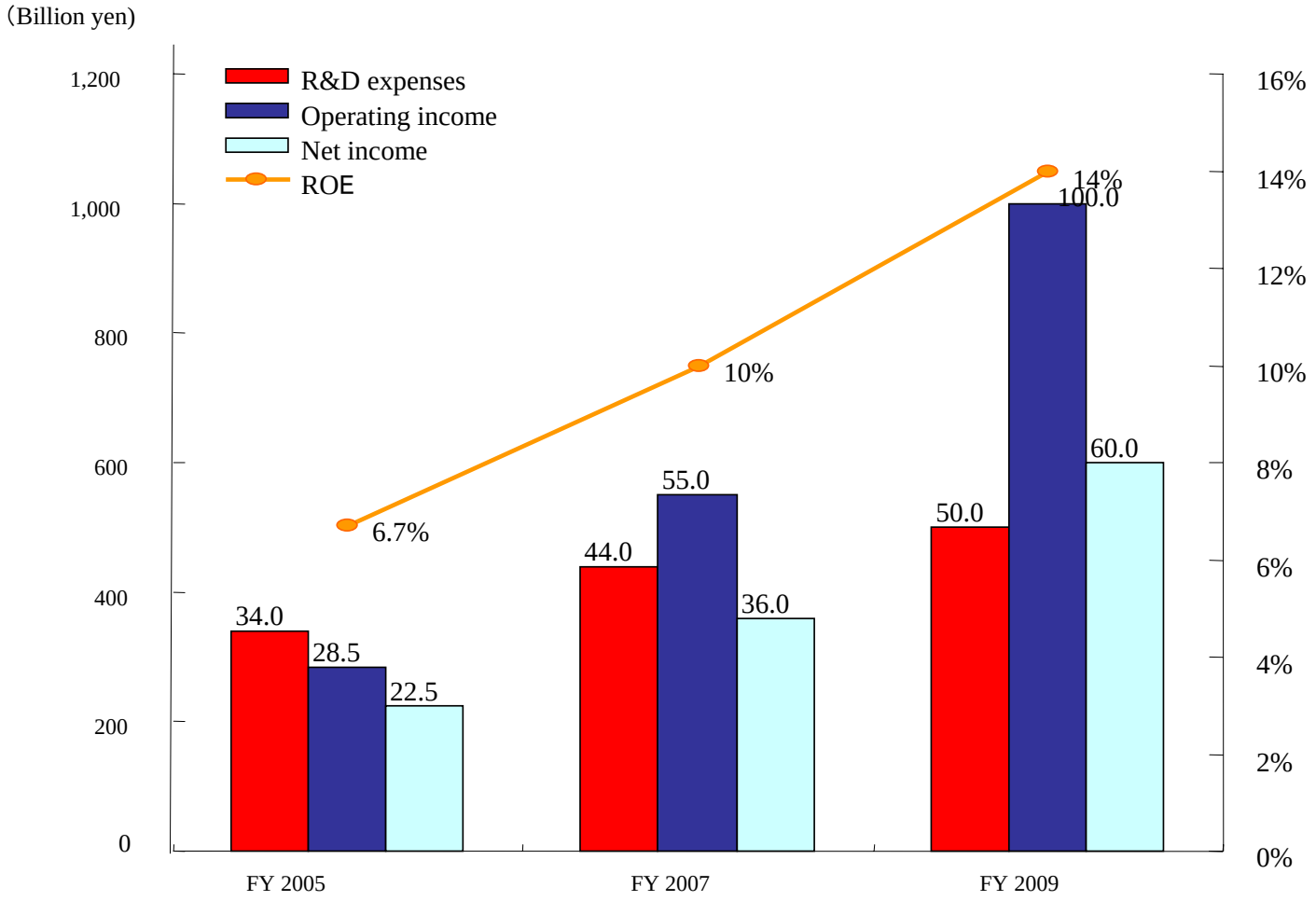
- Rooted new R&D processes with POC studies targeted
- Initiated a new education program for next-generation leaders

Allocate resources to targeted TAs
Thorough control of milestones

Organization



Forecasts of R&D Expenses, Income, and ROE (Consolidated)



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Progress in Fiscal 2005 and Milestones for Fiscal 2006 :
Infectious Disease Area

- **Finibax® , Avelox® , Finibax® kit product**
  - **Launched Finibax® and Avelox® during fiscal 2005**
    Additional clinical study is under way for Finibal after an approval
  - **Finibax® kit product launch is scheduled for the first half of 2006**
- **S-013420 (New Macrolide Antibiotic)**
  - **Moved to Phase 2a and clinical studies are under way**
  - **'Go/No-Go' decision during fiscal 2006**
- **S-364735 (Anti-HIV)**
  - **Reach FTIH (First Trial in Human) during fiscal 2005**
    (Scheduled for the end of March 2005)
  - **Scheduled Phase 2a during fiscal 2006**
- **Broad-spectrum cephem antibiotic for injection**
  - **Scheduled FTIH during fiscal 2006**

Progress in Fiscal 2005 and Milestones for Fiscal 2006 :
Pain Area

- **Oxycodone immediate-release formulation** (Cancer pain)
  - **Scheduled to launch during fiscal 2006**
- **Duloxetine (**Diabetic neuropathic pain)
  - **Started dose-response study in December 2005**
  - **Key break is scheduled for the end of fiscal 2006**
- **Side effects reliever for opioid analgesics** (Emesis and Constipation)
  - **Select the best compound and start FTIH during fiscal 2006**
- **Collaboration with Purdue Pharma L.P. in the USA**
  - **Started collaborative research on novel pain treatments for future global co-marketing**

Progress in Fiscal 2005 and Milestones for Fiscal 2006 :
Metabolic Syndrome Area

- **Crestor ®**
  - **Launched in 2005**
  - **Post-marketing surveillance is under way**
- **Irbesartan**
  - **Phase 3 clinical study is moving smoothly**
  - **NDA filing scheduled during fiscal 2006**
- **S-2367**
  - **Phase 2a study is under way in the USA**
  - **Scheduled to make a ‘go/no-go’ decision during fiscal 2006, then move to phase 2b as soon as ‘go’ decision is made**

Progress in Fiscal 2005 and Milestones for Fiscal 2006 :
Frontier Area

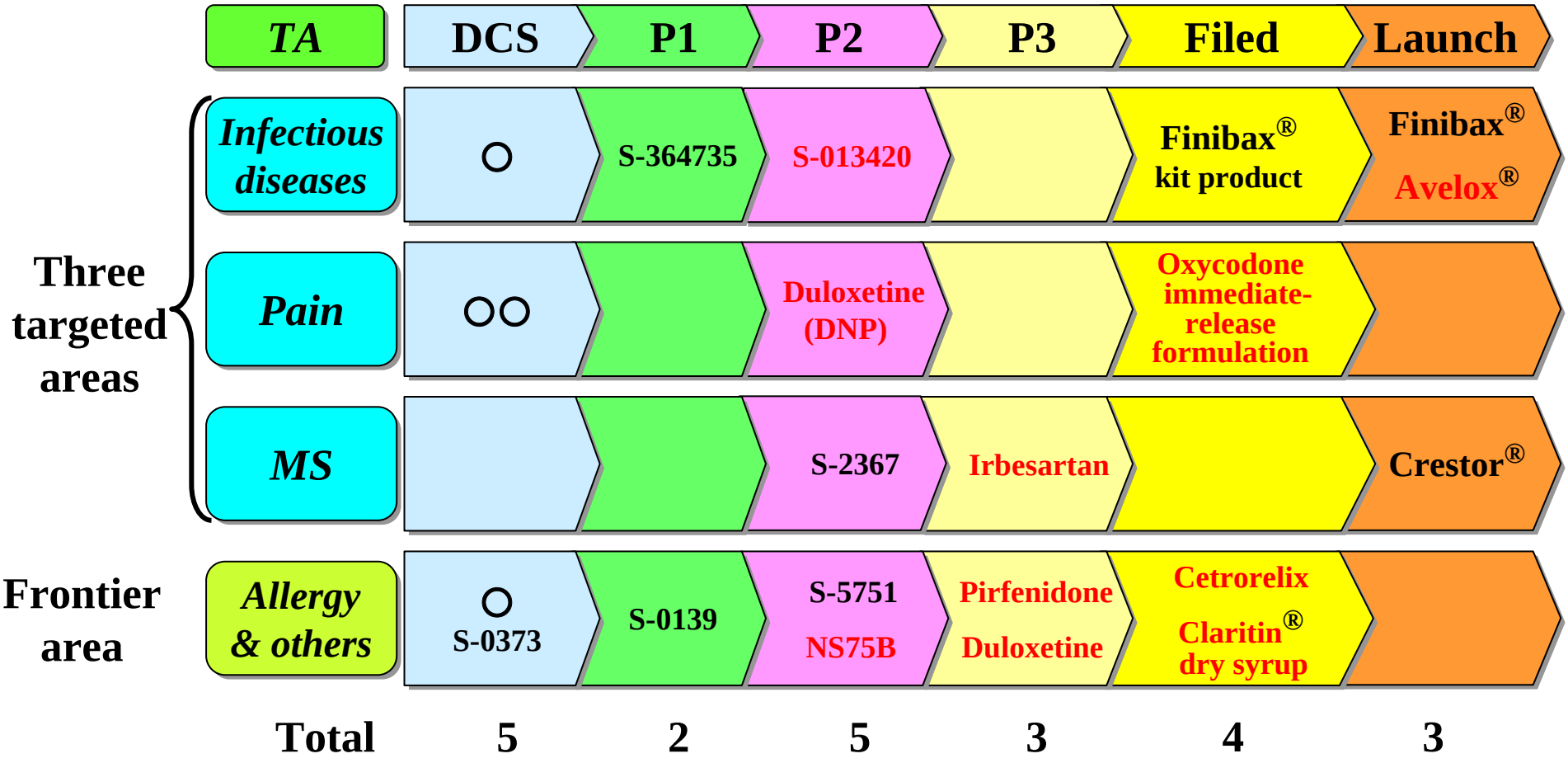
- **Claritin® dry syrup**
  - **Scheduled to launch during fiscal 2006**
- **Pirfenidone (Idiopathic pulmonary fibrosis)**
  - **Phase 3 clinical study is moving smoothly**
  - **NDA filing scheduled during fiscal 2006**
- **S-5751 (Asthma)**
  - **Moved to Phase 2a in fiscal 2005**

    Phase 2a study is under way both in the USA and Europe
  - **Scheduled to make a ‘go/no-go’ decision during the 2nd half of fiscal 2006**
- **Antipruritic treatment**
  - **FTIH is scheduled during fiscal 2006**

Progress in Fiscal 2005 and Milestones for Fiscal 2006 :
Other Important Compounds

- **Cetrorelix (Prevention of premature ovulation during a controlled ovarian stimulation followed by assisted reproductive technology)**
  - Scheduled to launch during fiscal 2006
- **NS-75B (Benign Prostatic Hypertrophy)**
  - Scheduled to enter Phase 2a during fiscal 2006
- **Duloxetine (Depression)**
  - Phase 3 comparative clinical study is under way
  - NDA filing scheduled during fiscal 2007
- **S-0139 (Cerebrovascular diseases)**
  - Planning to continue development by Shionogi from Phase 2a in EU
- **Adapalene (Acne Vulgaris)**
  - NDA filing scheduled by Galderma KK during fiscal 2006

Shionogi R&D Pipeline (In-licensed Compounds)



DCS: Drug Candidate Selection
MS: Metabolic syndrome
TA: Therapeutic area

In red: In-licensed compounds
○: Novel candidate

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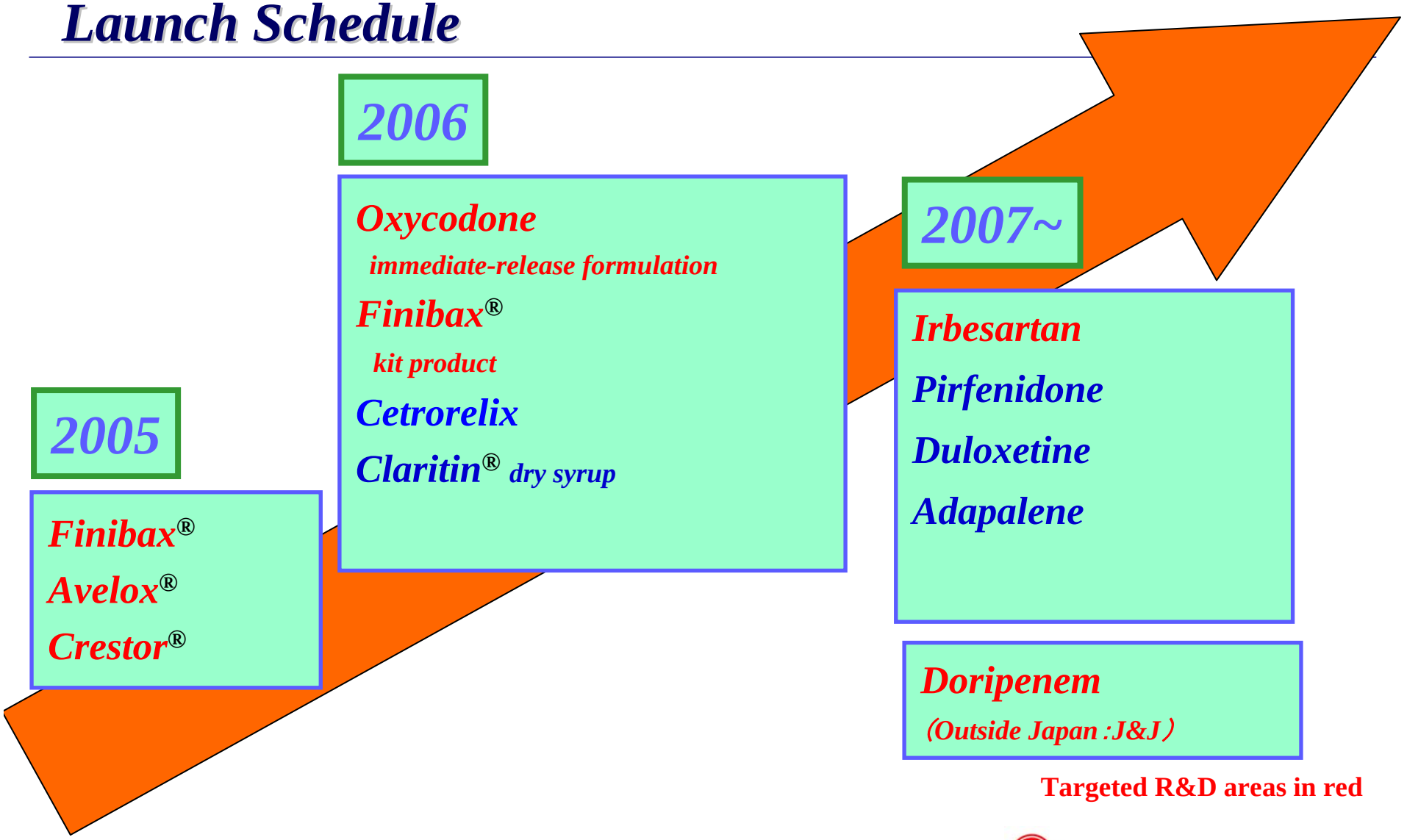
Launch Schedule



Targeted R&D areas in red

Targets for Fiscal 2006

Research

- Initiate clinical studies for 3 out of 4 current drug candidates
- Select 4 or more new drug candidates from research programs

Development

- Launch 4 products for which NDAs have been filed
  - Cetrorelix, Oxycodone immediate-release formulation, Finibax® kit product, Claritin® dry syrup
- NDA filings for 2 products
  - Irbesartan, Pirfenidone
- Move Phase 2a products to the next clinical stage
  - S-013420, S-2367, S-5751, Duloxetine (DNP)

