Achievements in the First Year of the Second Medium-Term Management Plan

In fiscal 2005, the first year of the second medium-term management plan, Shionogi effectively allocated resources in its targeted research areas and implemented bold reforms to meet plan objectives. The Company has designated infections, pain and metabolic syndrome as its three targeted research areas and subsequently established a future-oriented frontier research area. Organizationally, Shionogi implemented reforms to establish a therapeutic area-based framework in both research and development, with the three target areas and the frontier research area as the core. In conjunction with these reforms, the Company established the Therapeutic Area Conference (TAC) to horizontally link research, development, manufacturing and marketing in each targeted research area, as well as the Product Strategy Conference, which is in charge of strategic functions as a senior organization to TAC and serves as a venue for creative discussion.

In this way, the Pharmaceutical Research and Development Division made effective use of research, development, manufacturing and marketing resources while conducting activities as the core of a company-wide, comprehensive pharmaceutical development framework encompassing product portfolio evaluation and performance monitoring based on strategies for each targeted research area. Results of these efforts in the first year of the second medium-term management plan were as follows.

In research activities, Shionogi worked to expedite acquisition of Proof of Concept (POC) by developing strict standards for moving forward from the drug discovery stage in order to improve the quality of development candidate selection. At the same time, it worked to maximize drug discovery output by using milestone management to improve allocation of drug discovery resources. The Company enhanced its in-house research program, primarily in the three targeted research areas, while proactively conducting collaborative research with external research institutions. Through these activities, Shionogi selected four compounds at the drug discovery stage as development candidates for clinical trials. It also advanced one candidate compound to the clinical research stage.

In the area of infections, Shionogi commenced clinical trials on S-364735 (antiviral agent), and advanced an injectable

Strategic Alliances for Joint Research

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<td>Toxigenomics</td>
<td>National Institute of Health Science of the Ministry of Health, Labour and Welfare</td>
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<td>Glycoprotein synthesis</td>
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broad-spectrum cephem antibiotic to the development candidate stage. In the area of pain, Shionogi began collaborative research targeting receptors that modulate pain and neural pathways under an agreement with U.S.-based Purdue Pharma L.P. Through in-house research, the Company also successfully created a candidate compound that relieves nausea and other side effects of opioids. In the area of metabolic syndrome, Shionogi added to its expertise in developing glycoconjugate-based glycoprotein synthesis technology through joint research with Professor Shinichiro Nishimura of Hokkaido University. Shionogi is expediting research on diabetes treatments using a jointly developed automated carbohydrate synthesizer to develop glycoconjugate-based pharmaceuticals. In the area of frontier research, the Company selected a candidate compound with a novel mechanism of action that relieves itchiness. It is therefore expected to be effective in treating eczema and dermatitis.

For the technology platform that supports drug discovery in every field, Shionogi enhanced its basic research to speed up verification of target molecules, measurement of efficacy markers and other aspects of drug discovery. These efforts included ongoing participation in toxicogenomic research under the National Institute of Health Sciences of the Ministry of Health, Labour and Welfare; in the Japan Health Science Foundation’s Innovative Drug Proteome Factory Project Consortium; and in Kyoto University’s Biosimulation Project. In addition, Shionogi in-licensed new technology for producing phage antibodies from the German company MorphoSys AG. Shionogi has also made significant advances in new target gene drug discovery through collaborative research with organizations such as U.S.-based Quark Biotech, Inc. (osteoarthritis), OncoTherapy Science, Inc. (lung cancer, prostate cancer and breast cancer) and RIKEN Genomic Sciences Center (diabetic nephropathy).

In development activities, Shionogi continued working to build a management structure that promotes global development and to raise productivity. In Japan, Shionogi established a new management function in the Clinical Research Department to oversee outsourcing of clinical testing. This enhanced support for monitors and increased efficiency, enabling Shionogi to implement clinical testing on schedule. In global development, Shionogi enhanced the management framework of Shionogi USA, Inc. and upgraded its infrastructure to increase the efficiency of application processing and clinical testing. Based on the introduction of the targeted research system and infrastructure upgrades, Shionogi aggressively conducted Phase II clinical trials of two global strategic development products in the United States and Europe in close collaboration with Shionogi USA. In Japan, three products that are currently in Phase III clinical trials are proceeding on schedule.

