Contributing to People's Health through the Creation of Products and Services with Unique Characteristics

Pharmaceuticals Business: R&D

Material issues and related SDGs

Realizing a healthy future by creating innovation

Strengthening efforts to protect the global environment

Resolving social issues and coexisting with the community

Three foundations we value

- Pursuit of originality
- Continuously tackling the challenges of new modalities
- Giving our all in thinking about patients

Quickly delivering new world-class therapeutic agents to the patients who need them

Kazuchika Takagaki
Director, Research & Development

By actively engaging in R&D of drugs for intractable and rare diseases for which there have been no effective treatments, Nippon Shinyaku succeeded in developing Uptravi, a pulmonary arterial hypertension (PAH) treatment that has grown into a blockbuster, and Viltepso, a Duchenne muscular dystrophy (DMD) treatment, the first nucleic acid drug in Japan. Behind these successes are three principles that have been important to the R&D Division: 1) pursuit of originality in R&D, 2) Continuously tackling the challenges of new modalities, and 3) Giving our all in thinking about patients. As a result of continuing our R&D based on these three foundations, we believe that we have overcome the high and difficult barrier of developing new therapeutic agents for intractable and rare diseases, which have been considered difficult in the past.

We will continue to pursue originality, continuously take on the challenge of new modalities, and give our all in thinking about patients as the foundation of our R&D, but it is essential that we speed up R&D in order to deliver innovative new drugs to patients suffering from diseases as soon as possible. With regard to the R&D system and its mechanisms, we will work to optimize resource allocation, rationally prioritize projects, and improve the efficiency of R&D using AI and IT. In this way, we will increase the speed of development and the probability of success, and by actively introducing new and superior technologies from the outside through open innovation, we will realize the early launch of products unique to Nippon Shinyaku.

Review of the 6th Five-Year Medium-Term Management Plan and Remaining Issues

Under the 6th Five-Year Medium-Term Management Plan, we aim to increase our global significance as a company with a meaningful existence in the healthcare field, and as the R&D Division, we have taken on the challenge of creating new value through R&D.

In FY2023, the final year of the 6th Medium-Term Management Plan, we obtained manufacturing and marketing approval for two drugs. The first is high-risk acute myeloid leukemia treatment Vyxeos (code no.: NS-87), in-licensed from Jazz Pharmaceuticals, underwent Phase I/II study in Japan and we applied for approval in June 2023 and received approval in March 2024. The other is Fintepla (code no.: ZX008), for which we entered into an exclusive distribution agreement with UCB S.A. (formerly Zogenix, Inc.) in Japan. Fintepla received approval for the additional indication of Lennox-Gastaut syndrome by UCB Japan in March 2024. Progress has been made in the development phase of Fintepla, and in July 2023, we started a Phase III study in patients with CDKL5 deficiency. NS-863, which is currently under development for circulatory and metabolic diseases, began Phase I study in August 2023. In October 2023, Gazyva, a humanized anti-CD20 monoclonal antibody (code no.: GA101), began Phase III study in systemic lupus erythematosus without nephropathy.

Over the course of five years, we have launched four products: Viltepso (code no.: NS-065/NCNP-01) for the treatment of DMD, Defitelio (code no.: NS-73) for the treatment of sinusoidal obstruction syndrome, MonoVer (code no.: NS-32) for the treatment of iron deficiency anemia, and Fintepla. In addition, we added the indication for chronic thromboembolic pulmonary hypertension to the PAH treatment Uptravi (code no.: NS-304) and expanded the indication of myelodysplastic syndrome treatment Vidaza to the treatment of acute myeloid leukemia. As a result, we launched a total of six new products, achieving the target of launching more than one new product on average per year. On the other hand, there were termination of development for NS-18, and delays of development concerning NS-089/NCNP-02 for DMD treatment and NS-304's additional indication for ASO. These were intended to be launched during the period of the Medium-Term Management Plan, meaning our speed of clinical development is an issue yet to be addressed. Additionally, efforts to develop new modalities such as next-generation nucleic acids and gene therapies took longer than expected to develop candidates.