Research Areas

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Topics in Research Areas

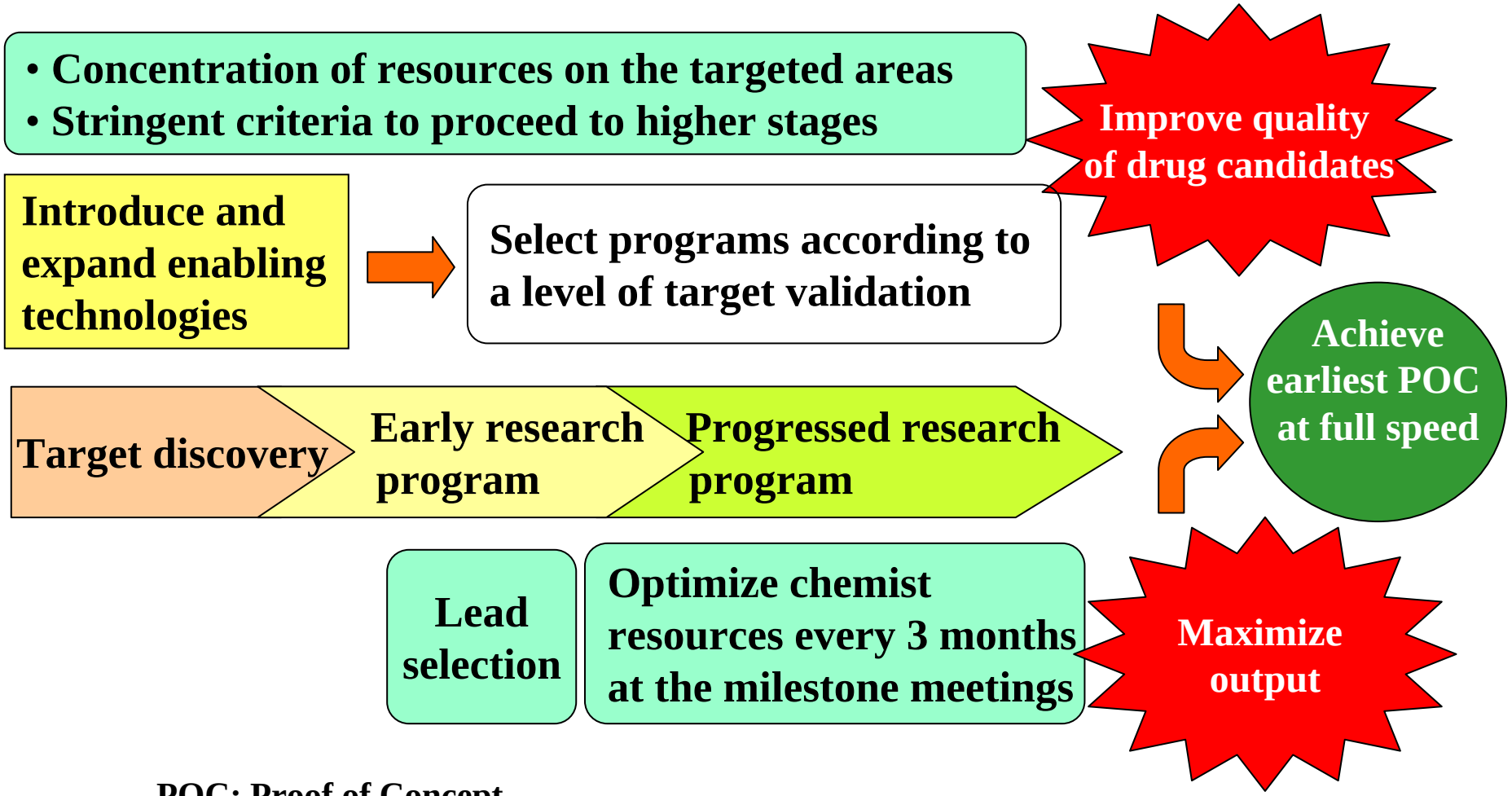
- **Infectious Diseases**
  - Scheduled to initiate clinical study for anti-virus drug
  - Discontinued development of cephem antibiotic for gram-negative bacteria
  - Completed DCS for injectable broad-spectrum cephem antibiotic
  - Enrich R&D assets in the infectious disease area
- **Pain**
  - Signed a contract with Purdue Pharma L.P. in the USA for research, development and marketing collaboration
  - Completed DCS (back-up) for opioid-induced adverse effects alleviator
- **Metabolic Syndrome（MS)**
  - Advanced programs both from in-house research laboratories and collaboration with external institutes to new research programs
- **Frontier**
  - Completed DCS for antipruritic drug
- **Innovative Technology**
  - In-licensed innovative technology for producing human phage antibody from MorphoSys AG in Germany

DCS: Drug Candidate Selection

Strategy for Drug Discovery

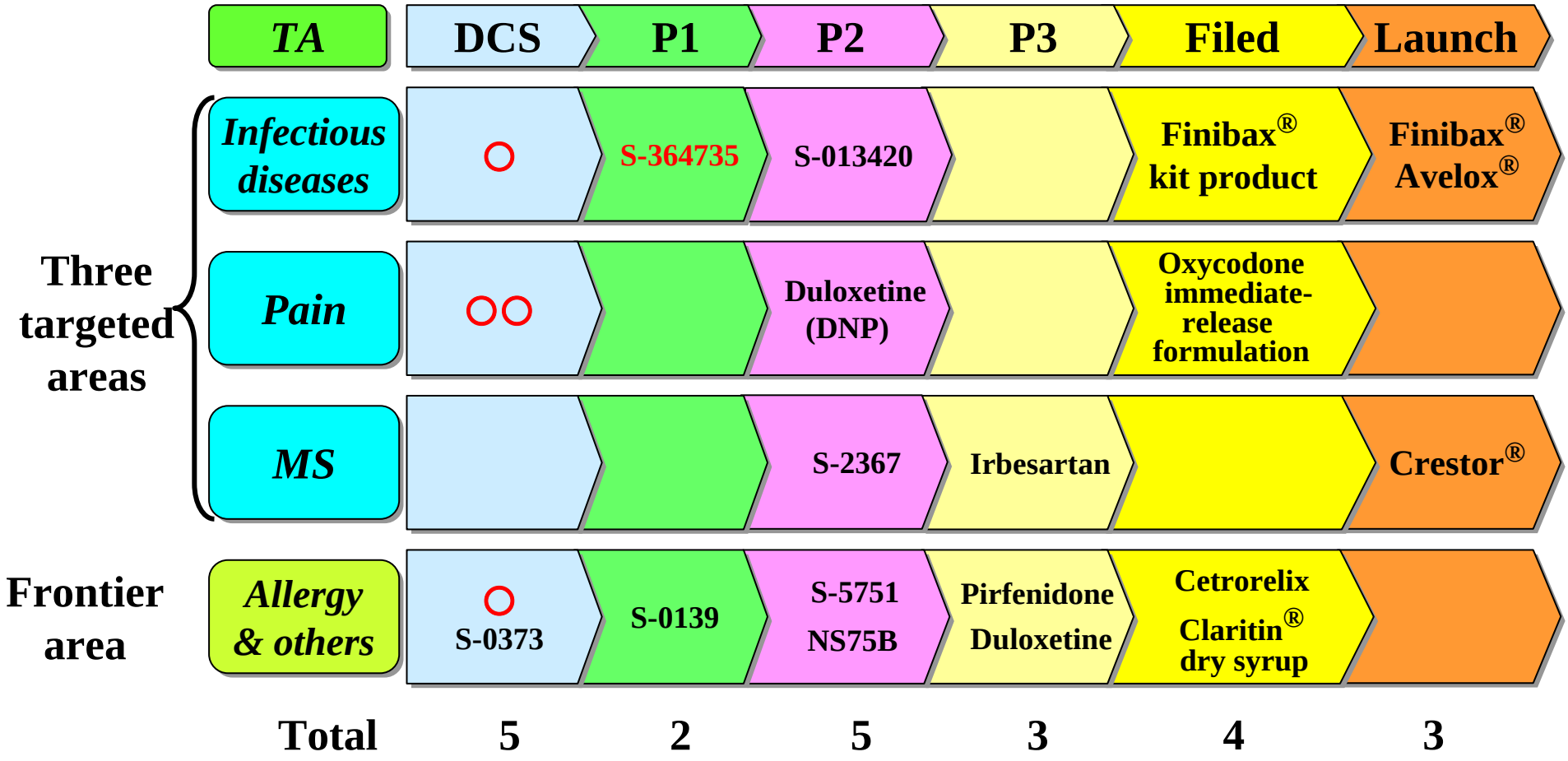
R&D Pipeline

Drug Discovery Strategy to Achieve POC Quickly



POC: Proof of Concept

Shionogi R&D Pipeline (DCS ~ Launch)



DCS: Drug Candidate Selection
MS: Metabolic Syndrome
TA: Therapeutic Area

In red: Compounds progressed to the next stage

○: Novel candidate

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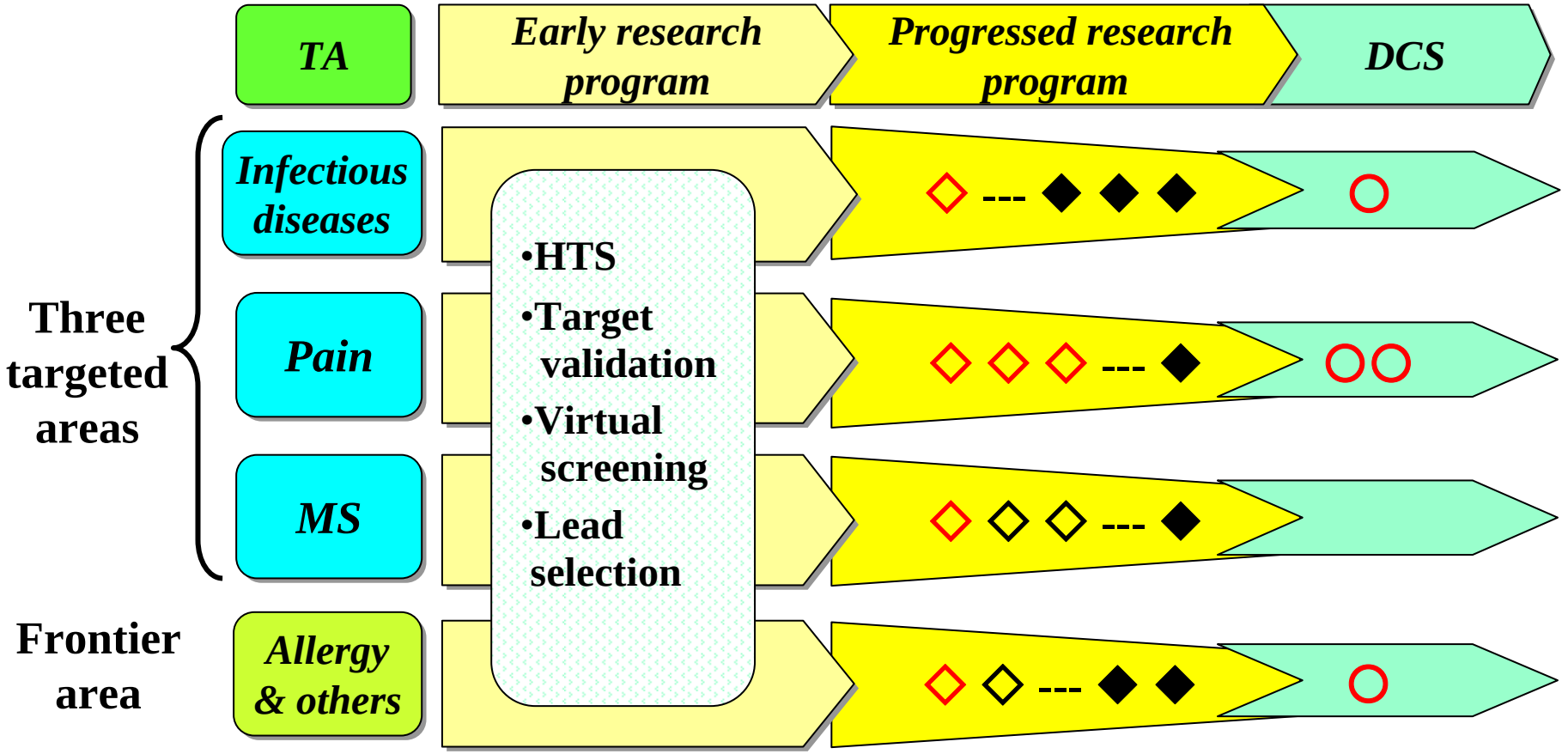
Shionogi R&D Pipeline (Research Area)



DCS: Drug Candidate Selection
MS: Metabolic Syndrome
TA: Therapeutic Area

◇ ○ : Novel program or candidate
◆ : Optimized compound

Infectious Diseases

R&D for Anti-virus Drug

♦S-364735

- Cleared toxicology studies to advance to FTIH
- To be developed by
  Shionogi-GlaxoSmithKline Pharmaceuticals, LLC

  ⇩

  Phase 1 start: March 2006

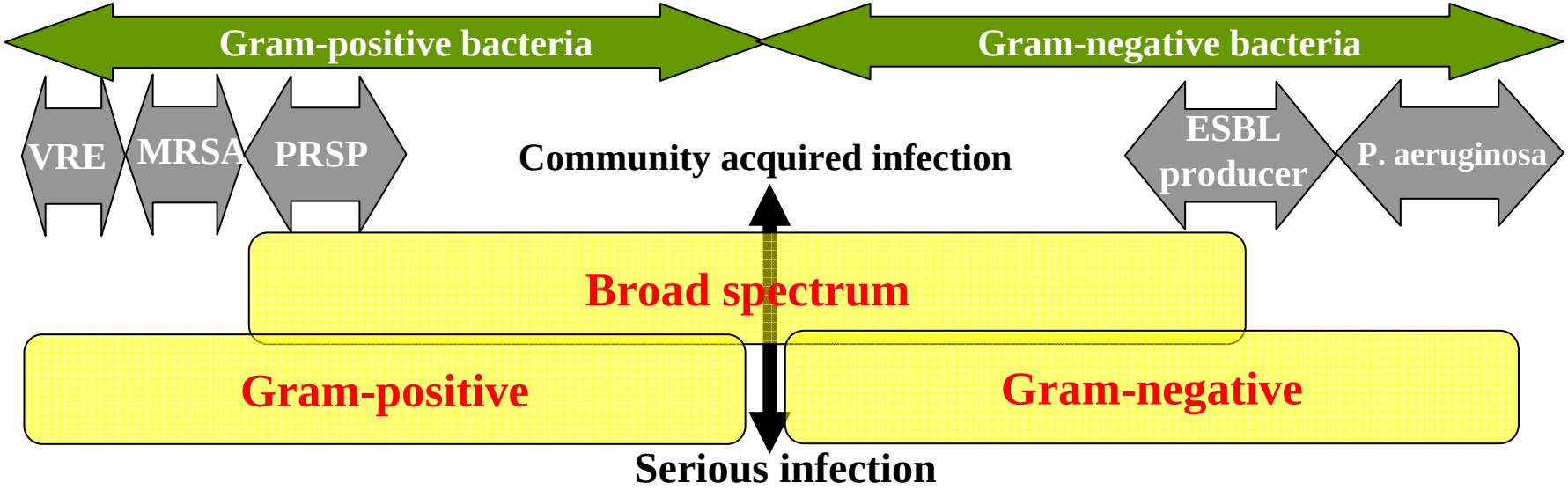
- Backup compound: already selected
- Follow-on compound: in discovery stage

♦Features

- ◆ Potent anti-HIV activity (1 nM level)
- ◆ Resistant mutations slow to emerge
- ◆ High safety margin
- ◆ Good pharmacokinetics profile
- ◆ Low risk of drug-drug interaction

