



Executive General Manager, Pharmaceutical Research Division

Kohji Hanasaki, Ph.D.

Pharmaceutical Research Division

In fiscal 2010, which marked the first year of Shionogi's third medium-term business plan, we took our first step toward realizing global growth—generating several new development candidates and undertaking three initiatives aimed at strengthening our operation. As a leading maker of drugs to treat infectious diseases, one of our notable achievements was the successful generation of potential new antibiotics targeting multidrug-resistant Gram-negative bacteria, identified as a major problem both in Japan and overseas. In fiscal 2011, the second year of the new medium-term plan, we will seek to fully capitalize on the Shionogi Pharmaceutical Research Center (SPRC) due for completion in summer. By encouraging active communication among researchers, we aim to consistently turn out high-quality drug candidates, contributing to global realization of our basic strategies.

Review of fiscal 2010 (first year of the new medium-term plan)

The Pharmaceutical Research Division aims to achieve world-class drug discovery research quality and productivity by focusing our resources in three areas: enhancement of early phase research portfolio; improvement of predictive performance for clinical efficacy; and centralization of functions and strengthening of flexibility. We have set two numerical performance targets: first, to select four or more new molecular entities (NMEs) for drug candidate selection per year, and second, to create NMEs with a success rate of 50% or more in POC* studies.

During the first year of our new medium-term plan, we advanced two compounds to clinical trials—the HIV integrase inhibitor S-265744 LAP* and peptide cancer vaccine S-488410 (for esophageal cancer, head and neck cancer, etc.)—as well as progressing several new development candidates (including one for Alzheimer's disease) to preclinical studies. We also succeeded in generating three new development candidates in our focused therapeutic areas: two candidates of antibiotics for serious infectious diseases and a drug candidate for treatment of chronic pain. In the field of cephem antibiotics targeting Gram-negative bacteria, the unmet medical needs* in treatments to combat drug-resistant bacteria has been increasing in recent years. Against this backdrop, Shionogi has leveraged its strength in antibiotic research to successfully discover effective antibiotics against a broad array of multidrug-resistant Gram-negative bacteria, including *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. In order to convey the results of this research to medical settings worldwide as quickly as possible, we have formed a global R&D partnership with GlaxoSmithKline.

Initiatives in fiscal 2011 (second year of the new medium-term plan)

Enhancement of early phase research portfolio

We think that if Shionogi is to overcome the "Crestor Cliff" and further grow our operations worldwide, we must create groundbreaking new drugs addressing unmet medical needs. To upgrade our early drug discovery portfolio, the Pharmaceutical Research Division has focused on seeking out new seeds of research innovation through external alliances with academia and bioventures in Japan. Thus far, these efforts have spawned several new drug discovery programs; besides the Shionogi Science Program, there is also the FLASH* initiative with the Osaka University Graduate School of Medicine to find further drug discovery seeds, and a network of joint research projects around the hub of the Shionogi Innovation Center for Drug Discovery, established on the campus of Hokkaido University. We plan to take our search for the seeds of drug discovery worldwide by deepening our ties with overseas academia, especially in Europe. In addition to small molecule drug discovery, which we consider to be an area of our strength, we are conducting joint research with bioventures such as OncoTherapy Science, Inc. and AnGes MG, Inc., with a view to accelerating development of highly innovative large molecule drugs.

Improvement of predictive performance for clinical efficacy

In May 2010, we opened the Osaka University PET Molecular Imaging Center, a joint initiative with the Osaka University Graduate School of Medicine. Equipped with the latest cyclotron and radio/image analysis devices, the Center has already succeeded in the synthesis of a novel positron probe and in imaging analysis in pharmacokinetics and drug efficacy experiments. In fiscal 2011, we plan to press ahead with these initiatives, as well as promoting translational research to facilitate microdosing clinical trials. To further improve clinical predictability, we will fully analyze and make practical use of POC data concerning the compounds we develop in-house, creating enhanced predictive animal models and screening evaluation systems for assessing drug efficacy and toxicity.

Centralization of functions and strengthening of flexibility

July 2011 marks the scheduled completion of the much-awaited new research building in Toyonaka, Osaka. The SPRC will bring the company's various disparate research functions—from basic research to exploratory research, synthetic research and early-stage formulation research—under one roof. Our aim in doing so is to achieve top-class global research productivity, with the aid of cutting-edge research facilities and intensive scientific discussion yielded by greater coordination among researchers. In cooperation with other members of the Shionogi value chain, the Pharmaceutical Research Division will work to realize our company policy from a global perspective, at every stage of research from sales and development support to new drug creation.

Intellectual Property

The Intellectual Property Department is focused on developing a global patent strategy closely coordinated with Shionogi's R&D strategies. In fiscal 2010, as in past years, the Department put emphasis on acquiring substance patents for a broad range of new compounds in a large number of countries. As a result of these efforts, approximately 100



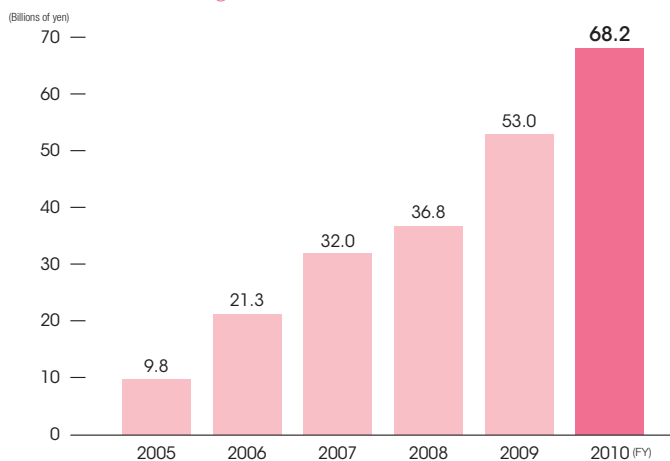
patents were filed, of which around 30% were for foreign patents (original invention filings).