Strategies and Focus Initiatives to Achieve the 7th Five-Year Medium-Term Management Plan

In the 7th Five-Year Medium-Term Management Plan, we have set "fostering growth drivers to replace Uptravi" and "continuous pipeline expansion" as key themes. As growth drivers during the 7th Medium-Term Management Plan, we will launch four DMD drugs, three hematological malignancy drugs, and an average of two or more new products per year through the expansion of indications for Uptravi, Fintepla, and Gazyva. In addition, we will focus on newly acquired products to further expand the number of our products on the market.

In addition, we will continue to expand our pipeline based on the three pillars of in-house drug discovery, in-licensing, and PLCM. With regard to in-house drug discovery, we will utilize open innovation and AI drug discovery to combine and bolster our strengths with the technologies of other companies. In nucleic acid drugs, we will work on drug discovery in the central nervous system area in addition to DMD, and promote the use of new nucleic acid drug discovery modalities through open innovation. With regard to in-licensing, we will prioritize items that lead to global sales and work to acquire at least one in-licensed product per year. With regard to PLCM, we will start working on secondary indication diseases earlier than in the past, and make efforts to maximize the value of our pharmaceuticals.

In the 7th Medium-Term Management Plan, we set out to "speeding up R&D" as one of the ways to strengthen our management foundation. In clinical development, multiple clinical studies were delayed during the 6th Medium-Term Management Plan, and in order to solve these issues, we will improve the probability of success and speed up the process by rigorously checking the progress of the entire Company, strengthening compliance with regulatory authorities in each country, bolstering project management, formulating robust trial plans, and pursuing the possibility of accelerated approval. In drug discovery research, we aim to shorten the time from the drafting of a theme to the entry into clinical study, and to

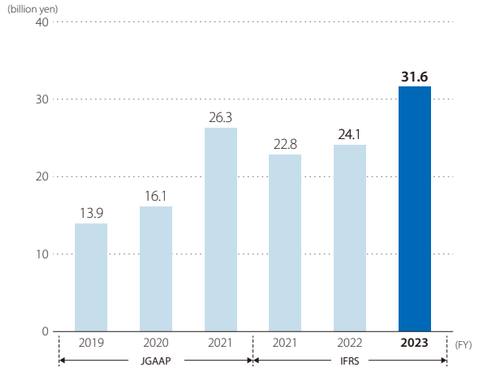
Contributing to People's Health through the Creation of Products and Services with Unique Characteristics

Pharmaceuticals Business: R&D

build a system that enables us to launch one product a year. In addition, as part of our financial strategy for sustainable growth set among the management foundations we plan to strengthen, we plan to invest 190 billion yen in R&D over five years and 38 billion yen in capital investment, including the construction of a new research building at the Discovery Research Laboratories to respond to new technologies and create innovation.

With the aim of realizing a healthy future by creating innovation, which we identified as one form of our materiality, the R&D Division will work together in accordance with the 7th Medium-Term Management Plan.

Research and development expenses



Accessing seeds of world-leading drug discovery

The area around Cambridge, Massachusetts on the East Coast of the U.S. is home to many world-leading academia and affiliated hospitals such as Harvard University and the Massachusetts Institute of Technology. Many startups and biotech companies are also concentrated, making it a hotspot for innovation. Our establishment of Innovation Research Partnering (IRP) here will increase early access to the world's most advanced drug discovery technology seeds and opportunities for co-creation with world-class scientists. This will enable Nippon Shinyaku to efficiently conduct information gathering and exploration activities that will lead to the introduction of innovative technologies and early products.