R&D Program Assets in the Infectious Diseases Area

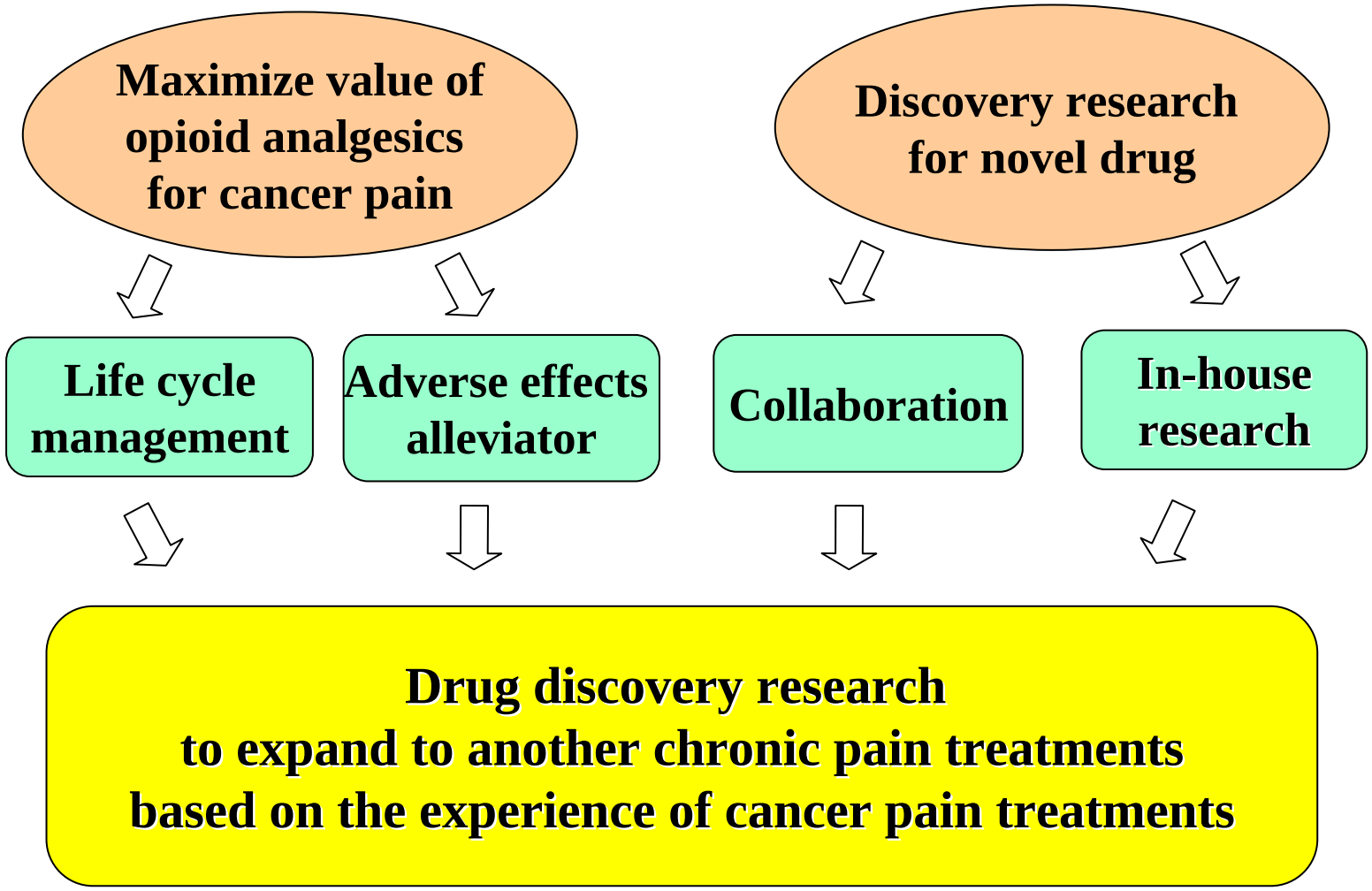
Route	Market	Spectrum	Development compound	Stage
Injection	Community acquired infection	Broad		DCS
	Hospital acquired or serious infection	Gram-positive		Progressed research program
		Gram-negative		
Oral	Community acquired infection	Broad	S-013420	Phase 2a



PRSP : Penicillin-Resistant Streptococcus Pneumoniae
ESBL : Extended-Spectrum β-Lactamase
DCS : Drug Candidate Selection

Pain

Drug Discovery Strategy in the Pain Area



Research Program Assets in the Pain Area

Investigated unmet needs and washed out target molecules for drug discovery

↓

Evaluation

↓

- **Many unmet needs**
- **Over 30 target molecules**

↓

Prioritization

1. **Aggressive execution**
2. **Feasibility investigation**
3. **Collection of information**
4. **No handling**

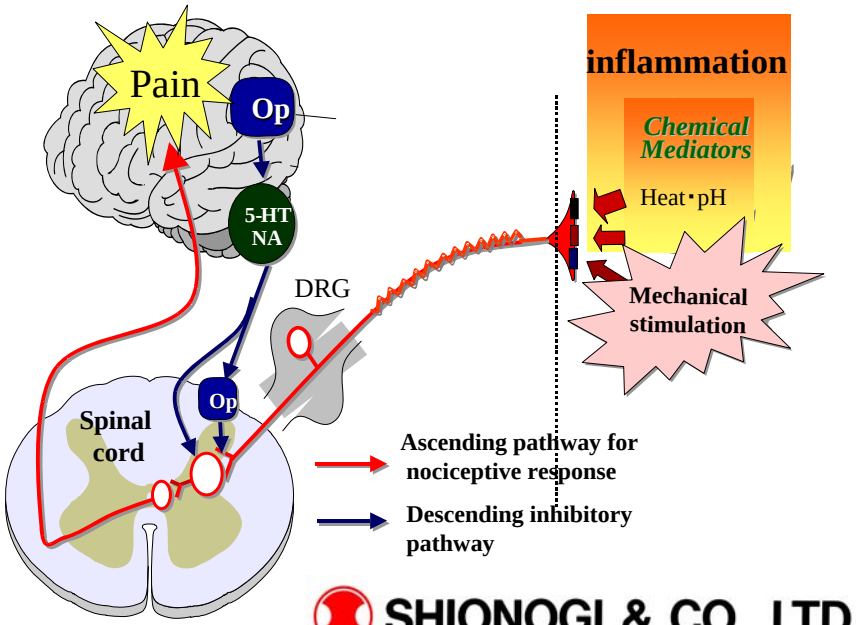
→ **In-house research programs**

→ **Collaboration research programs with Purdue Pharma L.P.**

Collaboration Programs with Purdue Pharma L.P. in the USA

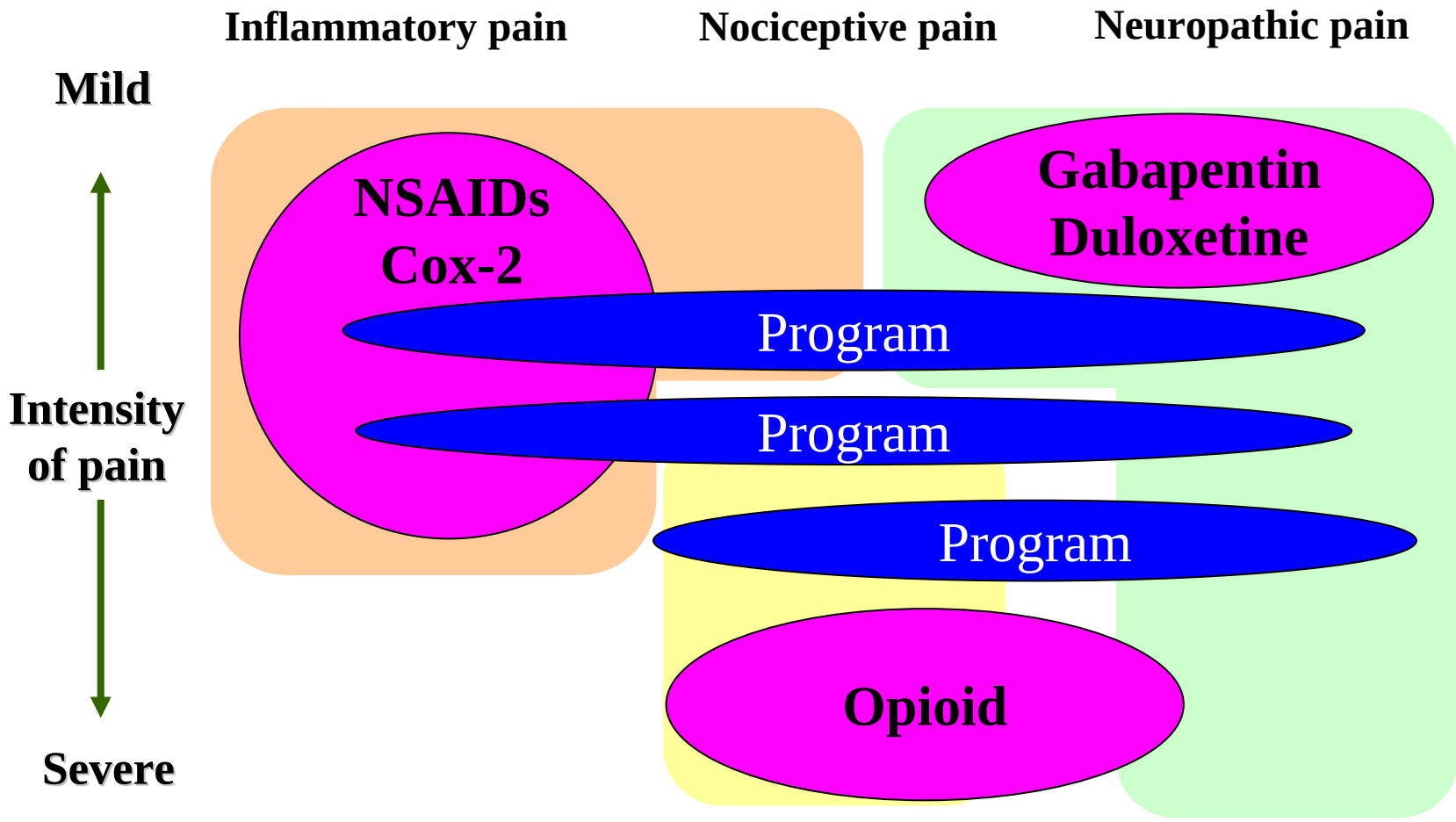
- **Develop novel compounds discovered in 3 research programs targeting the receptors and channels for pain relief**
- **Accelerate our original plan for the clinical study of drugs with novel mechanism for chronic pain by 1-2 years with this collaboration**

- **<u>Program A</u> ⟹ DCS（licensed from Purdue Pharma L.P.）**
  ＋Backup program
- **<u>Program B</u> ⟹ Optimization**
- **<u>Program C</u> ⟹ Optimization**



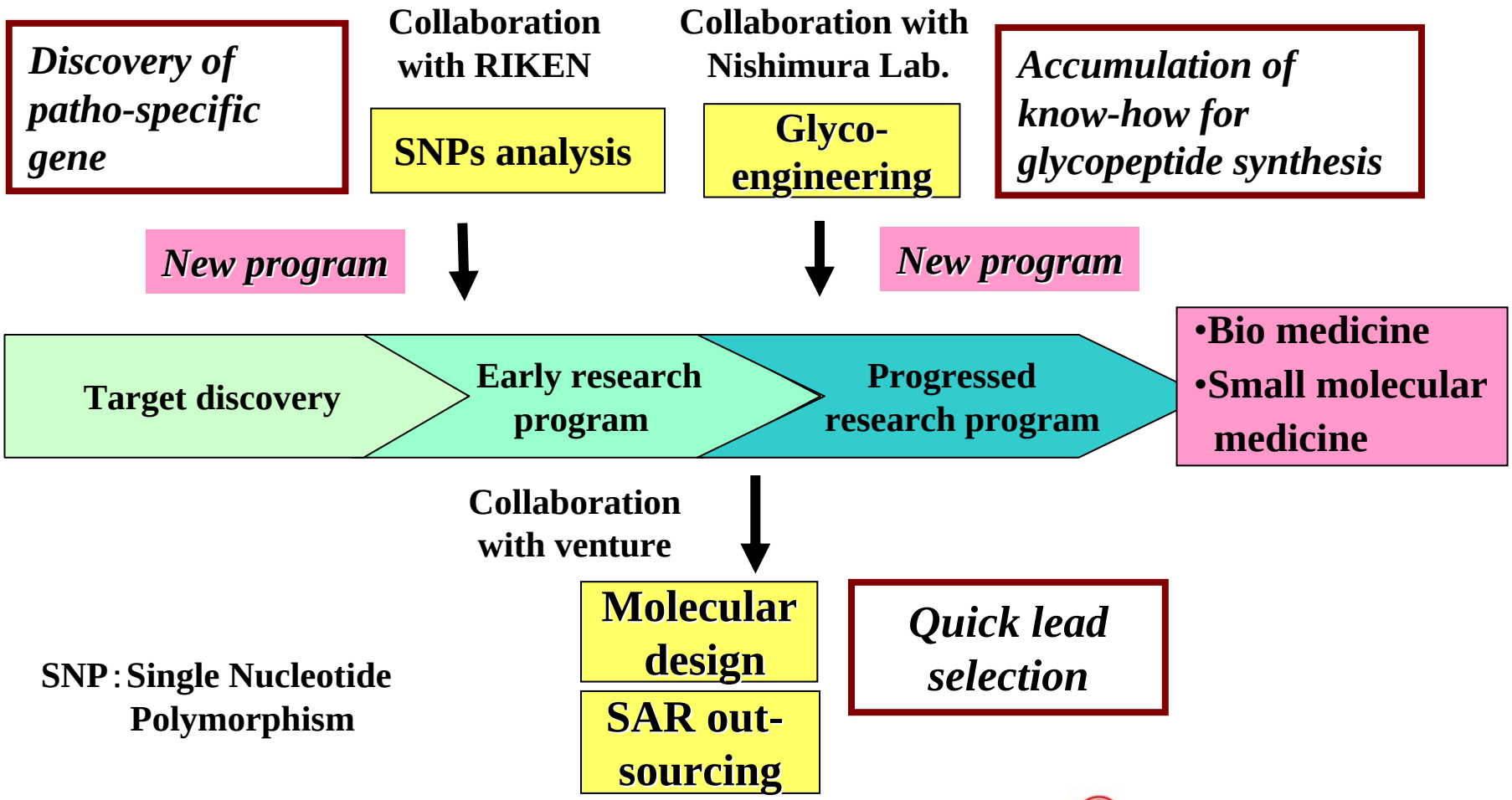
DCS：Drug Candidate Selection

Positioning of the Collaboration Programs



Metabolic Syndrome (MS)

Drug Discovery Research in the MS Area



New Technology-Glycoengineering

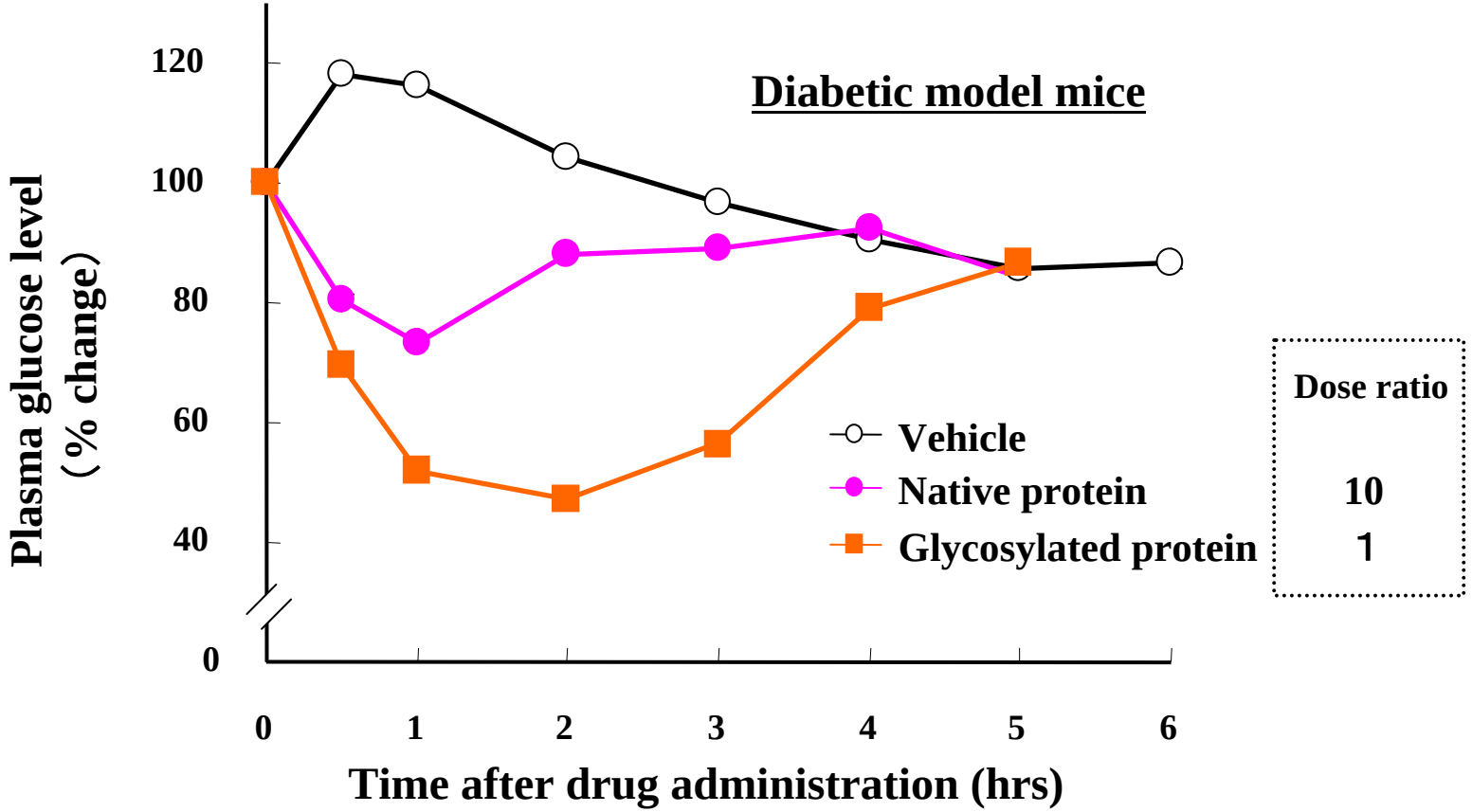
- **Synthesis of glycopeptide**
  - **Preparing the glycopeptide library using automatic sugar chain synthetic technology（NEDO project）→ Development of vaccine, etc.**
- **Analysis of sugar chain and glycoside structure**
  - **Development of automated analysis device for sugar chain (JST project)：Completed the setup of analytical conditions for serum pre-treatment → Planning the sugar chain analysis for patient sample**
- **Glycoprotein drug**
  - **Synthesis of glycosylated anti-diabetic protein**

