

Pharmaceutical Development

To respond to the increasingly diverse needs of medical therapy facilities and contribute to effective treatment for patients worldwide, Shionogi is seeking to accelerate its development programs and increase their success rate.

Progress of the Second Medium-Term Management Plan

Shionogi launched three new drugs in Japan during fiscal 2008, including an antihypertensive agent, long-acting angiotensin II receptor antagonist, Irbetan[®], in July 2008; the first topical preparation for acne vulgaris approved for manufacturing and marketing in Japan, Differin[®], in October 2008; and an idiopathic pulmonary fibrosis treatment, Pirespa[®], in December 2008.

As a result, the Company has succeeded in launching 9 new products during the past four years, and it has made great progress toward its medium-term management plan target of launching 10 new products in Japan during a five-year period.

Global Development Programs

In general, Shionogi's domestic and overseas clinical trial projects are smoothly advancing to new stages. An integrase inhibitor anti-HIV agent being developed by Shionogi-GlaxoSmithKline Pharmaceuticals LLC, S-349572, has moved up to the proof-of-concept (PoC) stage. Shionogi USA conducted year-long Phase IIb clinical trials of a neuropeptide Y Y5 receptor antagonist for treatment of obesity, S-2367, and found that the 800mg doses of the drug candidate attained the FDA's draft guidance standards. In view of this, the

potential of S-2367 for treating obesity has been confirmed.

* For information on drug candidates in each region, please see the chart on page 18.

Measures to Accelerate the Generation of New Drugs

Amid the recent trend of decline in drug candidate commercialization rates, it is clear that candidate compounds that have reached the PoC stage must be developed with due attention to the maximization of product value from an early point based on a life-cycle-management perspective. Accordingly, the Pharmaceutical Development Division has established two new functions—the Medical Science Department and the Marketing Department—and is moving forward with measures to leverage analyses undertaken from the perspective of medical science and to increase emphasis on life-cycle-management strategies.

Shionogi's development plan for fiscal 2009 calls for submitting an application for the approval of a neuraminidase inhibitor anti-influenza agent, S-021812, that has been the subject of Asian multinational Phase III trials; expanding the applications of duloxetine hydrochloride for the indication of diabetic neuropathic pain, as a life-cycle-management measure; and submitting an application for

Finibax[®] carbapenem antibiotic for the indication of treating severe and intractable infectious diseases.

Moreover, in February 2009, Shionogi entered into a licensing agreement that gives it globally exclusive rights to peptide vaccines for cancer treatment, and the Company has begun developing those vaccines. Going forward, Shionogi plans to continue proactive in-licensing/out-licensing activities as it strives to strengthen its development pipeline and ensure its future growth.

Advancing from the Accelerating Stage to the Significant Strides Stage

Currently, Shionogi is drafting its third medium-term management plan. This plan will call for achieving steady progress during the period from 2012 through 2014 in arranging the submission and approval of applications for global development drug candidates as well as the marketing of the resulting drugs. Both in Japan and overseas, the Group will create systems able to provide markets with steady supplies of products.

By means of proactive research activities, the Pharmaceutical Development Division has acquired capabilities for steadily moving distinctive in-house drug candidates ahead to more-advanced clinical study stages. To this end, it has fostered capabilities for perspicaciously evaluating compounds at early development stages, focusing and concentrating limited resources on selected projects, and increasing development efficiency. Moreover, it is evolving a culture that encourages drawing on the most advanced scientific technologies to boldly address challenging tasks that require innovative new approaches. By effectively leveraging these approaches, the division intends to play a key role in impelling Shionogi ahead from the stage of "accelerating toward significant strides" to the "brink of significant strides" and "significant strides" stages.





Shionogi USA: Building on Recent Successes



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CEO, Shionogi USA, Inc.

For Shionogi USA, fiscal 2008 represented a turning point in our goal to establish a truly global product development engine for Shionogi & Co., Ltd. Most notably, we completed the largest clinical study conducted independently by Shionogi outside of Japan—a Phase IIb study of S-2367 (velneperit) for obesity. The results not only demonstrate the potential for NPY5 receptor antagonism as a target for obesity treatment, but confirm that Shionogi is capable of executing global clinical studies for product candidates originating from our own pipeline. In addition, Shionogi USA supported the achievement of a successful Phase IIa proof-of-concept result for our HIV integrase inhibitor candidate, S-349572, which is being developed in collaboration with GlaxoSmithKline.

This fiscal year, S-2367 and S-349572 are slated to enter later-stage clinical trials, and Shionogi USA is progressing multiple new product candidates into clinical trials. Active clinical programs within Shionogi USA include S-888711 (TPO mimetic for thrombocytopenia), which will hit key U.S. milestones in fiscal 2009. To meet needs related to increasingly important global clinical trials, Shionogi USA expanded its teams of clinical development, medical, project management, and regulatory personnel.

Also in fiscal 2009, the portfolio of clinical stage candidates originated by our research group in Osaka will progressively expand, and the capable team at Shionogi USA is ready to aggressively support our corporate goal of launching new medicines globally.

Overview of Particularly Important Drug Candidates

LY248686 (Duloxetine hydrochloride) (Serotonin & noradrenaline reuptake inhibitor) for depression)

Application for duloxetine hydrochloride for treatment of depression in Japan was submitted in January 2008, and it is hoped that approval will be received during fiscal 2009. Besides enabling remission/alleviation of depression based on a single daily administration, duloxetine hydrochloride also improves body condition regarding aches and pains, etc. Duloxetine hydrochloride has already been approved in more than 90 countries, and Shionogi expects it to become a significant growth-driver product.

S-2367 (Velneperit) (Neuropeptide Y Y5 receptor antagonist for treatment of obesity)

Having completed U.S. Phase IIb clinical trials, the 800mg dosage group has demonstrated compliance with FDA draft guidance standards as well as a high level of safety. Plans call for discussions with the FDA concerning the possibility of trials in conjunction with other obesity treatment agents as well as for the start of development in Japan.

S349572 (Integrase inhibitor for treatment of HIV)

With strongly active inhibition of HIV replication and an excellent resistance profile, this drug candidate reaches therapeutic blood concentrations with one daily dosage administration and has a low likelihood of causing drug interactions. Phase IIb trials will soon begin.

S-021812 (Peramivir) (Anti-influenza agent, Neuraminidase inhibitor)

In addition to human type-A and type-B influenza viruses, this drug candidate has demonstrated strongly active antiviral efficacy toward highly pathogenic avian influenza (H5N1) viruses. It is expected to meet the needs of a broad range of patients, including ordinary patients as well as those with such high risk factors as asthma and diabetes.

S-888711 (Thrombocytopenia agent, TPO mimetic)

Having completed Japanese Phase I clinical trials, this drug candidate is currently undergoing U.S. Phase I trials. Once-daily administration elicits a rapid rise in blood platelet counts. This candidate is appropriate for diverse diseases accompanied by thrombocytopenia, and plans call for moving ahead to Phase IIa trials (global) during fiscal 2009.

Cancer Vaccines (Therapeutic peptide vaccines)

These drug candidates are peptides from proteins selectively over-expressed in cancer cells. Cytotoxic T lymphocyte (CTL) induction was confirmed in physician-guided translational research focused on bladder and esophageal cancers, and some patients demonstrated a response to the vaccines. Plans call for initiating Japanese Phase Ib trials during fiscal 2009.