Promotion of patient centricity-based drug discovery research

We have set a long-term goal for 2035 to use drug discovery research themes based on patient centricity to promote R&D activities aimed at bringing drugs to market, and we are now working toward this goal. In FY2023, we aimed to increase opportunities for drug discovery researchers to interact with patients or with people who are close to patients. We would like to introduce two specific initiatives. As the first initiative, we asked patients and their families to create video messages for our Company, which were viewed by all employees of the R&D Division. Employees who watched the videos commented, "It gave me an opportunity to rethink what I can do as an employee of a pharmaceutical company," and "I realized that our work has an impact on the lives and livelihoods of patients and their future." As a second initiative, in October 2023, Mr. Takeshi Shukunobe, President and CEO of PPeCC, gave a talk to employees entitled "The Significance of Listening to the 'Voices' of People with Illness," which was attended by approximately 330 employees. Employees who attended the talk commented, "I thought it would be difficult to hear directly from people with illnesses, but I was able to recognize that it is possible," "I felt that it is important to think together about how to live with hope in the future," and "It is important to incorporate this into the work of each department. I think it would be good if drug discovery researchers had more opportunities to hear directly from people with illness." At Nippon Shinyaku, there have not been many opportunities to hear directly from patients and their families. Through this initiative, we were able to reaffirm the importance of increasing opportunities to talk directly to and getting to know patients.

In order to achieve our vision for 2035, we believe that it is important not only to provide opportunities to interact with patients and those close to patients, but also to aim for drug discovery together, and we will continue working on the development of this system going forward.

Building where IRP is located

Increasing partnering opportunities and diversifying in-house drug discovery

For technologies and compounds under development that are in the preclinical stage or earlier, IRP and the Modality Strategy Team at the head office are responsible for partnering functions, and for developed compounds that are in the clinical stage and have confirmed proof of concept (POC), NS Pharma based in New Jersey, U.S., and the Licensing Department at the head office are responsible for partnering functions. In this manner, dividing work by stage of development and region enables efficient scouting activities and leads to an increase in partnering opportunities.

By partnering with academia and venture companies with distinctive technology seeds, we aim to create new therapeutic technologies not only by layering the pipeline of developed products, but also by combining Nippon Shinyaku's strengths with cutting-edge technologies. Since the development of new therapeutic technologies is one of the important factors in the development of drugs for intractable and rare diseases for which there are no effective treatments yet, and for drug discovery in new disease areas, we believe that the increase in partnering opportunities will bring diversity to our own drug discovery.

Consideration of animal welfare

Research using animals is indispensable to verifying the safety and efficacy of pharmaceuticals. Nippon Shinyaku has established internal rules regarding animal research in accordance with relevant laws, regulations and guidelines, and has established the Animal Research Committee. The committee screens all animal research to ensure that they are conducted with appropriate consideration based on the principles of the 3Rs (Replacement, Reduction, Refinement). Our implementation system for animal testing confirms compliance with relevant laws and regulations through periodic self-inspections, and is certified by the Japan Pharmaceutical Information Center (JAPIC), a third-party organization. In addition to optimizing the environment for raising animals and reducing stress, we provide education on animal welfare as part of regular training for those involved in animal testing.

NIPPON SHINYAKU PEOPLE

Bringing drugs to more patients as a team

I had been a project manager for hematological malignancy drugs such as NS-87 (Vyxeos: a treatment for high-risk AML) since April 2021. The main task of a project manager is to promote development and maximize product value with a view to post-launch. In that role, I was always thinking about what we could do to bring drugs to market as soon as possible and to as many patients as possible. I was impressed by the fact that the project team worked together to obtain approval for the manufacture and sale of NS-87 in March 2024, expanded the range of patients the drug could be administered to through consultation with the authorities, and was able to deliver the drug to a broader number of patients, and shortened the development period for another hematological malignancy treatment by more than one year.

Michiyo Akagi
Planning and Coordination Section 1, R&D Planning and Administration Department
(currently, Planning Section 2, Licensing Department)

Contributing to People's Health through the Creation of Products and Services with Unique Characteristics

Pharmaceuticals Business: R&D

Pipeline (As of August 7, 2024)