As a result of the above development activities, in Japan Shionogi launched Crestor (hyperlipidemia treatment) and Fini-bax and Avelox (both antibacterials), and acquired approval for Cetrotide (premature ovulation inhibitor). Aiming for NDA submission in 2006 or 2007, the Company continued Phase III clinical trials for irbesartan (antihypertensive), pirfenidone (treatment for idiopathic interstitial pulmonary fibrosis), and duloxetine hydrochloride (depression). Shionogi also advanced S-013420 (novel macrolide antibiotic), which was licensed from Enanta Pharmaceuticals, Inc. of the United States, to Phase II clinical trials. Overseas, S-5751 (bronchial
Asthma) and S-2367 (obesity) are currently in Phase II (POC) clinical trials. S-2367, for which an early launch is expected due to high demand, proved to be effective and safe in POC clinical trials. For the first time in the world, clinical trials proved that this antagonist, which acts on the neuropeptide Y Y5 receptor, is effective in treating obesity. This marks a new phase in Shionogi’s global research and development activities.

From the perspective of strategic product life cycle management, Shionogi vigorously conducted clinical testing to add indications. Phase II clinical trials are under way for duloxetine hydrochloride as a treatment for diabetic peripheral neuropathic pain, and a controlled-release injectable dosage form of Cetrotide (cetrorelix pamoate) to treat benign prostatic hypertrophy. In addition, Shionogi has filed NDAs for an additional indication of pediatric use for Claritin in a dry syrup formulation developed by Shionogi and an immediate-release formulation of oxycodone hydrochloride, and recently received approval for Finibax 0.25g IV Solution Kit.

In licensing activities, in addition to conducting collaborative research with Purdue Pharma, Shionogi executed a sales and marketing alliance with the French company Galderma S.A. for Adapalene (topical treatment of acne vulgaris). Galderma submitted an NDA for Adapalene in June 2006.

In parallel with these R&D activities, the Pharmaceutical Research and Development Division places importance on developing its human resources, which are the source of Shionogi’s value. As the first step of the second medium-term management plan, the Division conducted a thorough review of its human resource development plan. Coordinating its plan with the Company’s overall human resource development plan, the Division expedited the establishment of a program to develop next-generation leaders. The outcome was an extensive training menu that forms the basis of development plans in which many employees in R&D are currently participating.

In these ways, Shionogi’s Pharmaceutical Research and Development Division made steady progress in the first year of the second medium-term management plan, based on measures that balanced strategy and organization.

Commitment to Achieving the Second Medium-Term Management Plan

The goal of Shionogi’s research activities is to aggressively maintain a continuous supply of new drug candidates for development. Based on this bold, venturesome spirit, Shionogi has set medium- and short-term goals toward achieving the second medium-term management plan, as well as challenging long-term goals for the period beyond the plan.

Milestones to be achieved in fiscal 2006 under the second medium-term management plan include advancing three of the four candidate compounds to the clinical trial stage within the fiscal year and advancing at least four compounds in the late discovery stages to the candidate compound stage by the end of the fiscal year.

As a long-term challenge, Shionogi aims to generate high-quality candidate compounds by focusing on enhancing its technology platform and licensing new technologies while applying strict program selection that employs target validation when moving from the early target identification period to later discovery program stages. In other words, Shionogi aims to generate new drugs in rapid succession on a global scale by conducting collaborative research with external research organizations, primarily in the three targeted research areas and the frontier research area.

In development activities, Shionogi is working to meet the following goals in target areas and other key fields.

In the area of infections, since the start of fiscal 2006
Shionogi has launched Finibax 0.25g IV Solution Kit, following on the launch of Finibax and Avelox in fiscal 2005. The novel macrolide antibiotic S-013420 is currently in Phase IIa clinical trials and is expected to advance to Phase IIb trials during fiscal 2006. Shionogi is also developing an injectable wide-spectrum cepham antibiotic, aiming for clinical trials within the current fiscal year as well. Plans are also set to advance S-364735, an HIV integrase inhibitor that commenced Phase I trials in March, to Phase IIa during the same period.

In the area of pain, during fiscal 2006 Shionogi plans to launch immediate-release oxycodone hydrochloride, for which an NDA has been filed, and expects to receive the results of Phase IIa clinical testing of the new indication of duloxetine hydrochloride as a treatment for diabetic peripheral neuropathic pain.

In the area of metabolic syndrome, everyone at Shionogi is working together to maximize the value of Crestor. The Pharmaceutical Research and Development Division is also making a concerted effort through a cooperative framework centered on the TAC. During fiscal 2006, Shionogi plans to submit an NDA for irbesartan, an angiotensin II receptor antagonist for treatment of hypertension. It also plans to concentrate efforts on testing toward developing the obesity treatment S-2367 for the U.S. and European markets by accelerating the schedule for Phase IIb clinical trials in the United States based on the evidence of its effectiveness in POC clinical trials.