In the US, several generic drug companies filed Abbreviated New Drug Applications for generic drugs of the hyperlipidemia treatment Crestor®. In response to these filings, the Company brought a patent infringement action against these generic drug companies in the US. In July 2010, a US district court ruled that the substance patent was valid and enforceable. This matter is still being contested because the generic drug companies subsequently appealed the ruling. Separate from the above, the Company is contesting the filing of generic applications by another manufacturer in a district court. In Japan, the Company is a defendant in a pending lawsuit concerning technology relating to genetically modified mice for research.

The emergence of generics manufacturers in recent years has seen generics launched to coincide with the expiry of substance patents. In light of this situation, Shionogi plans to efficiently acquire patents regarding indication, crystalline form, manufacturing method, formulation and in other areas in various countries commensurate with cost. In this way, the Company is determined to do its utmost to continue maximizing the length of patent terms and protecting its earnings.

As of March 31, 2011, Shionogi owned approximately 240 patents in Japan and approximately 120 families of patents in overseas jurisdictions (registered patents based on original invention filings).

Patent and Licensing Revenues



Glossary

- * **POC (Proof of Concept)**
POC studies are human clinical trials designed to demonstrate early signs of a product's efficacy.
- * **LAP (Long acting parenteral formulation)**
- * **Unmet medical needs**
This refers to conditions for which there remains no satisfactory method of treatment.
- * **FLASH (PHarma-Link between Academia and SHionogi)**



Executive General Manager, Global Development

Takuko Sawada

Global Development

Among the goals outlined in Shionogi's third medium-term business plan, one is to file for overseas regulatory approval for four products by fiscal 2014. Our mission in fiscal 2011 will be to select the candidate compounds holding the key to Shionogi's future growth, and subject them to efficient global development. To this end, we established the Global Development as an organizational body for planning and overseeing new drug development globally. The Global Development, along with subordinate bodies the Global Project Management and the New Product Planning, will step up the pace of development of highly marketable compounds.

Mission and role of the Global Development and its two subordinate departments

Under Shionogi's new medium-term plan, the mission assigned to the Development Division was first to make submissions for overseas regulatory approval of four compounds originating from Shionogi or Japanese research institutes, and launch more than one product, and second to globally develop at least five late-stage products (Phase IIb and beyond). To achieve these missions, we will give top priority to carefully screening for highly marketable drug candidates that can drive future growth, and pursuing global development of the chosen compounds with high speed and efficiency and relatively low cost. The Global Development is positioned as an organizational body charged with consolidating control over important decisions concerning "when," "where," "who," and "what studies at what cost."

Unified management enables us to prioritize—that is, to selectively allocate resources to projects that we believe have higher added value and will confer a competitive advantage. Additionally, the Global Development is putting in place systems and processes for global project management, including budgetary allocation and control based on the

Target Milestones for FY2011

Code No.	Milestones for FY2011
S-349572 (Dolutegravir)*	Global: Phase III registration completed
S-2367 (Japan) S-234462	Go/No-Go decision
Ospemifene	US: BE study completion, NDA filing
S-555739	Japan: Phase IIa completion, Go/No-Go decision
S-297995	US: Phase IIa completion, Phase IIb initiation Japan: Phase IIb initiation
S-707106	US: Phase IIa completion, Go/No-Go decision
S-888711	Japan: Phase IIa completion, Go/No-Go decision
S-288310	Japan: Phase I/II in progress (registration completed)
S-488410	Japan: Phase I/II in progress (registration completed)
S-222611	EU: Phase Ib in progress (registration completed)
S-265744 LAP	US: Phase I completion
FTIH (First Time in Human): more than new 3 compounds	

*Developed by Shionogi-ViiV Healthcare LLC

mentioned prioritization, and information on the progress of projects.

In order to speed up global development through timely and flexible decision-making, we arranged the Global Steering Committee (approval of development strategy and clinical trial plans for global compounds) and established the Global Product Strategy Meeting (evaluation and prioritization of the global development compound portfolio). This has enabled speedier strategic decision-making and development.

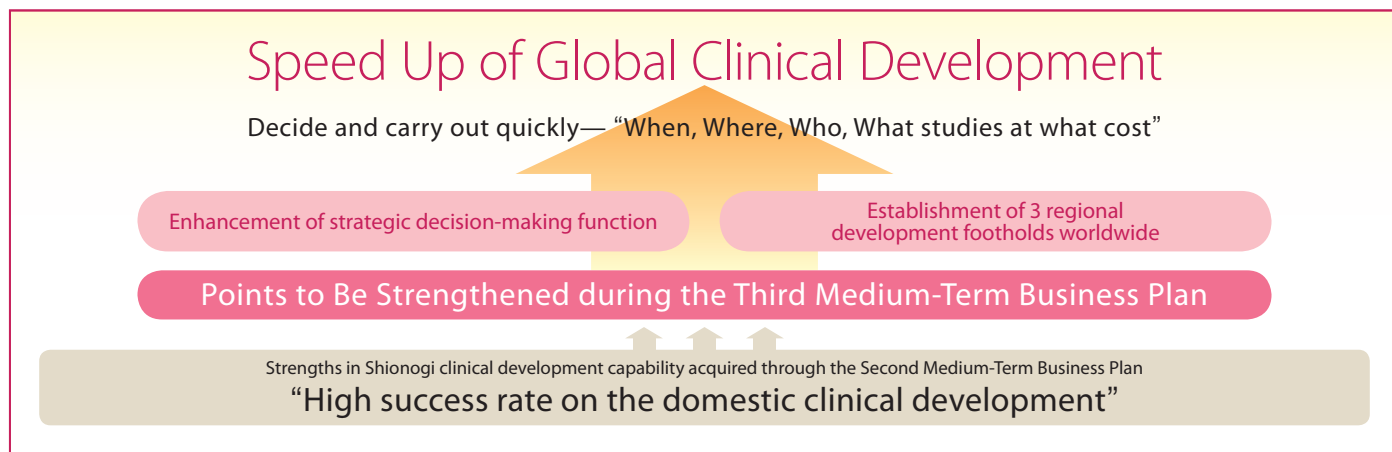
The functions of the Global Project Management and the New Product Planning, which were established under the Global Development, are as follows. The Global Project Management and its constituent Global Project Leaders are responsible for planning, implementing and supervising development strategies geared toward speedy and efficient global development in three regions: the US, Europe and Asia, including Japan. In specific terms, the Global Project Management is formulating plans for late-stage clinical development of global compounds once POC has been demonstrated in early-stage clinical studies domestically and overseas by the Pharmaceutical Development Division and our US subsidiary Shionogi Inc. Meanwhile, the New Product Planning conducts research on each therapeutic area and competing products, the goal being to create high added-value, namely, distinctive new products that can succeed through