  → Improved pharmaco-dynamic/kinetic profile
- **Glycosylated small molecule**
  - **Identified improvement of pharmaco-dynamic/kinetic profile**

NEDO：New Energy and Industrial Technology Development Organization
JST：Japan Science and Technology Agency

Drug Discovery Research on Diabetes

Glycosylated anti-diabetic protein（Collaboration with Hokkaido University: Nishimura Laboratories)



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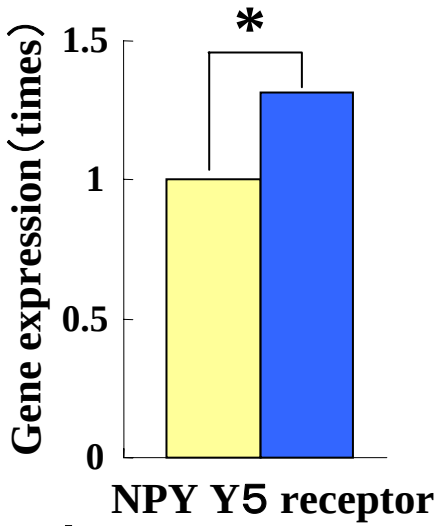
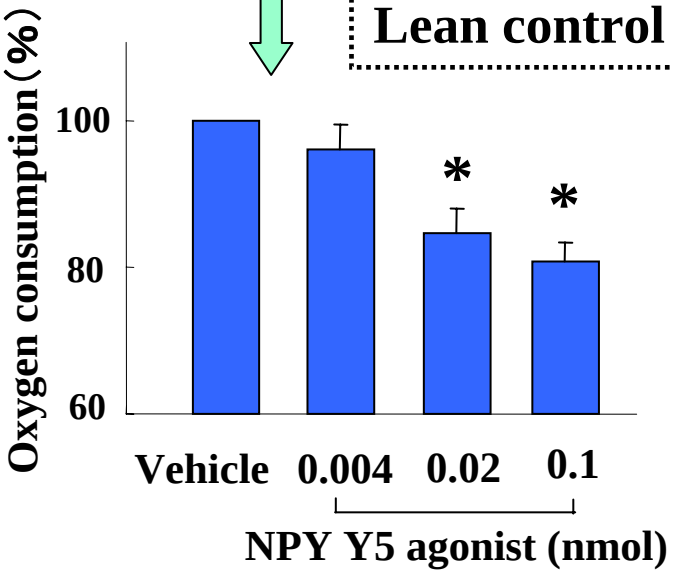
Role of Neuropeptide Y Y5 Receptor on Obesity

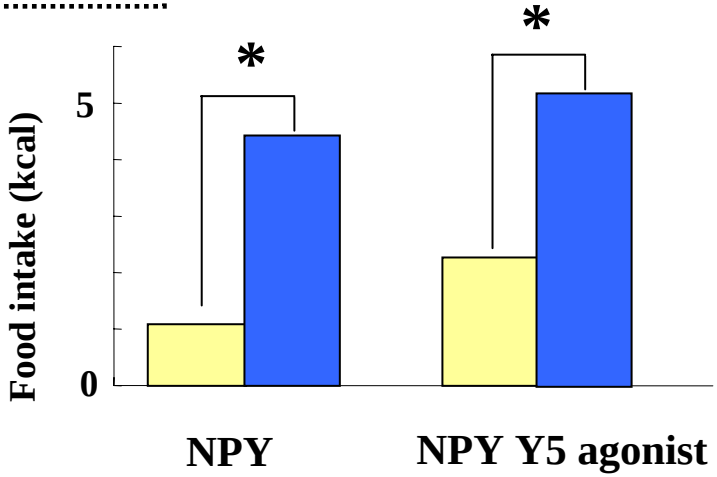
In mice fed high-fat diet（obese）:

- **NPY Y5 receptor gene expression was increased**
- **NPY Y5 agonists (icv) induced**
  - **Remarkable increase in food intake**
  - **Reduction of energy expenditure （oxygen consumption）**



Lean control mice（ ）





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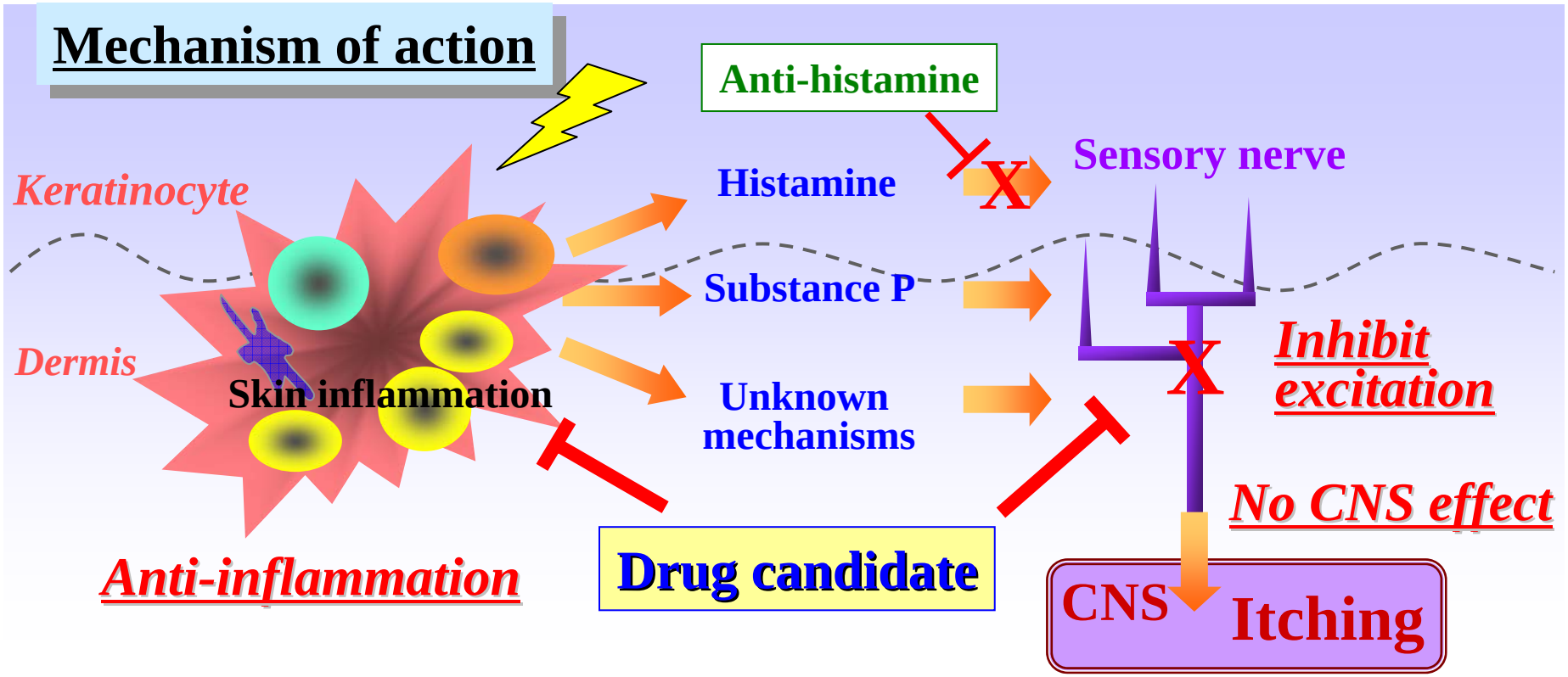
Frontier

R&D of Antipruritic Agent

・Novel mechanism: Antipruritic（peripheral）＋
Anti-inflammatory



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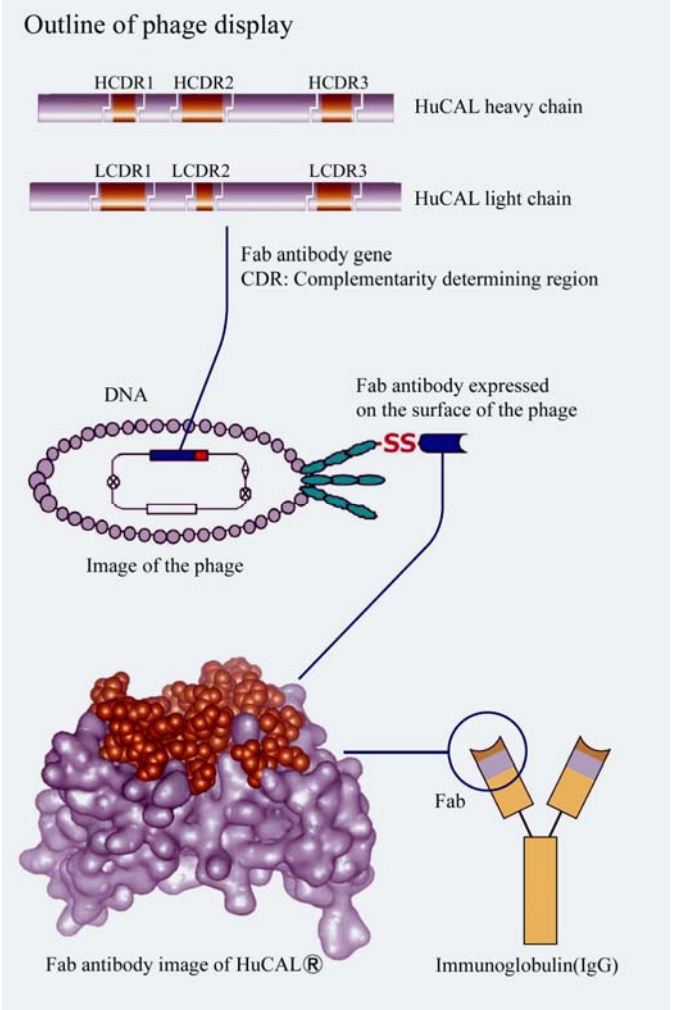
Expansion and In-licensing of Enabling Technology

Phage Antibody Technology from MorphoSys AG

Innovative technology : optimized human phage antibody library

Capability to produce useful antibody within 2 weeks

Useful for target molecule evaluation, compound screening and as the pharmacological marker
→Accelerate research/development in Shionogi



Summary

- **Progress in Fiscal 2005**
  - Selected 4 drug candidates
  - Initiated clinical study for anti-virus drug（S-364735）
  - Progressed research programs in the 3 targeted areas, and initiated collaborations with external institutes
  - Initiated global research in the pain area through the collaboration with Purdue Pharma L.P.
  - Expanded basic technologies through in-licensing innovative technologies etc.

- **Milestones in Fiscal 2006**
  - Select 4 or more new drug candidates
  - Initiate clinical study for 3 drug candidates

Development Area

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March 9, 2006

Clinical Development

- Aaiming to maximize output

  while promoting globalization

Reconstruction of Development Management System

Measures	**Introduced a therapeutic area-oriented system**
Objectives	**Strengthen pipeline management for each area** **Optimize resource management on a basis of targeted areas** **Build robust knowledge background and improve performance** **Promote MPDR cooperation and nature specialists**
Measures	**Established a new section to manage CRO**
Objectives	**Improve performance by promoting strategic management of procurement**
Measures	**Enhanced function of Shionogi USA Inc. by hiring new development director**
Objectives	**Strengthen cooperative system to promote global development**

Expected Result

Promote development under accurate target profiling
Move steadily to next stage and obtain approval

Initiatives Taken to Improve Productivity

Reconstruction of infrastructure for information technology	**Systems corresponding to Part11 and e-application of document management for globalization**
Improvement of the efficiency of clinical studies	**Introduction of EDC（Electronic Data Capturing）system in addition to strategic outsourcing**
Design optimal development process and efficient management	**Established cross-functional MPDR cooperation system to maximize product value**
Effective use of state-of-the-art technology to alleviate development risks	**Promoted genomic analysis and applied PET（Positron Emission Tomography）**

Progress in Development

Since April 2005

- **Crestor®** — Launched → Post-marketing clinical study
- **Finibax®** — NDA filed → Launched → Post-marketing clinical study
- **Avelox®** — NDA filed → Launched
- **Cetrorelix** — NDA filed → Passed MHLW Evaluation Committee
- **Irebesartan** — NDA filed → Phase 3 study
- **Duloxetin** — In preparation for Phase 2 study → Phase 2a study（DNP)
- **S-5751** — Phase 1 Multiple-dose study → Phase 2a study（Asthma: POC）
- **S-2367** — Phase 1 Multiple-dose study → Phase 2a study（Obesity: POC）
- **S-013420** — Phase 1 single-dose study → Phase 2a study
- **NS75B** — Phase 1/2 single-dose study → Moved to Phase 2 part
- **S-0139** — Phase 1 → In preparation for Phase 2a study
- **S-364735*** — Pre-clinical → Phase 1 study

* Shionogi-GSK (JV) Product

DNP: Diabetic Neuropathic Pain
POC: Proof Of Concept

Life Cycle Management

- ***New Products :***

  Claritin ® dry syrup preparation（NDA filed）
  Oxycodone immediate-release formulation（NDA filed)
  Finibax® kit product（NDA filed）
  NS75B（Cetrorelix sustained release formulation）(Phase 2）

- ***New Indications :***

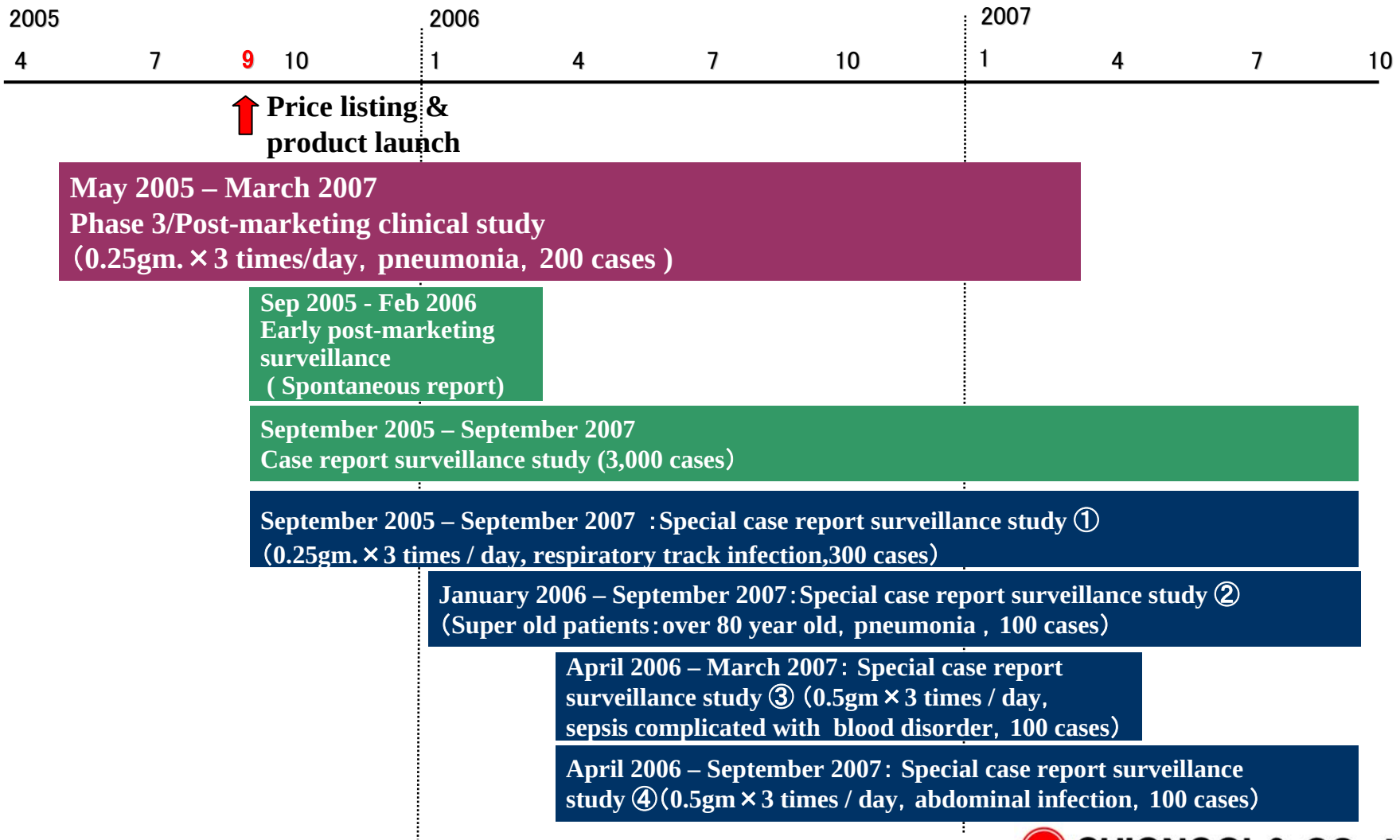
  Duloxetine － Diabetic neuropathic pain（Phase 2）
  NS75B（Cetrorelix sustained release formulation）－ Benign prostatic hypertrophy（Phase 2）
  Finibax® － Pediatric use（Planning）

- ***Post-Marketing Clinical Studies :***

  Crestor® － Prevention of plaque extension in coronary arteries （IVUS study）
  Finibax® － Establish 3 times /day administration based on PK/PD theory
  Imunace® － Pharmacogenomics test with renal cell carcinoma

Maximize existing product value by adding new formulations and indications, etc.