Japan

Code no. (generic name)	Domain classification	Indications	Origin	Development	Phase: I	Phase: I/II In preparation	Phase: I/II	Phase: II In preparation	Phase: II	Phase: III	NDA filing	Launch
NS-065/NCNP-01 (Viltolarsen)	Intractable and rare diseases	Duchenne muscular dystrophy	Co-development: National Center of Neurology and Psychiatry	Nippon Shinyaku								
LY3527727 (Pirtobrutinib)	Hematological malignancies	Mantle cell lymphoma*	Alliance: Eli Lilly Japan K.K.	Eli Lilly Japan K.K.								In preparation
NS-304 (Selexipag)	Intractable and rare diseases	Pediatric pulmonary arterial hypertension	Nippon Shinyaku	Co-development: Janssen Pharmaceutical K.K.								
ZX008 (Fenfluramine hydrochloride)	Intractable and rare diseases	CDKL5 deficiency disorder	Distribution partnership UCB S.A. (formerly Zogenix, Inc.)	UCB S.A (formerly Zogenix, Inc.)								
GA101 (Obinutuzumab)	Intractable and rare diseases	Lupus nephritis	Licensed-in from: Chugai Pharmaceutical Co., Ltd.	Co-development: Chugai Pharmaceutical Co., Ltd.								
GA101 (Obinutuzumab)	Intractable and rare diseases	Pediatric nephrotic syndrome	Licensed-in from: Chugai Pharmaceutical Co., Ltd.	Co-development: Chugai Pharmaceutical Co., Ltd.								
GA101 (Obinutuzumab)	Intractable and rare diseases	Systemic lupus erythematosus without nephropathy	Licensed-in from: Chugai Pharmaceutical Co., Ltd.	Co-development: Chugai Pharmaceutical Co., Ltd.								
LY3527727 (Pirtobrutinib)	Hematological malignancies	Mantle cell lymphoma	Alliance: Eli Lilly Japan K.K.	Eli Lilly Japan K.K.								
LY3527727 (Pirtobrutinib)	Hematological malignancies	Chronic lymphocytic leukemia	Alliance: Eli Lilly Japan K.K.	Eli Lilly Japan K.K.								
NS-304 (Selexipag)	Circulatory and metabolic system	Arteriosclerosis obliterans	Nippon Shinyaku	Nippon Shinyaku								
NS-580	Gynecological diseases	Endometriosis	Nippon Shinyaku	Nippon Shinyaku								
NS-580	Urological diseases	Chronic prostatitis / Chronic pelvic pain syndrome	Nippon Shinyaku	Nippon Shinyaku								
NS-089/NCNP-02 (Brogidirsen)	Intractable and rare diseases	Duchenne muscular dystrophy	Co-development: National Center of Neurology and Psychiatry	Nippon Shinyaku								
NS-229	Intractable and rare diseases	Eosinophilic granulomatosis with polyangiitis	Nippon Shinyaku	Nippon Shinyaku								
NS-401 (Tagraxofusp)	Hematological malignancies	Blastic plasmacytoid dendritic cell neoplasm	Licensed-in from: The Menarini Group	Nippon Shinyaku								
NS-050/NCNP-03	Intractable and rare diseases	Duchenne muscular dystrophy	Co-development: National Center of Neurology and Psychiatry	Nippon Shinyaku								
NS-917 (Radgocitabine)	Hematological malignancies	Relapsed/refractory acute myeloid leukemia	Licensed-in from: Delta-Fly Pharma, Inc.	Nippon Shinyaku								
NS-025	Urological diseases	Urological diseases	Nippon Shinyaku	Nippon Shinyaku								
NS-863	Circulatory and metabolic system	Circulatory and metabolic system diseases	Nippon Shinyaku	Nippon Shinyaku								

* Relapsed or refractory mantle cell lymphoma due to resistance or intolerance to other BTK inhibitors

Overseas

Code no. (generic name)	Domain classification	Indications	Origin	Development	Phase: I	Phase: I/II In preparation	Phase: I/II	Phase: II In preparation	Phase: II	Phase: III	NDA filing	Launch
NS-065/NCNP-01 (U.S.) (Viltolarsen)	Intractable and rare diseases	Duchenne muscular dystrophy	Co-development: National Center of Neurology and Psychiatry	Nippon Shinyaku								
NS-065/NCNP-01 (Global) (Viltolarsen)	Intractable and rare diseases	Duchenne muscular dystrophy	Co-development: National Center of Neurology and Psychiatry	Nippon Shinyaku								
CAP-1002 (deramiocel)	Intractable and rare diseases	Duchenne muscular dystrophy	Partnership: Capricor Therapeutics Inc.	Capricor Therapeutics Inc.								
NS-089/NCNP-02 (Brogidirsen)	Intractable and rare diseases	Duchenne muscular dystrophy	Co-development: National Center of Neurology and Psychiatry	Nippon Shinyaku								
NS-229	Intractable and rare diseases	Eosinophilic granulomatosis with polyangiitis	Nippon Shinyaku	Nippon Shinyaku								
NS-050/NCNP-03	Intractable and rare diseases	Duchenne muscular dystrophy	Co-development: National Center of Neurology and Psychiatry	Nippon Shinyaku								