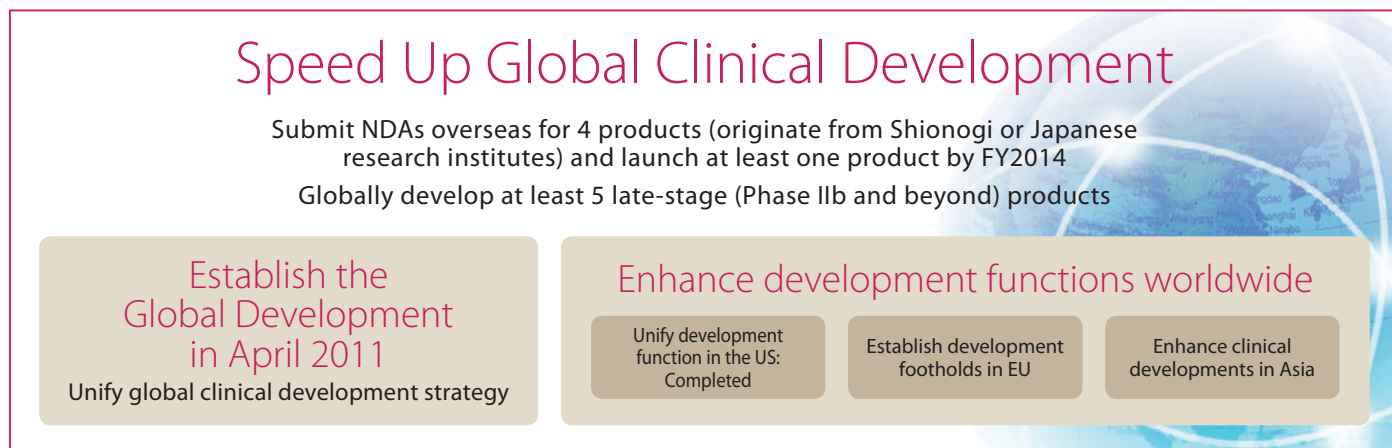
building a competitive advantage after launch.

The Global Development will work even more with the Pharmaceutical Development Division and Shionogi Inc. in an increasingly cross-organizational and borderless fashion, to ensure that all organizations act in unison and agreement, thereby generating maximum value from global development compounds.

■ Goals for the Third Medium-Term Business Plan ①



■ Goals for the Third Medium-Term Business Plan ②





Executive General Manager, Pharmaceutical Development Division
Takayuki Yoshioka, Ph.D.

Pharmaceutical Development Division

In fiscal 2011, the Pharmaceutical Development Division will engage in further collaboration with the Pharmaceutical Research Division, with a view to conducting early-stage development (to the point of determining POC) swiftly and accurately, and proceeding to clinical development resulting in regulatory approval in Japan and Asia. We will work actively to support attainment of the goals set in the new medium-term plan, providing backup to the Global Development while also assisting with application procedures in Japan and Asia, in terms of data analysis, handling of regulatory affairs and document preparation.

Review of fiscal 2010 (first year of the new medium-term plan) and prospects

In fiscal 2010, we scored notable achievements with three drugs: Rapiacta®, S-349572, and S-297995.

Rapiacta®, the influenza antiviral drug in-licensed from BioCryst Pharmaceuticals, Inc., gained Japanese regulatory approval for the additional indication for pediatric use. In children as in adults, this drug is expected to prove sufficiently effective with just a single dose. As it can also be used on patients with severe influenza virus infection and in cases where oral administration is difficult, we expect the drug to play a key role in preparedness efforts against pandemic influenza, which tends to involve a broad range of patients including children.

In Phase IIb trials, our global strategic product S-349572 (anti-HIV drug) showed strong antiviral activity not just in treatment-naive HIV patients, but also in treatment-experienced patients resistant to the existing integrase inhibitors. The drug is currently in Phase III trials around the world.

In a Phase IIa POC study in the US, S-297995 (for alleviating opioid-induced adverse effects) demonstrated efficacy against constipation, and entered Phase IIb trials in Japan and the US.

In other development news, the type 2 diabetes treatment S-707106 was observed to lower blood sugar levels in an exploratory Phase Ib study in the US, and a Phase IIa POC study is ongoing in the US. In the field of peptide cancer vaccine therapy, which is expected to become the fourth major form of cancer treatment alongside surgery, chemotherapy, and radiotherapy, S-288310 (bladder cancer) and S-488410 (esophageal cancer, head and neck cancer, etc.) are undergoing Phase I/II trials in Japan and are poised to enter clinical trials in Asia as well. All these drugs have the potential to become growth drivers, but in order to uncover new engines for growth we have been enriching our pipeline through the in-licensing of drugs such as S-524101 (for treating allergic rhinitis caused by house dust mite allergen), and peptide vaccines for ophthalmic disease (age-related macular degeneration and other retinal disorders).