Post Marketing Surveillance Program for Finibax®



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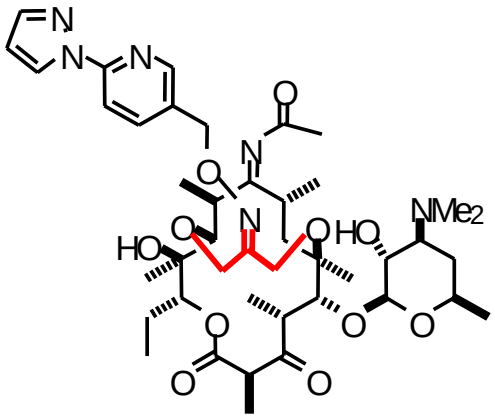
Outline of Main Products under Development

- **Product characteristics**
- **Expected indications**
- **Pre-clinical and clinical study data, etc.**

S-013420

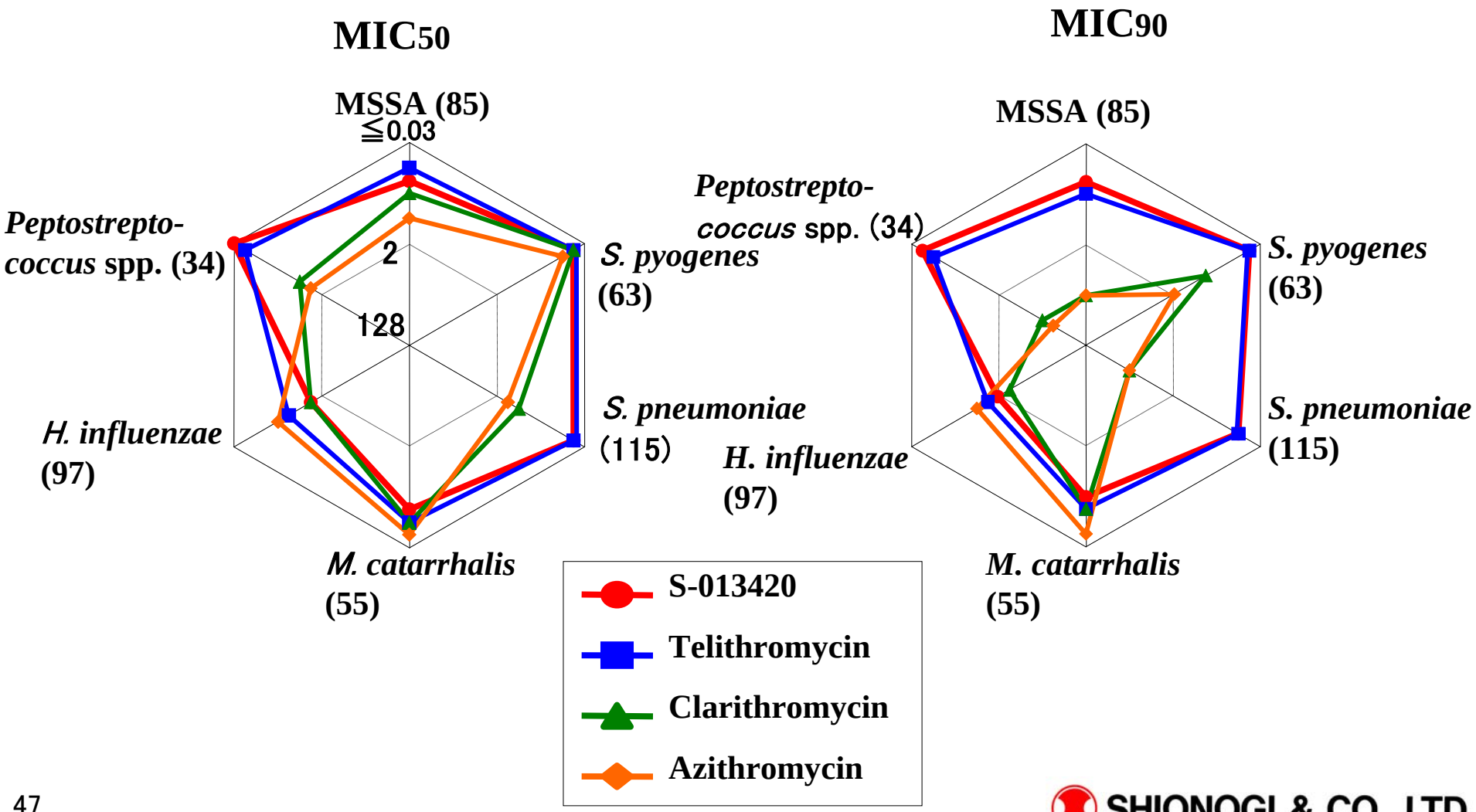


－Licensed from Enanta Pharmaceuticals（USA）

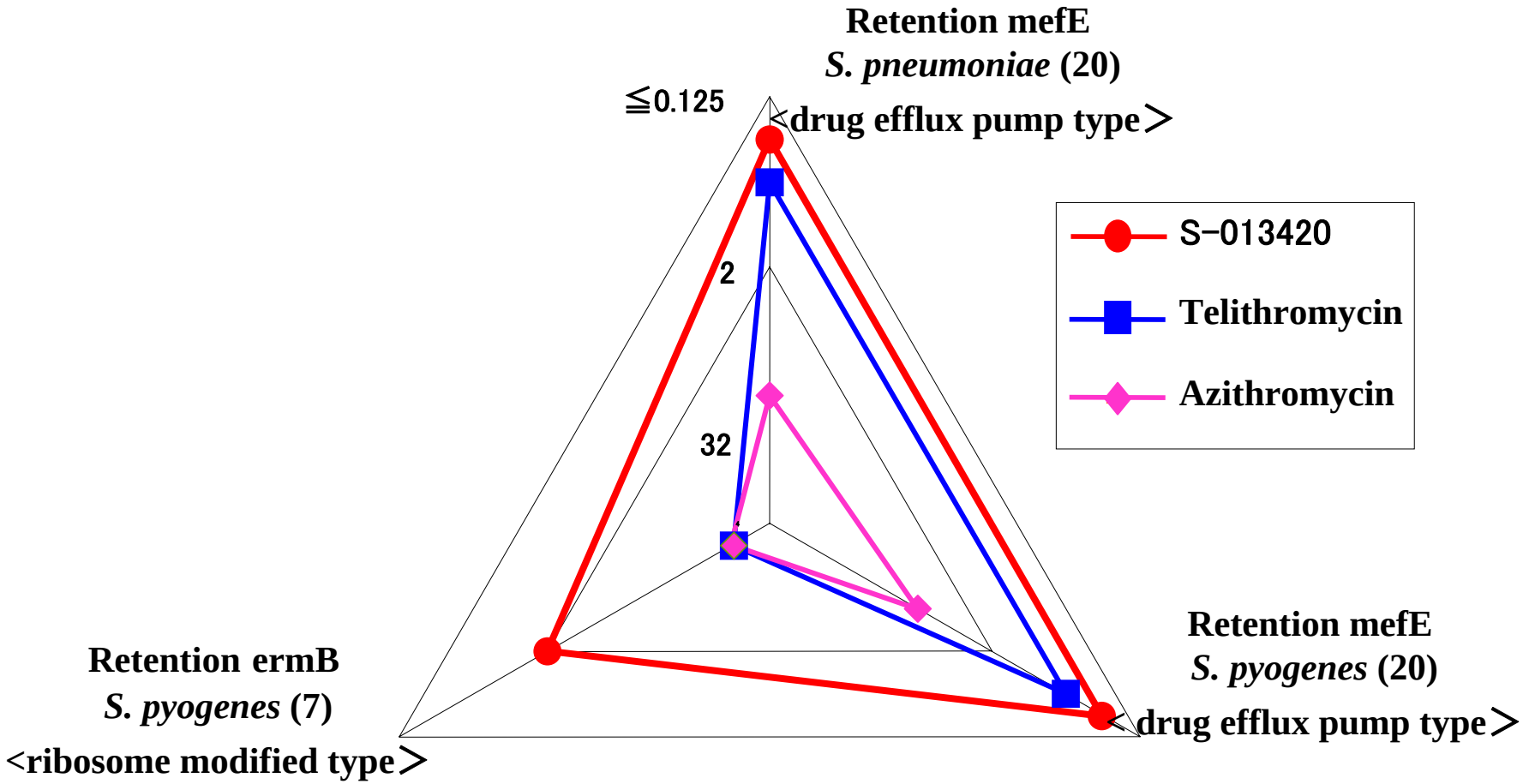
- Novel macrolide antibiotics（oral）
  （Novel characteristic of bridged structure）
- Broad spectrum enough to cover major bacteria causing respiratory infections
- Strong antibacterial activity against *S. pneumoniae* (including penicillin or macrolide resistant strains)
- Good PK profile
- Suitable for pediatric usage because of no bitterness

Initiation of Phase 2 study: Dec, 2005

Activity against Major Clinical Isolates



Antibacterial Activity against Macrolide Resistant Streptococcus spp.



Antibacterial Activity against Atypical Pathogens

Strains	MIC (μg/mL)				
	S-013420	TEL	CAM	AZM	EM
L. pneumophila					
ATCC33152	0.031	0.125	0.063	0.125	0.5
ATCC33215	0.031	0.063	0.063	0.125	0.5
M. pneumoniae					
ATCC15492	0.00049	0.0010	0.0039	0.00024	0.0078
ATCC15531	0.00049	0.00049	0.0020	0.00012	0.0039
C. pneumoniae					
ATCC53592 (AR-39)	0.0078	0.0156	0.0078	0.125	0.125
ATCC VR-2282 (TW-183)	0.0078	0.0156	0.0078	0.125	0.125

TEL: Telithromycin; CAM: Clarithromycin; AZM: Azithromycin; EM: Erythromycin

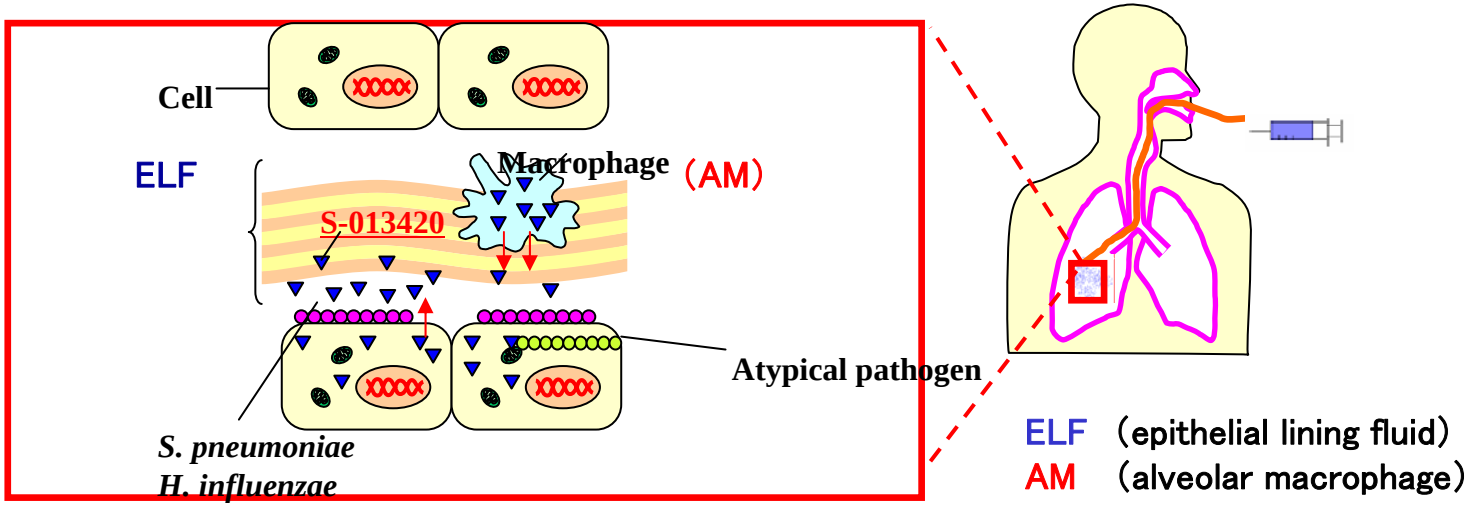
Summary of Phase 1 and Outline of Phase 2a Study in Japan

- **Summary of Phase 1 study**
  - **Pharmacokinetics：**
    - **Good PK profile（large AUC，long half-life），single dose a day will be possible**
    - **High distribution ratio to lung tissue**
  - **Safety：**
    - **No severe adverse events, safe and well-tolerated**
    - **Major adverse events: transaminase elevation, digestive symptoms (similar to that of analog drugs)**
- **Outline of Phase 2a study**
  - **Targeted disease**
    - **Pneumonia caused by bacteria or atypical pathogen**
  - **Design of study**
    - **Randomly allocated dose finding study**
  - **Accumulation of cases for initiation of Phase 2b study next winter**

Target Market and Positioning in Japan

- Market for macrolide antibiotics
  - **Current market size: ¥70-80 billion for Clarithromycin, Azithromycin etc.**
  - **Market for macrolide is increasing while that of other oral antibiotics is shrinking**
  - **Major players in the future are expected to be Azithromycin and Clarithromycin**
- Pediatric area
  - **Drugs effective against PRSP have long been desired by the market**
  - **High expectations for the macrolides which are effective against atypical pathogens and safe enough to pediatric usage**
- Aiming to be the first-line drug for oral antibiotics for respiratory infections
  - **in the market of macrolide antibiotics**
  - **in each market of cephalosporin, new-quinolone or penicillin**
- Shionogi will cover major oral antibiotics (cephalosporin, macrolide, new quinolone)

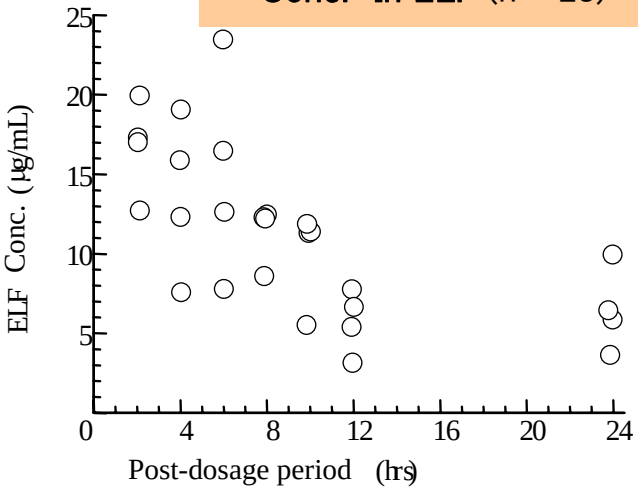
Lung Distribution



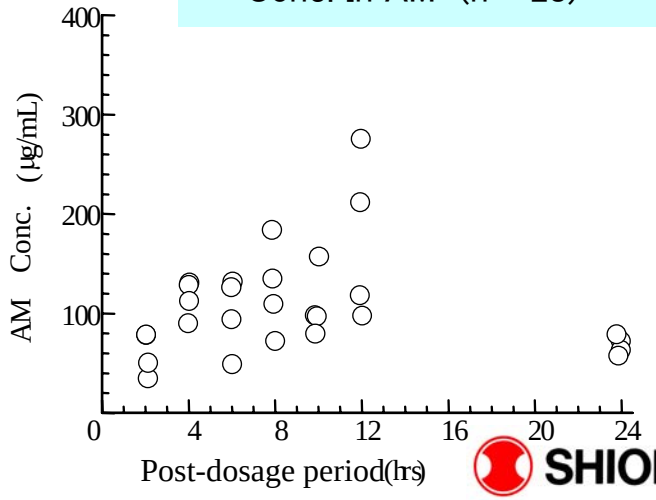
ELF (epithelial lining fluid)
AM (alveolar macrophage)