In the area of frontier research, in fiscal 2006 Shionogi plans to launch Claritin for pediatric use (with a new dry syrup formulation) and submit an NDA for pirfenidone, a treatment for idiopathic interstitial pulmonary fibrosis, which is currently proceeding smoothly through Phase III trials. The bronchial asthma treatment S-5751, which is currently undergoing clinical testing overseas, moved to Phase IIa in fiscal 2005. Shionogi plans to consider advancing it to Phase IIb in the second half of fiscal 2006. In addition, the Company is concentrating efforts aimed at bringing an antipruritic agent with a new mechanism of action developed in-house to the clinical testing stage during the current fiscal year. Shionogi’s aim is to further expand its presence in the field of dermatology, which has already been established by Rinderon and Claritin.

Other key products include the premature ovulation inhibitor Cetrotide, which received marketing approval in April 2006 and which Shionogi plans to launch in September, and Adapalene, for which the licensor submitted an NDA in June 2006, as previously mentioned. Cetrorelix pamoate, code number NS75B, is scheduled to begin Phase IIa clinical trials as a treatment for benign prostatic hypertrophy during fiscal 2006 as well. The antidepressant duloxetine hydrochloride is currently in Phase III clinical trials, and Shionogi plans to submit an NDA during fiscal 2007.

**Toward Sustainable Growth**

Through its research and development activities, Shionogi aims to develop safe, original ethical drugs under a corporate mission of “continually providing the superior medicines essential to people’s health.” Through close collaboration with other divisions and effective use of limited management resources, the Pharmaceutical Research and Development Division will continue working to fulfill its goal of continually developing new drugs. By doing so, it will enable the Company to survive in an increasingly competitive global business environment and to continue creating and providing ethical drugs that contribute to the health of people around the world. Based on this concept, Shionogi’s Pharmaceutical Research and Development Division will work to achieve overall Company strategies under the second medium-term management plan and expedite measures focused on global development.

**Overview of Intellectual Property**

**Patent Application Strategy and Status**

A single patent in the pharmaceutical industry affects a
company’s ability to compete and is extremely valuable compared to patents in other industries. Shionogi’s patent application strategy entails first gaining an accurate awareness of other companies’ patent applications in regard to promising drug discovery targets selected in the research process. Shionogi then focuses on efficiently acquiring strong, comprehensive patents for broad classes of compounds among the drug creation targets that demonstrate an activity. As part of efforts to strengthen protection of its own products, Shionogi carefully considers ways to extend the life cycle of products after their launches, and also aggressively acquires patents in areas including production processes, intermediates, uses (e.g., additional indications), formulations and crystalline structures. At the same time, Shionogi extends the life of the patents the Company holds for the maximum period allowed by the patent systems of various countries.

To implement this strategy, Shionogi works to educate researchers according to their level in order to raise their awareness of intellectual property; to identify inventions at early stages of research through the participation of Intellectual Property personnel in cross-functional teams that span internal and external organizations, including collaborative research between private corporations and educational institutions; and to search prior arts in a trustworthy manner. As a result, Shionogi has facilitated efficient patent applications (130 patent applications in fiscal 2005, 40 percent of which were filed overseas).

**Patent Portfolio Management**

Shionogi responds to changes in research and development and operating strategy, and periodically reviews its portfolio of patents on products and on products under development to optimize the patents the Company holds. As of the end of fiscal 2005, Shionogi held approximately 240 patents in Japan and a family of approximately 300 patents overseas. Income from licensing patents during fiscal 2005 totaled approximately ¥9.8 billion, an increase of about 60 percent compared with income of approximately ¥6.1 billion in fiscal 2004.

In 2006, Shionogi won the Japan Patent Office Commissioner’s “Intellectual Property Award of Distinction.” Reasons cited for the award include the highest rate of patents granted in the pharmaceutical product industry; the Company’s enhancement of the linkage between R&D strategy and intellectual property strategy by reorganizing the Intellectual Property Department, formerly a separate head office function, within the Pharmaceutical Research and Development Division; its active disclosure of the intellectual property portfolio to the Company’s management through measures such as placing the focus of intellectual property strategy decisions on the officers in charge of intellectual property and convening an intellectual property evaluation committee to strictly review and decide the necessity of patent examination and renewal requests; and its vigorous efforts to educate employees about intellectual property.

**Management of Trade Secrets**

Advances in information technology in recent years have increased the importance of managing intellectual assets, especially for trade secrets of companies engaged in manufacturing. Shionogi works to educate its employees about information security and prevent information outflow in situations such as when employees leave the Company for other employment or retire.

**Invention Reward System**

Since 1988, Shionogi has implemented an internal invention reward system to create fertile ground for new breakthrough drugs by enhancing the motivation of its researchers and engineers to conduct creative research and technology development, in compliance with Article 35 of the Japanese Patent Law. In fiscal 2005, Crestor® fulfilled the conditions of the performance-based bonus system that the Company introduced in 2001. Based on this, in 2006 Shionogi will pay the inventors a maximum of 0.05 percent of fiscal 2005 worldwide product sales, including licensee’s sales.