Shionogi has received approval for carbapenem antibiotic Finibax® in Japan for a new dosage regimen in adult patients with serious and intractable bacterial infections, and our next step is to seek authorization for the additional indication of pediatric infection in order to maximize product potential. Furthermore, we have also filed applications for regulatory approval for the additional indication of diabetic neuropathic pain for the antidepressant Cymbalta®, as well as for a cancer pain analgesic, and an additional formulation of oxycodone hydrochloride for injection, as part of product life-cycle management.

Overseas Business Activities

Shionogi Inc.



President and CEO, Shionogi Inc.

John Keller, Ph.D

A core component of Shionogi's globalization strategy, Shionogi Inc. is a US subsidiary of Shionogi & Co., Ltd. and has fully integrated capabilities spanning clinical development, registration and regulatory affairs, business development, and commercialization. Aided by the establishment of the Global Development, we will work in close collaboration with research and development divisions in Japan—while also independently developing, registering, and marketing our own products in the US, the world's largest pharmaceutical market—to contribute globally to maximizing Shionogi value.

Shionogi Inc.'s role and mission within the Shionogi Group

Shionogi Inc. is intensively pursuing business development opportunities with a view to helping the Shionogi Group attain the goals set in its third medium-term business plan. We have more than ten marketed products in the US, including two new products launch in early 2011—Kapvay™ and Cuvposa™.

In April 2011, we completed the integration of our operations from Atlanta into one site in New Jersey, and clarified the targets of Shionogi

Inc. We expect that achieving the goals of "managing our costs to stabilize our earnings," "maximizing the commercial value of our existing portfolio," "expanding the US portfolio through business development," and "supporting the development of Shionogi pipeline products," will not only bring financial stability but also create a platform for Shionogi Inc. to grow.

Key to the future success of Shionogi Inc. is our focus on new products. We believe that products in-licensed through current business development activities will establish a strong base for the marketing and sale in the US of internally discovered compounds. To that end, it is important also to pursue alliances with leading global companies possessing both deep expertise and stability. Globally, Shionogi has an excellent track record of innovative and successful alliances, based on respect for the expertise and vision of our partners. As Shionogi Inc. pursues new US commercialization partnerships, it is imbued with the same spirit as its parent. In that sense we are seeking out growth-stage pharmaceutical companies and proposing what we believe to be mutually beneficial alliances.

Shionogi Inc. also has a key role in the US development and registration of Shionogi pipeline compounds, and following the establishment of the Global Development, all development efforts throughout Shionogi have become more tightly integrated. With this, the entire Shionogi Inc. workforce will work as one to further strengthen the US operation and enhance the Shionogi Group's growth prospects.



Pipeline

Attention Products

◆S-349572

(HIV integrase inhibitor)

S-349572 displays stronger antiviral activity than existing integrase inhibitors, as well as an excellent resistance profile and favorable pharmacokinetics (maintaining sufficient plasma concentration with once-daily administration without a booster). It is moreover an oral drug that can be administered in combination with other HIV medications. As there is still a need for additional treatment options for HIV, including concomitant administration and combination therapies, Shionogi is concurrently developing a drug combining S-349572 with Epzicom® (abacavir/lamivudine). This combination therapy is currently the subject of several Phase III trials.

◆S-297995

(Peripheral opioid receptor antagonist for alleviating opioid-induced adverse effects)

S-297995 is an oral medication that has minimal CNS effect and selectively targets peripheral opioid receptors. It is therefore effective in alleviating opioid-induced adverse effects including nausea/vomiting and constipation, yet exerts no adverse impact on the analgesic effect of opioids. It is distinguished from existing treatments by being effective at smaller doses not only for nausea/vomiting but also constipation. Phase IIa studies in the US confirmed the drug's safety and efficacy, in light of which a Phase IIb study has now commenced in Japan and the US.

◆Ospemifene

(Selective estrogen receptor modulator for post-menopausal vulvar and vaginal atrophy)

Ospemifene is an oral medication that stimulates estrogen receptors in the vaginal mucosa. It is being developed as a treatment for post-menopausal vulvar and vaginal atrophy, a condition in which declining estrogen levels have adversely affected the thickness of vaginal epithelial cells, elasticity, and vaginal secretion. Ospemifene differs from currently available selective estrogen receptor modulators (SERMs) like raloxifene and tamoxifen, which have an antagonistic action on estrogen receptors, and therefore lacks the side effects associated with traditional estrogen-related products, such as thromboembolism and endometrial thickening. Phase III studies are complete and a study is now under way to determine bioequivalence to the commercial product.

Areas	Code No. (Generic name) [Product name]	Category (Administration)
Metabolic Syndrome	S-474474 (Irbesartan/trichlormethiazide combination)	Angiotensin receptor blocker/diuretic combination (Oral)
	S-2367 (Velneperit)	Neuropeptide Y Y5 receptor antagonist (Oral)
	S-707106	Insulin sensitizer (Oral)
	S-234462	Neuropeptide Y Y5 receptor antagonist (Oral)
Infectious Diseases	S-4661 (Doripenem hydrate) [Finibax®]	Carbapenem antibiotic (Injection)
	S-349572* (Dolutegravir)	Integrase inhibitor (Oral)
	S-265744 LAP	Integrase inhibitor (Injection; Long acting parenteral formulation)
Pain	LY248686 (Duloxetine hydrochloride) [Cymbalta®]	SNRI (Serotonin & noradrenaline reuptake inhibitor) (Oral)
	S-811717 (Oxycodone hydrochloride)	Natural opium alkaloids (Injection)
	S-297995*	Peripheral opioid receptor antagonist (Oral)
Women's Health	PSD502 (Lidocaine/prilocaine)	Eutectic mixture of anesthetics (Metered-dose topical aerosol spray)
	Ospemifene*	Selective estrogen receptor modulator (Oral)
Other	S-555739	Prostaglandin D2 receptor antagonist (Oral)
	S-888711	Small molecule TPO mimetic (Oral)
	S-288310	Peptide cancer vaccine (Injection)
	S-488410	Peptide cancer vaccine (Injection)
	S-222611	HER2/EGFR dual inhibitor (Oral)
	S-524101	Sublingual tablet of house-dust mite allergen extracts for immunotherapy