Phase 1 lung distribution study, (400mg single dose)

Conc. In ELF (n = 28)



Conc. In AM (n = 28)



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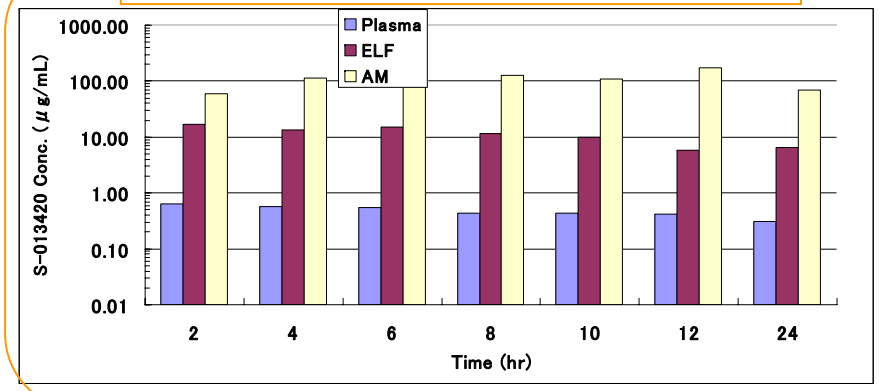
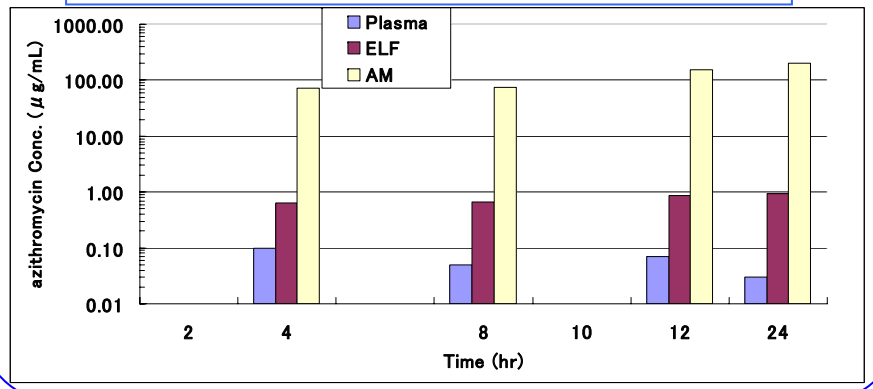
Lung distribution

【S-013420】 400mg single dose



【azithromycin】
Repeated dose（500mg×1day ＋ 250mg×4 days）



- **High distribution rate to lung tissue (Conc. in ELF was higher than plasma by ca 20 times.)**
- **Higher conc. of the drug than MIC $_{90}$ of major causing bacteria（PRSP, *H influenzae*, etc.）of respiratory infections. Superior efficacy on the respiratory infections can be expected because of high distribution rate to lung tissue.**

ELF （epithelial lining fluid）
AM （alveolar macrophage）

reference
CHEST 2004; 125: 965-973

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S-2367

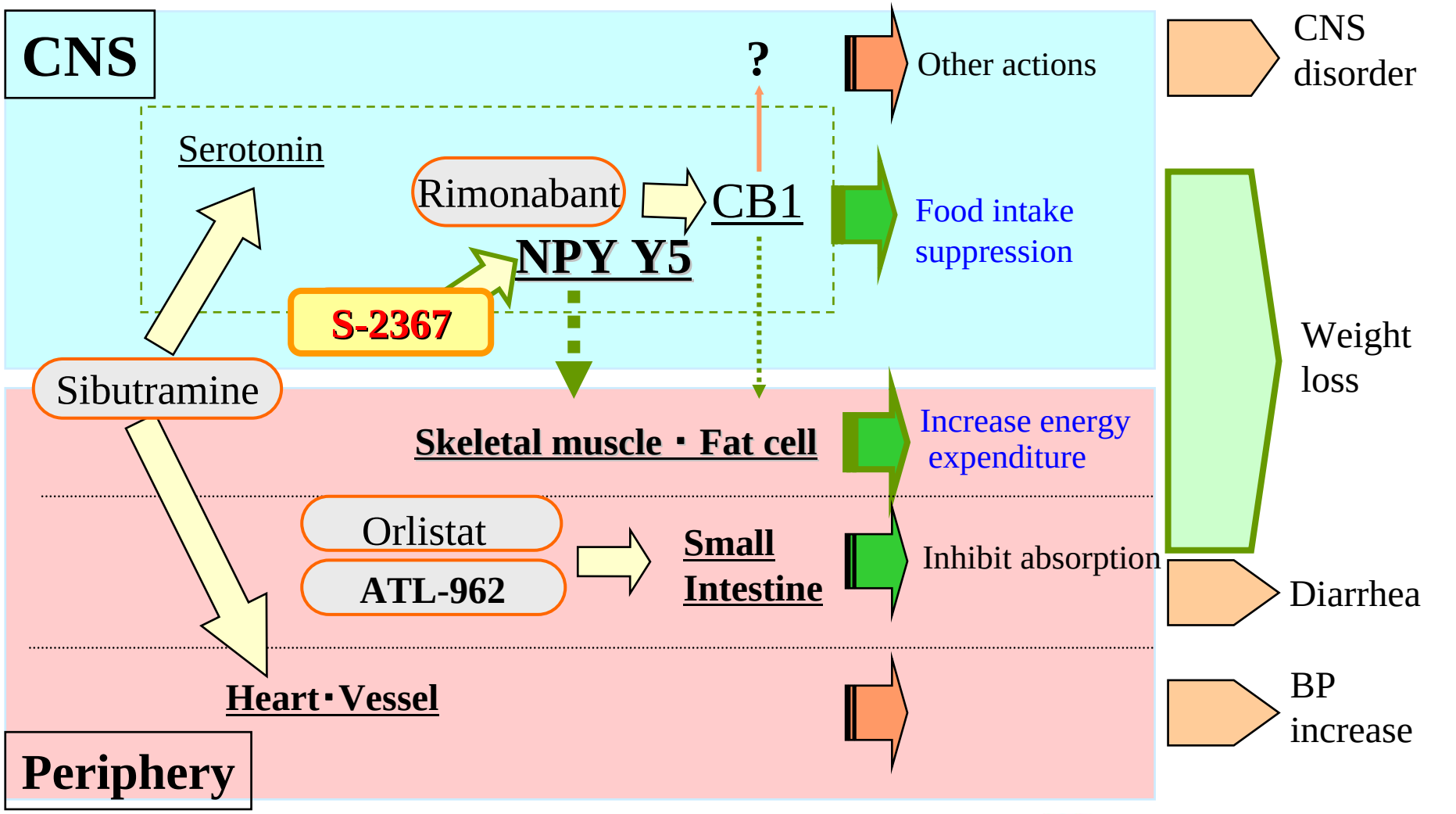
- Anti-obesity agent (Oral)
- Neuropeptide Y (NPY) Y5 receptor antagonist
- Expected weight reduction without rebound
- Suppression of visceral fat accumulation, improvement of blood glucose level and serum lipid level
- Phase 1 single and multiple dose studies have been finished in the USA
- Once-daily administration is possible（T ½ : about 20 hours）
- No drug-related serious adverse events were observed, excellent PK profile was confirmed.
- No serious findings in reproductive and developmental toxicity studies
- Phase 2 proof of concept study is under way in the USA

US Market for Anti-obesity Drug

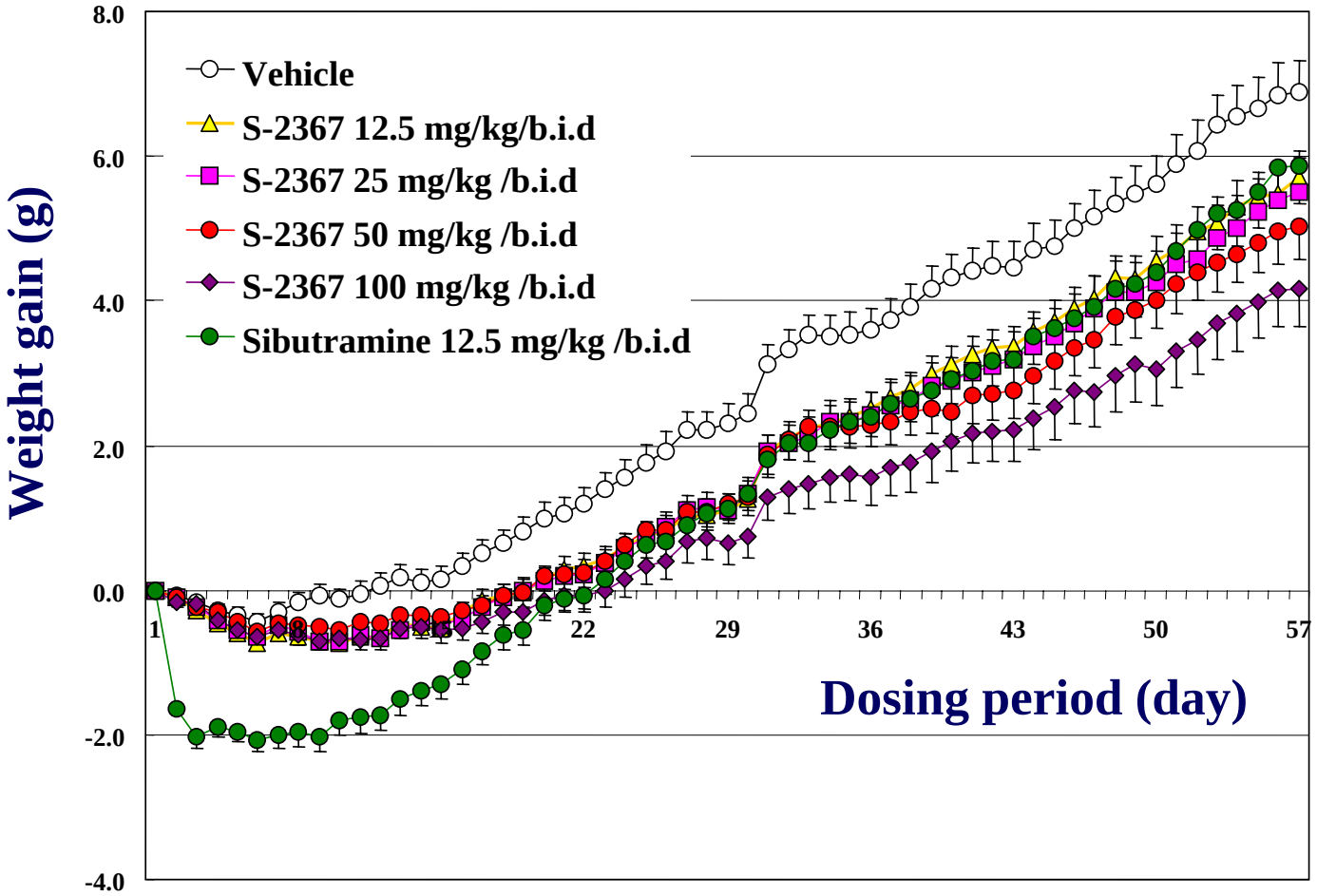
- **About 30% of adults (about 60 million people) are obese in the USA**
  （Source : NHAMES LIMITED）
  - **Obesity has been associated with a number of co-morbidities such as hypertension, dyslipidemia and diabetes**
- **Unmet needs for anti-obesity drugs are high**
  （Source : Datamonitor plc）
- **US market size: 2001 $444 mil. (peak)→ 2004 $353 mil.**
  - **The market shrank due to insufficient efficacy and side effects of existing prescription drugs**
- **New drug launches in the near future**
  - **Rimonabant（cannabinoid receptor［CB1］antagonist）**
  - **ATL-962（lipase inhibitor）and others**
- **Rapid market expansion is expected for anti-obesity drug**
- **Predicted US market size in 2012 : $1,860 mil.**

  (Source : Datamonitor plc)

Pharmacological Action and Characteristics of Anti-obesity Agents



Suppression of Weight Gain in High-fat Diet-induced Obese Mice



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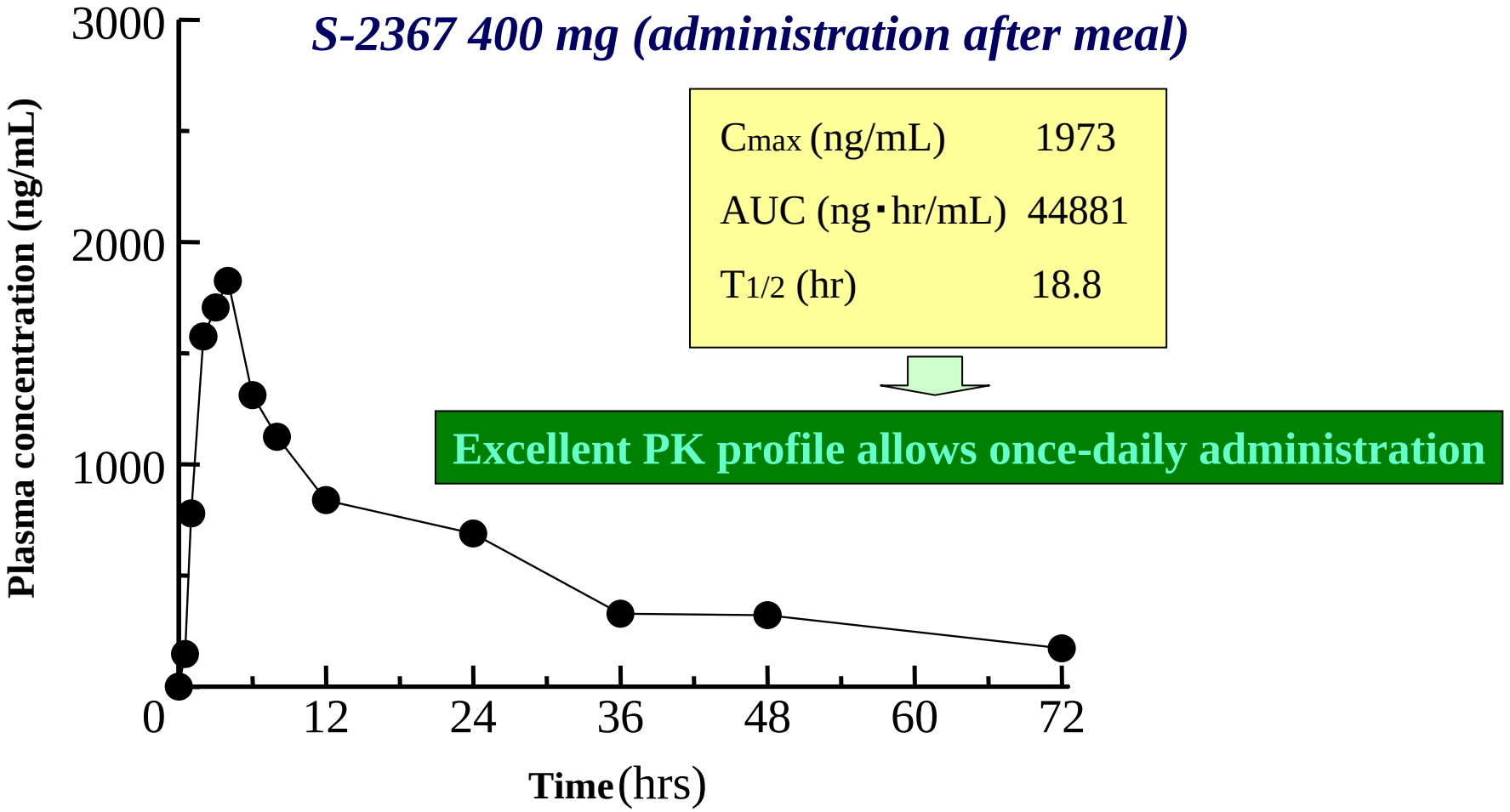
Plasma Concentration Change in Phase 1 Single Dose Study



