

We are aiming at growth in the “Medicine/Welfare and powerful anti-cancer drugs as the base, and focusing new medicines.



Director of
Pharmaceuticals Group

Haruo Inose
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STRATEGY 1

Rapid responses to a rapidly-changing market

Drastic reform of Japan's health care system, including large-scale reductions in drug price standards, is forcing drastic changes in the pharmaceutical market. With the globalization of new-drug development, the presence of overseas companies in the Japanese market is also expanding. These factors have heightened the struggle for survival that all pharmaceutical companies are facing. In addition, increased sharing of expertise and information on treatment directly with the patient, and the standardizing of treatment methods, are changing the health care field faster than ever before. While business improvements are now being demanded at medical institutions, it is expected that in the future a form of “health care planned from the patient's perspective” will be put into practice. This entails explanations of available treatment regimes, or a “menu,” for each illness, including the cost of each form of treatment, with treatment started only after agreement is reached between both parties. To secure our profits, under these circumstances, Nippon Kayaku is working for growth in the “Medicine/Welfare and Care” field. Based on our current anti-cancer drugs, we are focused on rapid development of products that benefit the patient, in cancer prevention to diagnosis, treatment, and care.

STRATEGY 2

Focusing on the cancer field

We expect that the needs related to anti-cancer drugs will continue to grow in the coming years. Pharmaceuticals Group has focused its efforts on cancer-related products, and strengthened our base in this field. We have worked to improve our research and marketing abilities, as well as accelerate our development process. In the future, this group will perform research and development specifically for cancer treatment and related business areas. The Research and Development Division has been involved in developing pharmaceutical agents using applied nano-technology, and has attracted the attention of the industry with its progress in trials of macromolecular micelles containing anti-cancer drugs that precisely target and attack cancer cells. This division will proceed with further research, and apply this technology to other anti-cancer drugs, creating a base for product development. It is also putting efforts into the early detection of cancer, which is strongly demanded by society.

STRATEGY 3

New drugs to counteract large-scale price revisions

The prices of our main products in this field have been affected by the government's review of the drug price standard system, which was conducted to eliminate differences in drug prices. However, to prevent our business performance from being

Care” field by using our on development of

affected by the continual lowering of drug price standards, we are planning to cover these changes with new products. In Japan, particular examples include AREDIA (a bone resorption inhibitor) and VITAJECT (a multivitamin product), which were licensed in Nippon Kayaku last year, SALIGREN (a drug for treatment of dry-mouth symptoms), MS-TWICELON (a sustained-release drug for cancer pain), which were launched last year, and IMMUCYST (a drug for treating bladder cancer), for which approval is expected in October 2002. We are also working to get additional indications for BESTATIN, RANDA, and SPANIDIN. Overseas, we are planning to expand our company’s global sales system, particularly for SPANIDIN, which is being developed in Europe.

STRATEGY 4

Constructing a system for rapid introduction of pharmaceuticals needed by the market

In the future, it will be required for medical institutions to explain to patients the available treatment options (or “menu”) and obtain their consent to start treatment. In order to adapt to this trend, this group will address the various pharmaceuticals required for treatments in the menu, and in areas where Nippon Kayaku medical information coverage is intensive. We are constructing an integrated system for research, production, and sales in order to rapidly introduce pharmaceuticals that are low-priced and convenient, and which can be administered in a manner that meets treatment needs.

STRATEGY 5

Strengthening our information service system by specialist medical representatives (MR)

An important key in the pharmaceutical market is the use of specialist MRs who can promptly respond to the needs of medical institutions, and both collect and provide accurate information. Nippon Kayaku currently has 500 certified MRs. Each of approximately 60 MRs are assigned to two strategically important areas: anti-cancer drugs and pharmacological drugs such as vasodilators. These MRs are placed in four major cities – Tokyo, Nagoya, Osaka and Fukuoka – where large numbers of specialist physicians are condensed at medical institutions. By assigning MRs with wide and updated knowledge of cancer and pharmacological activity to these areas, we better understand the needs of specialists in the medical fields, and strengthen our promotion activities. In addition, all MRs are provided with PCs in which special software developed by Nippon Kayaku is installed. This software aids in constructing networks with medical institutions, providing and collecting medical information, and streamlining sales.

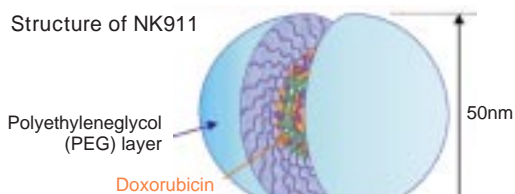
Topics

Start of joint development with NEC in anti-cancer drug field

In July 2002, Nippon Kayaku and NEC Corporation began joint research aimed at the construction of a highly advanced “in silico” drug discovery system using computer simulation, for use in the search for new anti-cancer drugs. Since the successful decoding of the human genome, there has been rapid progress in gaining a molecular-level understanding of biological mechanisms and disease mechanisms. If next-generation anticancer drugs can be developed that selectively act on the target proteins in these mechanisms, it will be possible to reduce the amount of side effects. For this joint research, Nippon Kayaku provides information about these proteins and compounds. Our two companies are together constructing an “insilico” system that selects and designs candidate substances for molecular-targeted pharmaceuticals that exclusively attack cancer cells without damaging normal cells. We expect to discover candidate pharmaceutical agents within the next 2 years. By creating a simulation based on 3-dimensional models of the interaction between proteins and compounds, we expect to achieve a large-scale reduction in the time and costs required in developing new pharmaceutical drugs. Nippon Kayaku aims to efficiently expand its product lineup, and to increase the number of cancer-related products that constitute our greatest focus.