Out-Licensing Activity

S-4661 (Doripenem hydrate)	Carbapenem antibiotic (Injection)
S-3013 (Varespladib methyl)	Secretory PLA2 (sPLA2) inhibitor (Oral)
S-0373	Non-peptide mimetic of TRH (Oral)

(As of August 2011)

Indication	Stage					Origin	Development
	Phase I	Phase IIa	Phase IIb	Phase III	Submission		
Hypertension	Japan: Phase III					Irbesartan: Sanofi Aventis (France) Trichlormethiazide: Shionogi	In-house
Obesity	Japan: Phase II					In-house	In-house
Type 2 Diabetes	USA: Phase IIa					In-house	In-house
Obesity	USA: Phase I					In-house	In-house
Pediatric infection	Japan: NDA submission (in preparation)					In-house	In-house
HIV infection	Global: Phase III					Shionogi-GlaxoSmithKline	Shionogi-ViiV Healthcare LLC
HIV infection	USA: Phase I					Shionogi-GlaxoSmithKline	Shionogi-ViiV Healthcare LLC
Diabetic peripheral neuropathic pain	Japan: NDA submission (September 2009)					Eli Lilly and Company (USA)	Shionogi/Eli Lilly Japan K.K.
For the treatment of moderate to severe pain in patients with cancer pain	Japan: NDA submission (September 2010)					Napp Pharmaceuticals Limited (UK)	In-house
Alleviation of opioid-induced adverse effects	Japan: Phase IIb					In-house	In-house
	USA: Phase IIb						
Premature ejaculation	USA, Europe: Phase III					Plethora Solutions Holdings PLC (UK)	Shionogi/Plethora Solutions Holdings PLC
Post-menopausal vaginal atrophy	USA: Phase III					QuatRx Pharmaceuticals Company (USA)	Shionogi/QuatRx Pharmaceuticals Company
Allergic disease	Japan: Phase IIb (in preparation)					In-house	In-house
	Europe: POM (Proof of Mechanism)						
	USA: NDA submission (in preparation)						
Thrombocytopenia	USA, Europe: Phase II					In-house	In-house
	Japan: Phase IIa						
Bladder cancer	Japan: Phase I/II					OncoTherapy Science, Inc. (Japan)	In-house
Esophageal cancer	Japan: Phase I/II					OncoTherapy Science, Inc. (Japan)	In-house
Malignant tumor	Europe: Phase Ib					In-house	In-house
Allergic rhinitis caused by house-dust mite allergen	Japan: Phase I					Stallergenes SA (France)	In-house
Bacterial infection	USA: NDA submission (June 2007) Hospital-acquired (nosocomial) pneumonia including ventilator-associated pneumonia					In-house	Johnson & Johnson (USA)
Acute coronary syndromes	USA, Europe: Phase III					Shionogi/ Eli Lilly and Company (USA)	Anthera Pharmaceuticals Inc. (USA)
Spinocerebellar ataxia	Japan: Phase II					In-house	Kissei Pharmaceutical Co., Ltd. (Japan)

Management

Shionogi's Business Activities

Shionogi's CSR Activities

Management System

Financial Section

Corporate Information



Executive General Manager, Human Health Care Division

Masaaki Goshima

Human Health Care Division

In fiscal 2010, the first year of our third medium-term business plan, the trial introduction of a new drug pricing system (NHI Drug Price Premiums for Promoting the Creation of New Drugs and the Elimination of Off-Label Drug Use) triggered dramatic change in the pharmaceutical sales and marketing environment in Japan. Despite the drug price revisions, Shionogi outpaced the market average in terms of growth in sales of prescription drugs in Japan for the first time in 12 years. Rather than relying on the off-patent drugs* that have been NHI-listed for many years, we will continue putting our all into promoting and carrying out educational activities on the new products, especially Crestor® (hyperlipidemia treatment), Irbetan® (antihypertensive) and Cymbalta® (antidepressant).

Review of fiscal 2010 (first year of the new medium-term plan)

We intend to achieve the goals set in our new medium-term plan by continuing to grow sales at a pace outstripping the average for the pharmaceutical market. In fiscal 2010, the first year of our new business plan, Shionogi's prescription drug sales grew 4.3% year on year, versus 2.5% growth for the market as a whole, according to Crecon data*. In this manner, growth outstripped that of the Japanese market for the first time in 12 years. We attribute our success in growing sales according to plan to strategic expansion in sales of eight strategic products: Crestor®, Irbetan®, Cymbalta®, OxyContin®/OxiNorm®, Finibax®, Differin®, Pirespa®, and Rapiacta®.

While leveraging Shionogi's long-standing strength in one-on-one sales activities by medical representatives (MRs), we also held a number of small seminars to promote "doctor to doctor" communication. We believe this action provided doctors, who share their experiences actually treating patients, with the information they need.