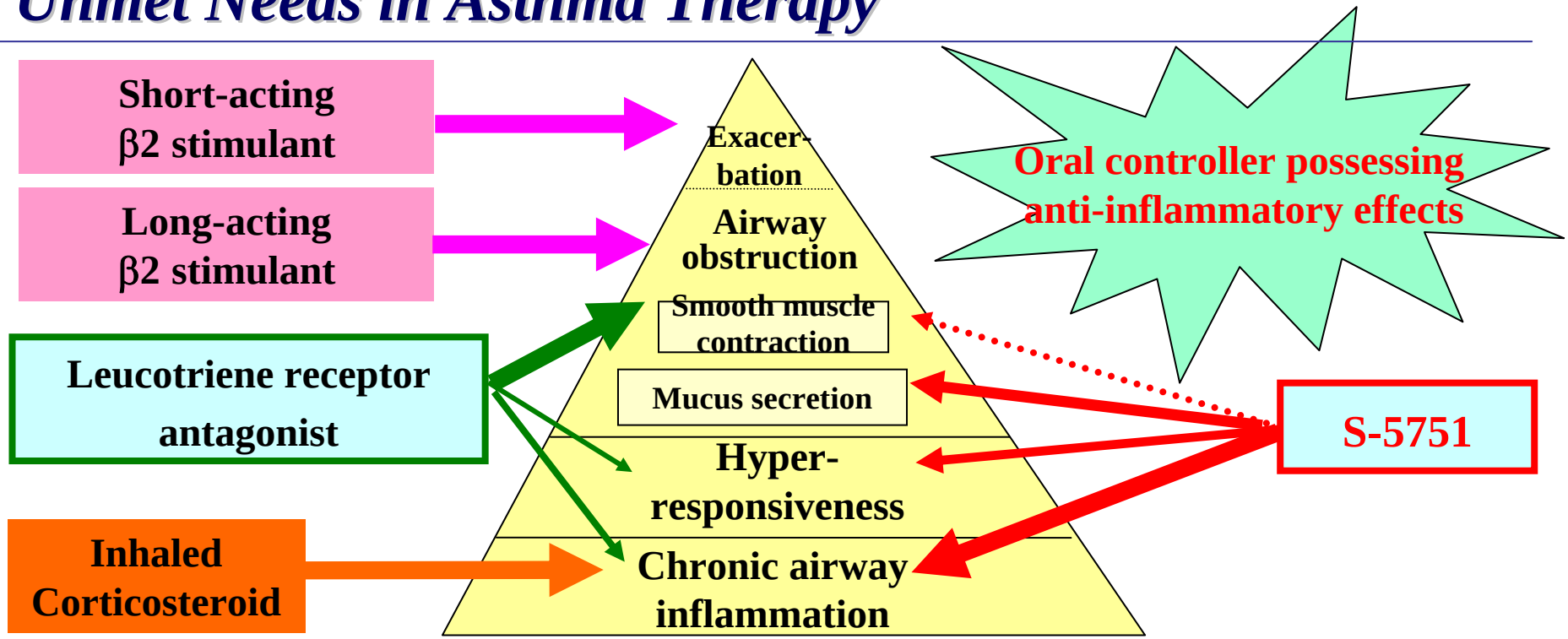
Phase 2a Proof of Concept Study

- **Underway at 20 sites in the USA**
  - **Double blind placebo controlled study**
  - **Subject**
    - **Healthy obese males/females including obesity patients with medically stable hypertension and hyperlipidemia**
  - **Two arms to be examined**
    - **Group to confirm the efficacy of weight loss** *(main efficacy as anti-obesity drug)*
    - **Group to confirm the efficacy of weight maintenance after losing weight through a diet treatment** *(to confirm the efficacy of NPY Y5 receptor antagonist under high NPY level)*
  - **Enrollment already completed, key break due to 2Q of FY2006**

S-5751

- **Prostaglandin D_2 Receptor Antagonist (oral)**
- **Observed marked efficacy in animal asthma models**
  - **in rats, guinea pigs and sheep**
    - **improved lung function after antigen challenge**
    - **suppressed airway hyper responsiveness**
    - **suppressed invasion of inflammatory cells involving airway inflammation**
- **Target positioning: Oral asthma controller based on anti-inflammatory effects**

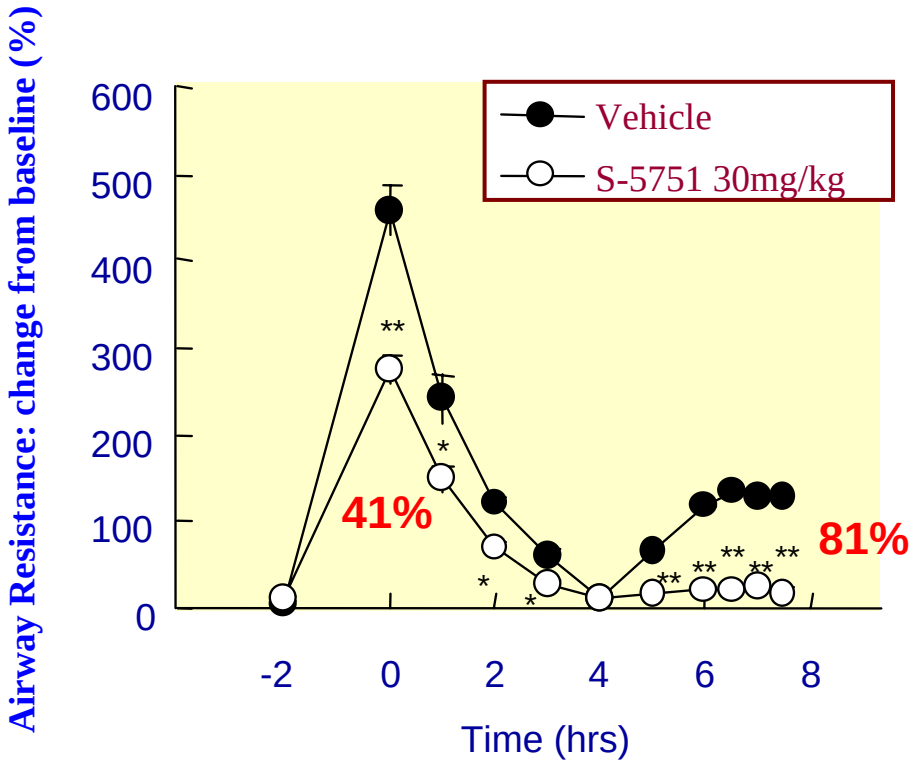
Unmet Needs in Asthma Therapy

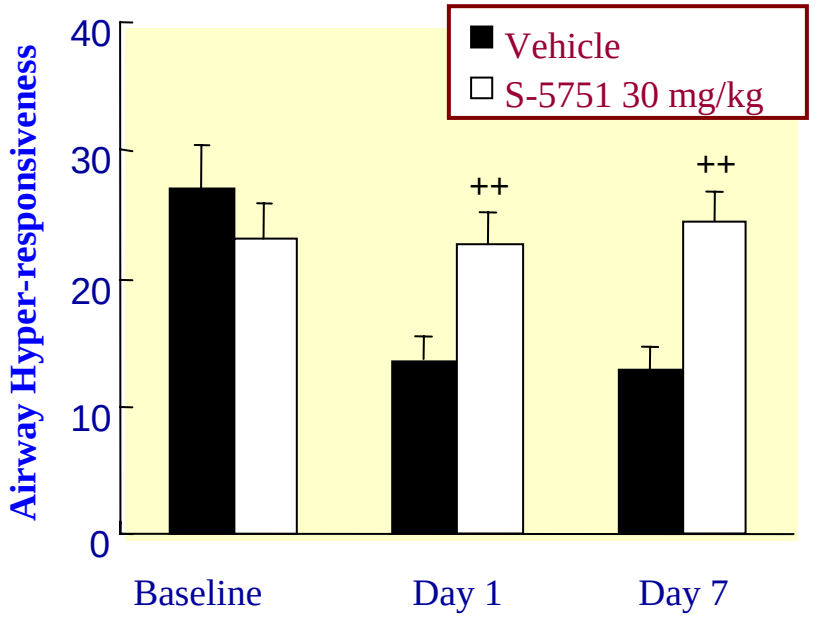


Unmet needs

anti-inflammatory effects (non-steroid)
safety (non-steroid), good compliance (oral)

Efficacy in Sheep Asthma Model





Airway hyper responsiveness: amount of carbachol required to provoke 400% increase in lung airway resistance (PC_{400}; Beath units). Lower PC400 means higher sensitivity.

Effects on airway resistance after bronchial antigen challenge

Effects on hyper responsiveness after bronchial antigen challenge

Past Clinical Studies

- **Clinical studies were conducted for Allergic Rhinitis (AR) as an indication**
  - **Phase 1 studies in healthy volunteers (5 studies)**
  - **Pharmacodynamics studies for AR (2 studies)**
  - **Phase 2 study in seasonal AR patients**
- **Over 400 subjects experienced S-5751 administration**
- **No significant side effects relating to safety**

Phase 1 Study in Asthma Patients

- **Conducted before Phase 2 study in asthma patients**
- **January 2005: IND**
- **April to August 2005: study conducted**
  - **assessed safety in asthma patients**
  - **subjects: mild to moderate asthma patients**
  - **14-day multiple dose**
  - **27 subjects were dosed with S-5751**
  - **no significant side effects relating to safety**

Clinical Development Status

- **Phase 2 study in asthma patients is ongoing**
  - **objectives: evaluate therapeutic effects and safety in asthma patients**
  - **subjects: mild to moderate asthma patients**
  - **300 patients to be randomized**
  - **8-week treatment period**
  - **about 30 sites in the USA and Eastern Europe**
  - **patient enrollment is progressing well**
  - **results to be available by the second half of fiscal 2006**

Duloxetine (Diabetic Neuropathic Pain; DNP)

- **Originator : Eli Lilly & Company**
- **Nonproprietary name : Duloxetine hydrochloride**
- **Serotonin Norepinephrine Reuptake Inhibitor (SNRI)**
- **Target Disease : DNP**
- **First-line drug for DNP, so far there is no approved drug with high efficacy in Japan.**
- **Expansion and strengthening of pipeline in MS area and pain area**
- **Life cycle management after approval for depression**

  ＊Eli Lilly obtained this indication in the USA in September 2004.

Phase 2 Clinical Trial

♦ Dose-Response Study

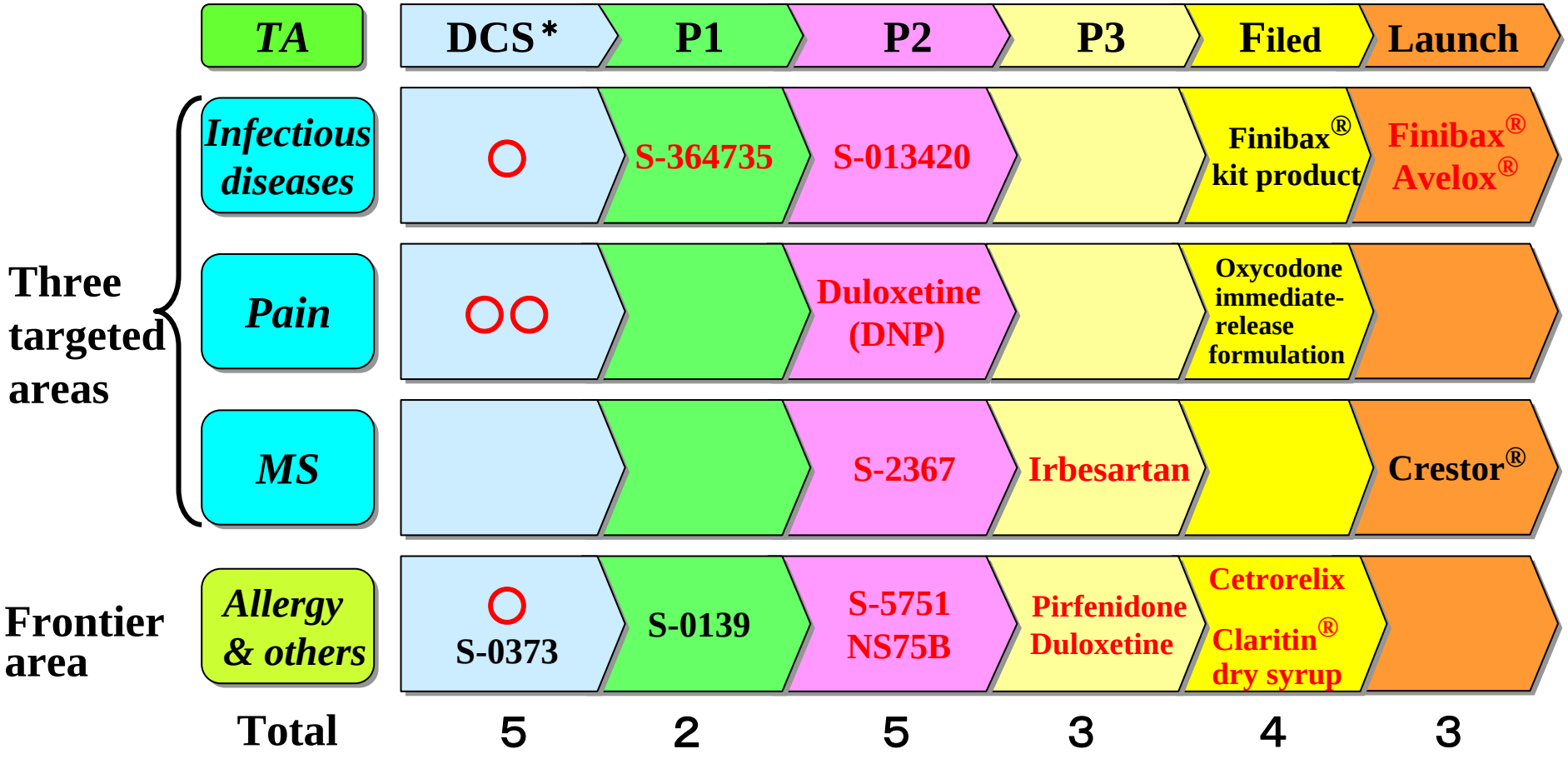
- Dosing period : 13 weeks
- Target sample size : 200 patients
- Study schedule :
  - FPI *: December 2005
  - Code break: March 2007

♦ Continuation study following "Dose-Response Study"

- Dosing period : 52 weeks
- Target sample size : At least 50 subjects who have proceeded from "Dose-Response Study"
- Study schedule :
  - FPI *: February 2006

* First Patient In

Shionogi R&D Pipeline (DCS ~ Launch)



DCS: Drug Candidate Selection
MS: Metabolic syndrome
TA: Therapeutic area

In red : Stage up compounds
○: Novel candidate

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Milestones for fiscal 2006

♦ Advance development on schedule

- **Launch 4 products（Cetrorelix，Claritin® dry syrup，Oxycodone immediate-release formulation，Finibax® kit product）**
- **NDA filing for 2 products（Irebesartan，Pirfenidone)**
- **Make a ‘go/no-go’ decisions for 4 products in Phase 2（S-013420，Duloxetine（DNP），S-2367，S-5751）**

Shionogi's Licensing Activities

SHIONOGI & CO., LTD.