Start of clinical trials of drug delivery system (DDS) for pharmaceutical using applied nano-technology

In July 2001, clinical trials began at the National Cancer Center for NK911 (micelle doxorubicin hydrochloride), a product based on micelle pharmaceutical technology, which is a form of applied nano-technology. The development of NK911 was consigned by Japan Science and Technology Corp. NK911 is a special granule, referred to as a macromolecular micelle, which is hydrophilic outside and lipophilic inside. It contains an anti-cancer drug, and enables concentrated delivery of medication specific to the cancer tissue, maximizing the power of the anti-cancer drug. In addition, reduced side effects with this system can also be expected.



DDS pharmaceutical license agreement with NanoCarrier, a company with unique nano-technology

In June 2002, we concluded a license agreement for paclitaxel DDS pharmaceuticals with NanoCarrier Co., Ltd. This is our second foray into the field of DDS pharmaceuticals using applied nano-technology. Paclitaxel is an anti-cancer drug that is used worldwide to treat cancer of the lung, stomach, breast, and ovary, and is distinguished by its resistance to dissolution in water. This paclitaxel DDS pharmaceutical is paclitaxel contained in nano-granules of a special polymer base material

which improves its ability to dissolve in water. This agent functions by remaining in the bloodstream longer than conventional anti-cancer drugs, and is expected to increase the drug's anti-tumor effects while lessening the side effects. Research and development are proceeding using a fusion of NanoCarrier's unique pharmaceutical technology and Nippon Kayaku's polymer technology. We are aiming to begin clinical trials in the latter half of 2003. With this agreement, we have obtained exclusive rights to its manufacture and sale in the Asian region, including Japan, and non-exclusive sales rights in other regions.

Investment in Reverse Proteomics Research Institute

In June 2002, we invested in Reverse Proteomics Research Institute, an institute for researching the functions of proteins that are useful in the development of pharmaceuticals. This institute makes use of gene information based on human full-length cDNA clones obtained jointly by the Institute of Medical Science, the University of Tokyo; Kazusa DNA Research Institute; and Helix Research Institute, Inc. It is engaged in research of the interactions between the proteins created by genes and existing pharmaceuticals, for the purpose of constructing a research base for the creation of revolutionary new drugs. Nippon Kayaku intends to make effective use of this type of outside research resources to create new drugs in cancer-related areas, our primary field.

SALIGREN – a new drug for treatment of dry-mouth symptoms

In September 2001, we began sales of SALIGREN, which is a drug for treatment of dry-mouth symptoms, for sufferers of Sjögren's syndrome. Sjögren's syndrome is a type of autoimmune disease in which an immune system abnormality results in damage to the exocrine glands. It occurs most often in women in their 40s to 60s, and the primary symptoms are a dry mouth resulting from a reduction in saliva, and dry eyes resulting from a reduction in tear gland production. SALIGREN stimulates a type of acetylcholine receptor that is present in the salivary glands to promote saliva secretion and improve the quality of life of those who suffer from this ailment.



SALIGREN

Status of New Product Development by Stage

Stage	Development code/product name (generic name)	Dosage form or route of administration	Therapeutic category (indications)	Major domestic developer	Characteristics/others
				Origin	
NDA	IMMUCYST (NDA Dec. '00) (BCG formulation)	Intravesical instillation	Anti-cancer drug for malignant tumors (bladder cancer)	Joint dev. with Aventis Pasteur Aventis Pasteur (Canada)	Orphan drug, approved in 50 countries
	NS75A (NDA Dec. '00) (cetorelix)	Injection	Anti-hormone drug (infertility)	Joint dev. with Shionogi, Kayaku Zentaris Zentaris (Germany)	LHRH (secretion of pituitary gonadotropin) antagonist
	BESTATIN (NDA Sep. '01) (ubenimex)	Oral preparation (capsule)	Anti-cancer drug for malignant tumors (for prolonging the survival period after surgery for lung squamous cell carcinoma)	Own development Institute of Microbial Chemistry	Additional indications
	DDP-H (NDA Mar. '02) (cisplatin)	Injection (hepatic arterial infusion)	Anti-cancer drug for malignant tumors (hepatic cancer)	Joint dev. with Bristol Pharmaceuticals NCI (USA)	Additional indications (new dosage form, new route of administration)
P	SL-1100 (estradiol)	Gel preparation	Estrogen (climacteric disorder)	Joint dev. with Shiseido Besins International (France)	First estradiol gel preparation in Japan. Approved in 54 countries.
P	NKT-01 (gusperimus hydrochloride)	Injection	Immunosuppressant (Wegener's granulomatosis)	Own development Institute of Microbial Chemistry	Developed overseas. Early Phase testing completed in Germany. Currently preparing for late Phase . Designated as an orphan drug by EMEA in March 2001. (Bulk manufacturing: Takara Shuzo)
	NS75A (cetorelix)	Injection	Anti-hormone drug (hysteromyoma)	Joint dev. with Shionogi, Kayaku Zentaris Zentaris (Germany)	LHRH (secretion of pituitary gonadotropin) antagonist
P	HFT-290 (fentanyl citrate)	Patch	Narcotic analgesic (cancer pain)	Joint dev. with Hisamitsu Pharmaceutical Hisamitsu Pharmaceutical	Even patients who have difficulty taking oral preparations because of vomiting and nausea caused by anti-cancer drugs can take this.
	NK911 (micelle doxorubicin hydrochloride)	Injection	Anti-cancer drug for malignant tumors (solid cancers)	Own development Tokyo Women's Medical University	Macromolecular micelle anti-cancer drug. Phase started in July 2001. Development consigned by Japan Science and Technology Corp.
PC	SS750 (triazole)	Oral preparation /injection	Anti-fungal drug (mycosis)	Joint dev. with SSP SSP	In addition to being effective against candida and trichophyton, it also acts against aspergillus. Phase started in the U.S. (SSP).