Shionogi's new medium-term plan also targets closer relationships with hospitals. This will require improved communication between Shionogi and hospitals (doctors), toward which end we have been holding web conferences with highly topical themes specifically catering for busy hospital doctors. These seminars offer doctors the convenience of participating online while remaining at their hospitals, and in fiscal 2010 our web conferences continued to attract large numbers of medical professionals.

In terms of initiatives undertaken to promote individual products, for Crestor® and Differin® we conducted our first direct-to-consumer educational campaigns. Based in part on television commercials, these programs were aimed at increasing public awareness of the two therapies, encouraging asymptomatic dyslipidemia patients and acne sufferers to seek help from medical institutions.

In April 2010, we entered the area of treatments for central nervous system (CNS) disorders when launching the antidepressant Cymbalta®, at which time we formed a special team of MRs dedicated to Cymbalta® detailing*. We will continue using MRs to maximize sales of our eight strategic products, while at the same time conducting marketing activities specifically tailored to each product's attributes.

Initiatives in fiscal 2011 (second year of new medium-term plan)

It goes without saying that our performance in fiscal 2011, the second year of our new medium-term plan, will be critical to achieving the plan's objectives. The Human Health Care Division will again concentrate its resources on expanding sales of Shionogi's eight strategic products, with the goal of achieving detailing synergies between products. We have positioned three products—Crestor® above all, followed by Irbetan® and Cymbalta®—as our core strategic products and aim to increase total sales



from them to ¥100 billion in fiscal 2014.

In marketing targeted at patients suffering from both dyslipidemia and hypertension, we anticipate detailing synergies between Crestor® and Irbetan®. In May 2011, approval was given for long-term prescription of Cymbalta®. As many depression sufferers are found to be afflicted also by lifestyle diseases such as metabolic syndrome or hypertension, we envision an increase in efficiency through concurrent detailing of Cymbalta®, Crestor®, and Irbetan®.

In terms of the other five strategic products, we conduct detailing activities, always aware of total care for patients. Although OxyContin®/OxiNorm®, both developed as analgesics for cancer pain, could relieve pain of most cancer patients when applied with appropriate dose setting, some cancer patients are still suffering from pain. Shionogi is therefore inspiring public opinion through multiple advertisements to make patients aware that cancer pain could be relieved with oral medication. At the same time, our MRs hold seminars for physicians as well as other medical professionals such as pharmacists and nurses. We are thus using every opportunity to provide information about cancer pain treatment. Moreover, Shionogi is tackling infectious diseases head-on, in an



environment where various infectious diseases have become social problems in recent years. We have produced a booklet called “What is SHIONOGI,” which looks back at our efforts in respect of infectious diseases over the past 100 years. Through this publication, we are providing information about Shionogi’s corporate commitment. In the context of treatments for infectious diseases, in April 2011 our carbapenem antibiotic Finibax® obtained or gained approval for an additional dosage and administration regimen (3g as a maximum daily dose), which we think will produce increased efficacy in patients with serious infections. At the 51st Annual Meeting of The Japanese Respiratory Society, new guidelines were released for NHCAP (nursing and healthcare-associated pneumonia). As an antipseudomonal drug, Finibax® (generic name: doripenem hydrate) was recommended at the meeting for patients at risk of infection with drug-resistant pathogens, and for those requiring treatment in intensive care unit settings. In fiscal 2011, we plan to continue the public awareness campaign begun in fiscal 2010 for Differin®, a topical treatment for acne vulgaris. We hope to return smiles to the faces of acne sufferers by encouraging them to seek help from dermatologists. With Pirespa®, the only drug indicated for idiopathic pulmonary fibrosis, receipt of regulatory approval in Europe has also had a favorable impact on domestic sales. Finally, Rapiacta® demonstrated the usefulness of injections in the treatment of influenza. In fiscal 2011, we will ramp up detailing activities with a view to carving out a role for Rapiacta® in treating all influenza patients.

Glossary

- * **Off-patent drugs**
Off-patent drugs for which generic equivalents exist
- * **Crecon data**
Market analysis data provided by pharmaceutical industry research organization Crecon Research & Consulting Inc.
- * **Detailing**
Providing doctors or other healthcare professionals with detailed information about drugs in a timely fashion.



Executive General Manager, Manufacturing & Technology Division

Takuo Fukuda

Manufacturing & Technology Division

Under the third medium-term business plan, the Manufacturing & Technology Division has the goal of strengthening the production system and ensuring a stable supply to support the global launch of in-house products. In fiscal 2010, the first year of our new medium-term plan, our emphasis was on putting in place new infrastructure to support these activities.

The Great East Japan Earthquake in March 2011 damaged the Kanegasaki Plant in Iwate Prefecture, where some of our key products are manufactured. It was not long, however, before production resumed after a concerted effort to get the plant up and running again.

Employees showed enormous passion and adaptability in undertaking restoration efforts and determination to make up for time lost due to the natural disaster. These qualities are strengths of the Manufacturing & Technology Division. I am convinced that they will enable us to speed up globalization and ensure stable product supplies, without affecting victims of the disaster.

Review of fiscal 2010 (first year of the new medium-term plan) and prospects

At the Manufacturing & Technology Division, we are actively working to bolster our existing manufacturing infrastructure and technology base in order to ensure reliable global supplies. In fiscal 2010, we enhanced the production line at the Settsu Plant in Osaka to support Cymbalta®, which was launched in April 2010, and also instigated a project to improve global GMP* compliance. At the Kanegasaki Plant, we began construction of a new formulation facility for injectable beta-lactam antibiotics in a move designed to consolidate and increase production.

In CMC* research activities so as to manufacture newly developed products and raise quality further, we embarked on construction of a D&M* facility that will be used for manufacturing APIs* in late-stage trials, and for commercial APIs in initial production. We also strove to establish technical expertise in biopharmaceuticals.