March 9 , 2006

Shionogi's Licensing Function

Search

- ◆Compound selection
- ◆Scientific evaluation

In-licensing

- ◆Fundamental strategy
- ◆Deal terms and conditions
- ◆Negotiation & agreement

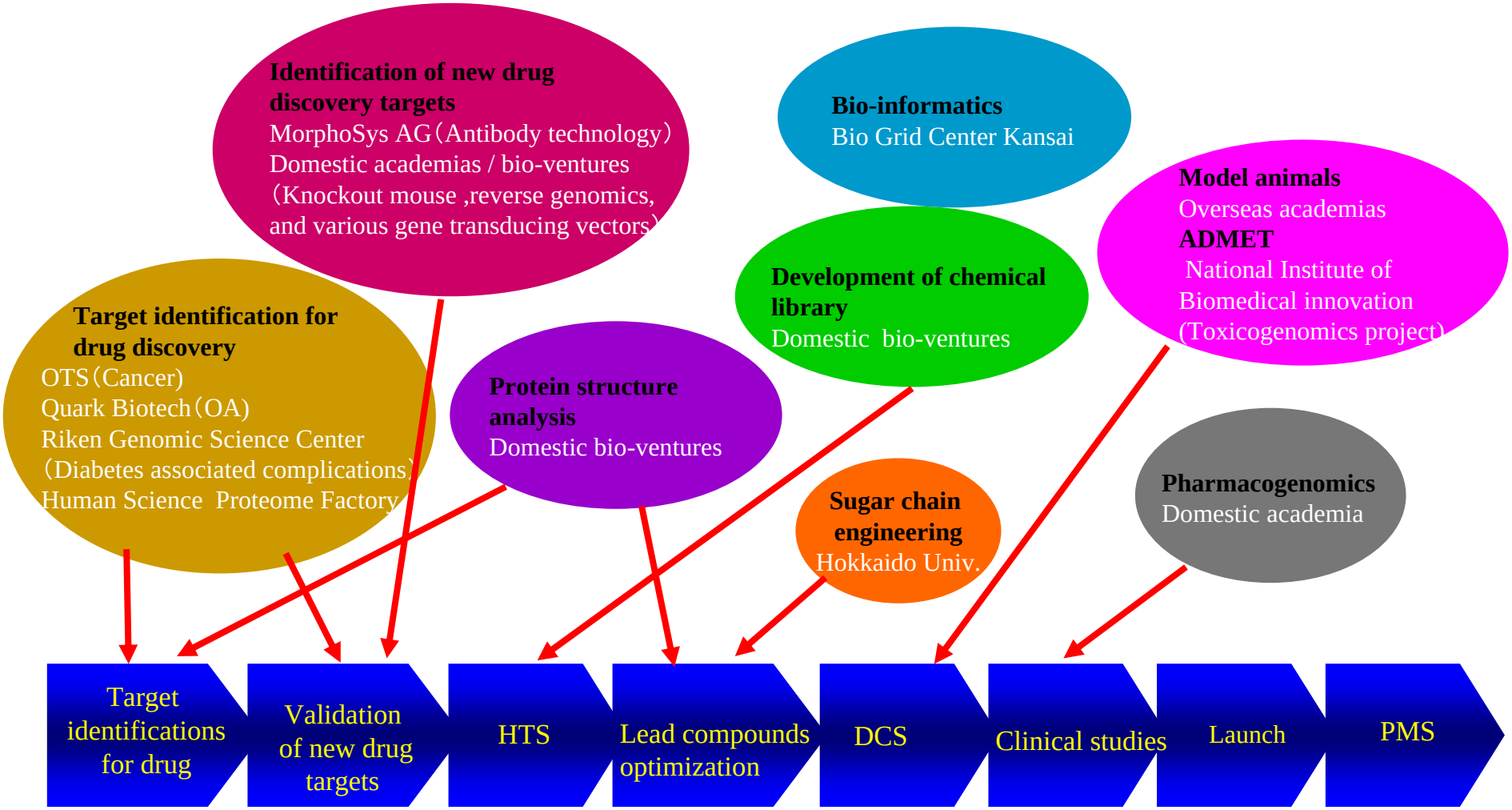
Value maximization

- ◆Construction of the governing organization
- ◆Alliance health check

Consistent process through continuous activity structure

High output through continuing cooperation with knowledge sharing

Shionogi's Productive Alliance Activities with Academia and Bio-ventures



DCS: Drug Candidate Selection

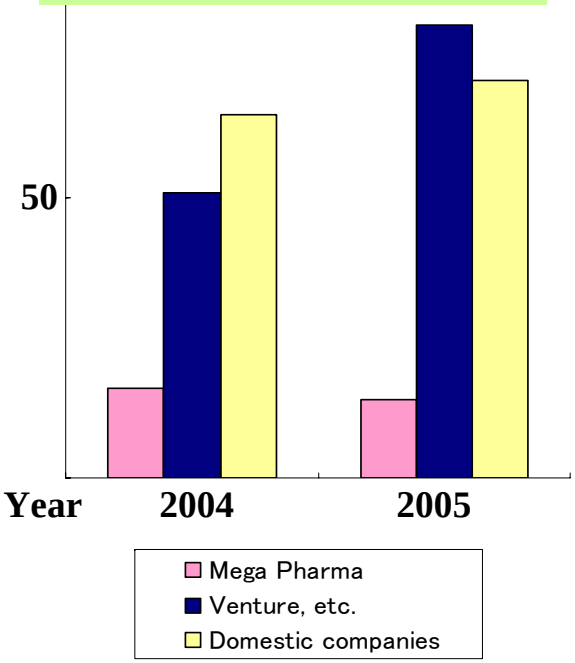
Approach to Licensing Opportunities

- **Worldwide information exchange with about 170 pharma and bio-ventures**
- **At academic conferences in target R&D areas**
- **At partnering conferences with bio-ventures**
- **Trimming in-house database**

Promote activities for exchange and collection of information

Expand licensing opportunities

Number of companies exchanging information



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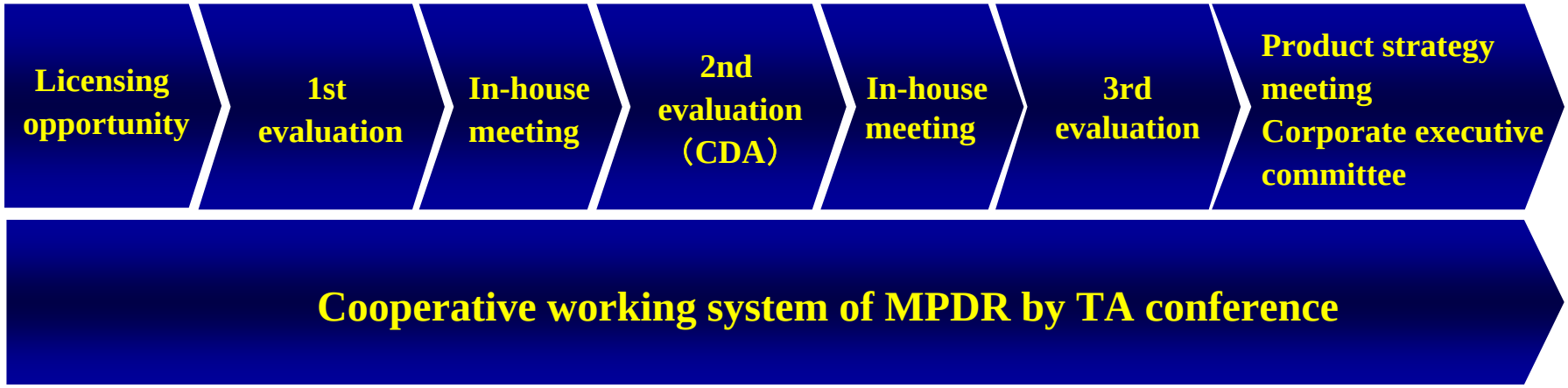
Evaluation System for Licensing



R&D Strategic Planning License Dept.

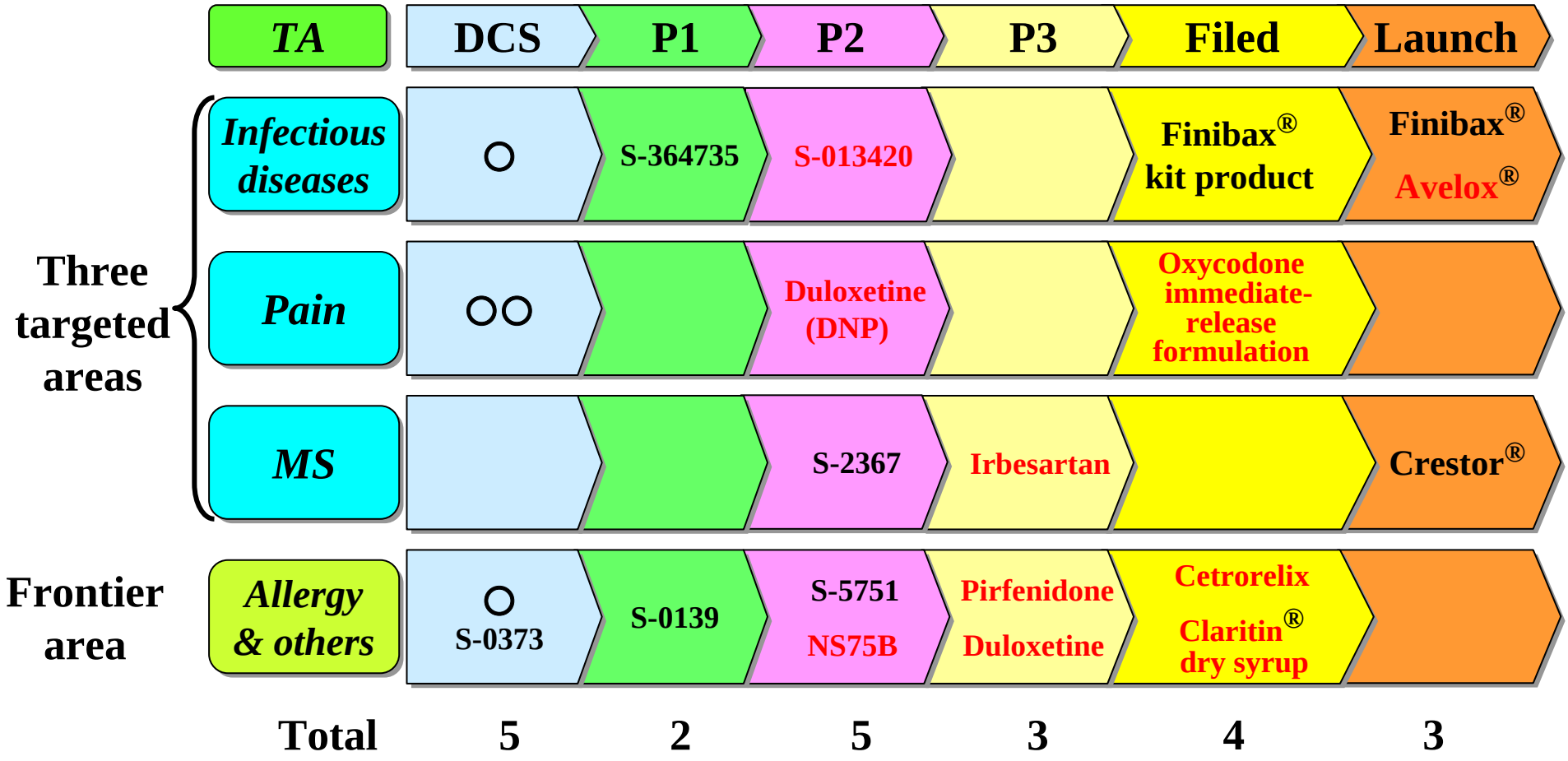
- R&D Strategic Planning
- Discovery Research Labs.
- Developmental Research Labs.
- Strategic Development Dept.
- Intellectual Property Dept.
- Manufacturing Technology Research Lab.

- Pharmaceutical Research & Development Div.
- Human Health Care Div.
- Corporate Administration Div.
- Manufacturing Div.

Internal and external coordination by License Department

Decision-making based on solid discussion

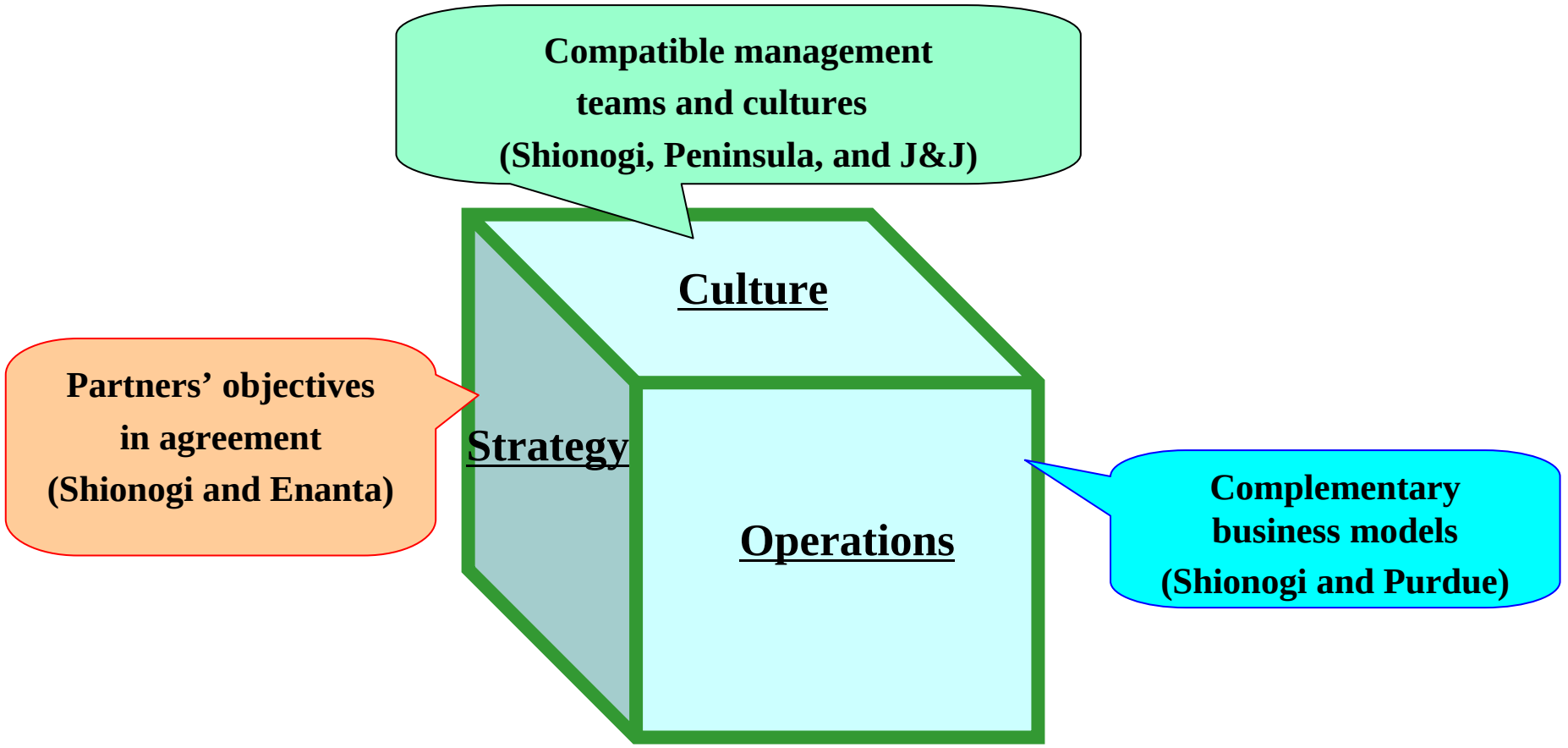
Shionogi R&D Pipeline (In-licensed Compounds)



DCS: Drug Candidate Selection
MS: Metabolic syndrome
TA: Therapeutic area

In red: In-licensed compounds
○: Novel candidate

Conditions for Success in Alliance



…there is good alignment!

References : The Warren Company, an Andersen Consulting alliances partner

Alliance Management with J&J

Peninsula

- **Share expertise and knowledge**
- **Close and constant monitoring**

Establishment of governance

Joint Steering Committee (JSC)

Joint Marketing Committee (JMC)

Joint Development Committee (JDC)

J&J | **Shionogi**

CL **CMC** **Marketing** **NCL** **PV** **AM**

Decision-making by the committee

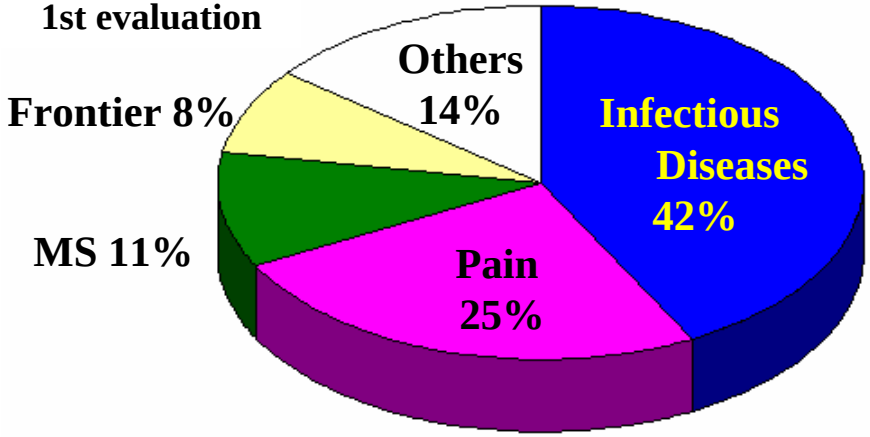
Communication at practical level

Goal

In- and Out-licensing Activities – Toward 2006

Fiscal 2005

Breakdown of 1st evaluation



Collaborative research agreement with Purdue

Paid utmost respect to the alliance with Mundipharma Purdue through MS Contin and Oxycontin

Marketing alliance agreement with Galderma

Obtained an understanding about the benefit of the alliance with Shionogi

Fiscal 2006

Platform technologies

To discover, foster and connect cutting-edge technologies to create novel drugs through alliances with both domestic and international academia and Bioclusters

In- and out-licensing

To focus activities on the three target areas
Possible partnering of S-2367 & S-5751
Three Fs: Fast, Footwork & Finding - Find promising opportunities with nifty footwork

Alliance management

To maximize product value of Finibax ®
Promote efficiency in managing the alliance with Purdue
Accelerate collaborative research activities for pain

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