IMMUCYST (a drug for treating bladder cancer) market entry expected in early 2003

IMMUCYST, a drug for treatment of bladder cancer, with approval expected in October, is a type of BCG formulation, and was developed as an orphan drug for treatment of superficial bladder cancer and epithelial cancer of the bladder. Currently, the estimated number of bladder cancer sufferers in Japan is approximately 10,000, and it is expected that this drug will be administered to approximately 60% of these patients.

Development of MS-TWICELON and ASTRIC DRY SYRUP for cancer treatment

During the year, we launched MS-TWICELON, a drug to reduce pain that accompanies terminal cancer, and ASTRIC DRY SYRUP, an anti-viral chemotherapeutic drug. ASTRIC DRY SYRUP is a generic drug for acyclovir, which is recognized as an effective drug for combating the herpes virus. In the cancer field, it contributes to cancer treatment by preventing infection from the herpes virus which can result from diminished immune system function during



MS-TWICELON



ASTRIC DRY SYRUP

chemotherapy, and after bone marrow transplants in particular. Nippon Kayaku is working to construct a specialized cancer treatment base, and is actively proceeding with research and development in cancer-related fields such as these.

Construction of a global Nippon Kayaku sales system

In August 2001, the decision was made to construct a Nippon Kayaku sales system for pharmaceuticals in Europe and North America. The first concrete step in this plan was NKT-01, a drug for treatment of refractory vasculitis that was developed using an independent clinical research organization. In Japan it is known as SPANIDIN, and has been sold since 1994 as an anti-rejection drug for treatment following kidney transplantation. This drug has recently been designated by the European Agency for the Evaluation of Medicinal Products (EMEA) as an orphan drug for treatment of Wegener's granulomatosis, a type of autoimmune disease. We are proceeding rapidly with the details required for approval. We are also preparing for clinical development of the same treatment in the U.S. In addition, in order to improve sales of our anti-cancer drugs in eastern Europe, the Ukraine, and China, in March 2002 we increased the number of medical representatives, and are working to develop a global sales system.

[Group Companies]

Nippon Kayaku America, Inc.

This company was originally founded in New York in 1982. In June 1995 it was incorporated as an overseas affiliate, and in February 1997 it relocated to Westchester in the suburbs of New York City. Currently, it concentrates on identifying pharmaceuticals and generic drugs that hold promise in cancer-related fields, and plans to introduce them in Japan.

Euro Nippon Kayaku GmbH

This company was founded in Düsseldorf in 1988 for the purpose of licensing and sales support activities in Europe. In 1995, the office was relocated to Frankfurt. It is engaged in development and sales of pharmaceuticals, centered on clinical trials of NKT-01 in Germany.

Taiwan Nippon Kayaku Co., Ltd.

This company was started as an overseas affiliate in July 1993 for the purpose of pharmaceutical sales and promotion in Taiwan. In 1996 it received approval to conduct import and sale of pharmaceutical products, and in 1998 it began direct dealings with Nippon Kayaku. In 2000, it received approval to carry out the sale of environmental sanitation chemicals, cosmetics, food supplements, agrochemicals, fertilizers, and other products.

Topics in Other Businesses

Integrating materials and construction with FLOWSEALER, a repair material for waterproofing concrete

FLOWSEALER, a crack-penetration type of repair material for waterproofing, is a new type of water-based material for stopping water leakage. Because it is made of a combination of a safe water-soluble organic polymer and an inorganic silicon-based compound, its advantages include a safe work environment and little burden on the natural environment. In 2001, Nippon Kayaku founded Nippon Kayaku Wasser, a company which is engaged in developing integrated materials and construction using the Wasser method for injecting waterproofing materials under pressure.



Before application After application