As part of our program to further develop the manufacturing infrastructure and technology base, we made consolidated subsidiary an API manufacturer Nichia Pharmaceutical Industries Ltd. a wholly owned subsidiary and renamed it Shionogi Pharma Chemicals Co., Ltd., as well as merging it with another wholly owned subsidiary, Shionogi Engineering Service Co., Ltd., to strengthen engineering functions.

In the field of infectious diseases, which is a priority therapeutic area for Shionogi, in 2010 we inked an agreement with GlaxoSmithKline to conduct joint research, development and commercialization regarding cephem antibiotics targeting Gram-negative bacteria. We intend to quicken the pace of development by appropriate manufacturing technologies at the early stage of R&D.

Impact of Great East Japan Earthquake and efforts to restore manufacturing facilities

The Great East Japan Earthquake on March 11, 2011 caused damage to our Kanegasaki Plant, where we manufacture mainstay antibiotics and cancer pain analgesics. At one point, we suspended all operations.

Thereafter, the entire company pitched in to aid the manufacturing division in restoring the plant, because it is precisely in circumstances such as this that we have a responsibility to provide patients with reliable access to Shionogi products. Production recommenced approximately a month later and has since been progressively ramped up as a result of prompt action to secure essential supplies, repair damaged facilities, accurately ascertain plant inventory levels, procure raw materials, and reschedule and redeploy manpower for resuming production. While we are still grappling with various issues in the aftermath of the natural disaster, the Manufacturing & Technology Division will continue making every possible effort to reinforce Shionogi quality while ensuring the stable supply of products.

Glossary

- * GMP (Good Manufacturing Practice)
- * CMC (Chemistry, Manufacturing and Controls)
- * D&M (Development & Manufacturing)
- * APIs (Active Pharmaceutical Ingredients)



Executive General Manager, Quality, Safety and Regulatory Affairs Management Division

Hirosato Kondo, Ph.D.

Quality, Safety and Regulatory Affairs Management Division

The first year of our third medium-term business plan has come to an end, and we are now into the second year. At the Quality, Safety and Regulatory Affairs Management Division we set three main goals in the first year of the new medium-term plan. First, to build and implement a global quality assurance system. Second, to upgrade predictive and preventive risk management. Third, to focus on human resource development. Each individual is working to advance the Company's pursuit of globalization, and the fruits of those efforts are considerable.

At the same time, we made it clear as to what aspects we should strengthen. For example, in our bid to build and implement a global quality assurance system, we consider it to be essential that the quality assurance and safety and regulatory affairs management for the Shionogi brand should function properly to ensure that patients around the world are able to use Shionogi products with confidence.

In the year ending March 2012, for a little closer to that objective, we will work cohesively to transform the Quality, Safety and Regulatory Affairs Management Division into an organization that acts rather than responds, viewing continued innovation as our overarching goal.

Review of fiscal 2010 (first year of the new medium-term plan)

In January 2010, in relatively quick time, we received regulatory approval for Rapiacta®, the world's first injectable treatment for influenza virus infections. To promote correct and safe usage after launch, the Quality, Safety and Regulatory Affairs Management Division is collecting data on all patients who receive the drug after launch to ensure safety, something never before undertaken in Japan.

In July 2010, we established a planning office to oversee the entire division, focusing specifically on our efforts to build a global quality assurance system, upgrade predictive and preventive risk management of Shionogi products, and engage in the necessary human resource development.

As the upshot of a joint project begun in early 2010 with Shionogi Inc. to build a new system for managing safety information globally, in March 2011 we also introduced and launched the Argus safety database for storing and managing adverse event information. This has enabled unified management of adverse event information and expedited the sharing of such information between Japan and the US, thereby allowing the Shionogi Group to take a cohesive approach to evaluating, ruling on, and responding to, adverse events. And, in November 2010, we established the "Shionogi Product Policy" to serve as an important guideline for Shionogi products. This policy emphasizes the pursuit of globally acceptable product quality.

On the other hand, fiscal 2010 saw us recall the OTC product Belix® and diagnostic agent Shionospot® BNP. After finding the cause of the problems based on information obtained from a contract manufacturer and an overseas manufacturer, we quickly recalled the products and took all the necessary improvement steps. Fortunately, there was no damage to human health. In light of these recall experiences, however, we will redouble our efforts to reinforce quality assurance for Shionogi products.

Initiatives in fiscal 2011 (second year of the new medium-term plan)

Under the aegis of the Global Development established in fiscal 2011 to steer and oversee global drug development, the Quality, Safety and Regulatory Affairs Management Division plans to work more closely with Shionogi's overseas affiliates to further strengthen quality assurance and ensure that patients worldwide can use Shionogi products with peace of mind. Following a management review conducted in accordance with international quality assurance guidelines, top management now has active involvement in this aspect of operations.

Turning to the Great East Japan Earthquake, we sustained damage to one manufacturing facility—the Kanegasaki Plant—and also to our Tokyo Distribution Center. In the event of future emergencies we may be required to make some changes to manufacturing processes. However, as a pharmaceutical manufacturer we will continue to devote every possible resource to ensuring the "quality," "safety," and "reliability" of our products, and to doing our utmost to achieve stable supply.

Major Products

Prescription Drugs

In fiscal 2011, which marks the second year of Shionogi's third medium-term business plan, we are targeting further growth through strategic expansion of sales for the eight core products underpinning our first basic strategy.

Crestor® Tablet (Hyperlipidemia Treatment)

Evidence from many clinical studies in Japan and overseas indicates that the statin therapy Crestor®, developed internally by Shionogi, is a leader among dyslipidemia treatments. Crestor® has been proven highly effective in lowering LDL cholesterol, thereby helping more dyslipidemia patients to reduce their risk of atherosclerotic diseases, and affording physicians and patients alike a greater sense of satisfaction and reliance.



Irbetan® Tablet (Antihypertensive)

Irbetan® is a long-acting angiotensin II receptor blocker (ARB) suited for use as a first-line therapy for hypertension. In addition to its superior antihypertensive effect, Irbetan® is also a first-choice treatment for the growing number of Japanese suffering from a combination of hypertension and metabolic syndrome. As a second-generation ARB, Irbetan® is the subject of much anticipation, and is also referred to as "metabosartan."



Cymbalta® Capsule (Treatment for Depression and Depressive Symptoms)

Cymbalta®, which won domestic approval in January 2010 after receiving US and European regulatory approval in 2004, is a serotonin and noradrenaline reuptake inhibitor (SNRI) approved in 99 countries around the world for the treatment of depression. It is expected to be a useful drug formulation for relieving the symptoms of depression and enabling those who suffer to achieve remission, recovery and a return to society.



Finibax®, Finibax® Kit (Carbapenem Antibiotic)

Developed in-house by Shionogi, Finibax® is a carbapenem antibiotic for injection with broad antibacterial activity against various bacteria. In April 2011, Finibax® received approval in Japan (ahead of elsewhere in the world) for an additional dosage (3g as a maximum daily dose). Shionogi is confident that this product will be effective for patients with serious infections.



Differin® Gel (Acne Vulgaris Treatment)

Differin® Gel, which uses adapalene and received an A grade recommendation for treating comedo as well as light to severe symptoms of inflammatory skin rashes in guidelines on the treatment of acne vulgaris, is Japan's first novel topical acne treatment with retinoid-like activity. We hope it will return smiles to the faces of acne sufferers.



Pirespa® Tablet (Idiopathic Pulmonary Fibrosis Treatment)

Offering the effect of inhibiting pulmonary fibrosis, Pirespa® (general name: pirfenidone) is the only drug that is indicated for idiopathic pulmonary fibrosis. In 2008, Shionogi became the first company in the world to obtain manufacturing and marketing approval of the drug in Japan. US company InterMune, Inc. received approval for pirfenidone in Europe in March 2011, and now plans to launch it across the region.



OTC Drugs

OxyContin® Tablet, OxiNorm® Powder
(Cancer Pain Analgesic)

The World Health Organization recommends treating cancer-related pain with oral analgesics that include immediate-release and sustained-release formulations of the same active ingredient. A combination of Shionogi's 12-hour sustained-release OxyContin® Tablet and immediate-release OxiNorm® Powder is clinically proven to be highly effective in cancer pain management.

Sedes® First
(Non-pyrazolone Analgesic Antipyretics)

We regard Sedes® First as a frontline analgesic antipyretic, in that it combines the three attributes patients demand from such drugs: it does not make you sleepy, is gentle on the stomach, and has a film coating that renders it easy to swallow.



Sedes® Hi G
(Pyrazolone Analgesic Antipyretics)

Sedes® Hi G is the first granular formulation in the Sedes® series, and like its predecessor Sedes® Hi contains isopropylantipyrene, which has an excellent antipyretic and analgesic effect. In its capacity as an analgesic antipyretic, Sedes® Hi G combines the clinical efficacy of Sedes® Hi with a granular formulation's ease of ingestion.



Pylon®
(Vitamin C-based Combination Cold Remedy)

Soluble in either hot or cold water, the lemon-flavored Pylon® is easy to ingest. Its seven active ingredients, starting with the analgesic antipyretic acetaminophen, and also including vitamin C, levels of which are quickly depleted during a cold, are effective in easing various cold symptoms including fever, chills, and sore throat.



Diagnostics

Rapiacta® Bag, Rapiacta® Vial
(Antiviral Drug for Influenza)

Rapiacta® was launched in January 2010, as the world's first influenza treatment administrable through a single-dose intravenous drip infusion. As an intravenous injection, Rapiacta® can be used to treat all age groups, from children to the elderly, and can be administered to seriously ill patients as well as patients who have difficulty swallowing tablets. These attributes aid it in fulfilling the mission of an anti-influenza drug, that of protecting the life of the patient.



MI02 Shionogi® BNP, Shionospot® BNP
(BNP Kit)

Because blood levels of the hormone BNP (human brain natriuretic peptide) rise when heart functions are even lightly impaired, BNP is a useful indicator when diagnosing and assessing cardiac insufficiency. With recent therapeutic guidelines citing testing of BNP blood levels as a useful means of screening people with hypertension for signs of cardiac insufficiency, BNP has gained a strong reputation at the frontlines of medicine.



Allerport® TARC
(Th2 Chemokine/TARC Kit)

TARC (thymus and activation-regulated chemokine) is believed to play a key role in the pathogenesis of atopic dermatitis, as serum levels of TARC are observed rising in step with worsening skin condition. Action to normalize serum TARC levels has proven highly effective in treating atopic dermatitis and for this reason such levels are regarded in clinical settings as an objective indicator of the condition. As a reagent used to measure serum levels of TARC, Allerport® TARC can be used to support treatment of atopic dermatitis.



Allerport® HRT (HRT Kit)

Launched in May 2011, Allerport® HRT (Histamine Release Test) is a reagent for use in automated assays measuring the histamine released due to allergens, of which 32 are now listed as causing food allergies in the Japanese Pediatric Guideline for Oral Food Challenge Test in Food Allergy.

Quick Chaser® Flu A,B
(Influenza Virus Diagnostic Kit)

Quick Chaser® Flu A,B is a reagent for determining whether a patient is infected by the influenza virus, featuring a product design that is easy for patients and medical professionals to understand. Together with Rapiacta®, Shionogi's anti-viral drug for influenza, Quick Chaser® Flu A,B is helping to improve patients' quality of life through the early detection and treatment of influenza virus infection.