Intellectual Property

The Nippon Shinyaku Group is committed to tackling the challenge of new modalities in drug discovery and globalization in order to realize our Business Philosophy of "Helping People Lead Healthier, Happier Lives." We recognize that intellectual property (IP) plays an important role in promoting these purposes, and through the protection and utilization of IP, we will strengthen the superiority of our business and continuously improve corporate value. We also adopt the basic attitude of respecting third-party IP rights, practicing thorough IP-related risk management including ownership investigations.

R&D activities and intellectual property

The Intellectual Property Department collaborates with the R&D Division from the early stages of research. By doing this, we can protect pharmaceuticals and functional foods produced in-house in a long-term, multifaceted and strategic way, using not only substance patents, but also use patents, process patents, formulation patents, dosage and administration patents and so on. In addition, we are considering building and utilizing a patent portfolio to strengthen our global R&D strategy and business strategies in an internal committee consisting of multiple department managers. This includes determining patent application and maintenance policies based on our own R&D and business strategies and those of other companies.

Understanding and analyzing intellectual properties

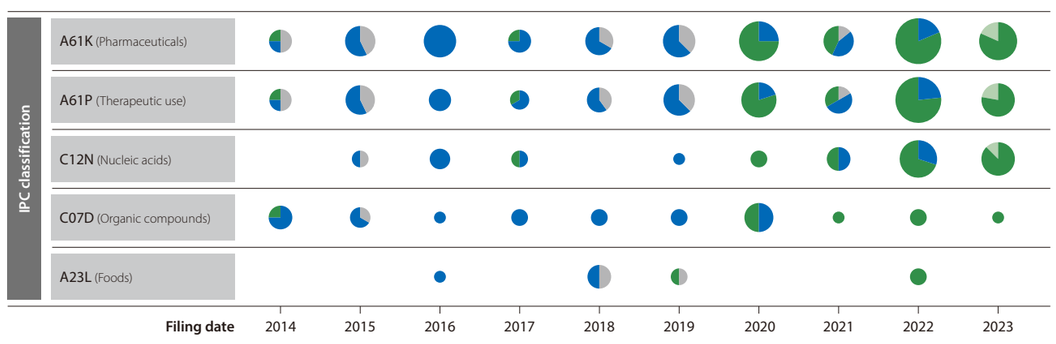
With the basic attitude of respecting third-party IP rights, the Nippon Shinyaku Group regularly conducts ownership investigations regarding its products. We conduct patent trend analysis and IP analysis of competitors in specific technical fields believed to be important for us over the medium to long term. As a result, we manage IP risk at an early stage and utilize the obtained analysis results in our R&D strategy and business strategy.

Furthermore, the Group analyzes IP protecting its products and their surroundings and utilizes these rights, including strategic licensing, to create opportunities for in-house R&D and business expansion.

Building our reputation and brand based on trademarks

We determine the appropriate product names according to the medicines and functional foods produced in-house. By protecting them with trademark rights, we build the reputation and brand of our products.

Application trends by International Patent Classification (IPC) (Top 5 classifications)



Invalid: A patent that has already expired or has been abandoned, or an application that has not been granted (e.g., rejected during review, abandoned by the applicant, etc.)
Valid: A patent that has been registered and the rights have been validly accrued
Pending review: A patent application that is under review in the patent office of the respective country
In the PCT international phase: A patent application that has been filed under the Patent Cooperation Treaty (PCT) but has not yet been reviewed by the national patent offices.

* Data analysis and compilation was conducted independently by Nippon Shinyaku using PatSnap Analytics.

Contributing to People's Health through the Creation of Products and Services with Unique Characteristics

Functional Food Business

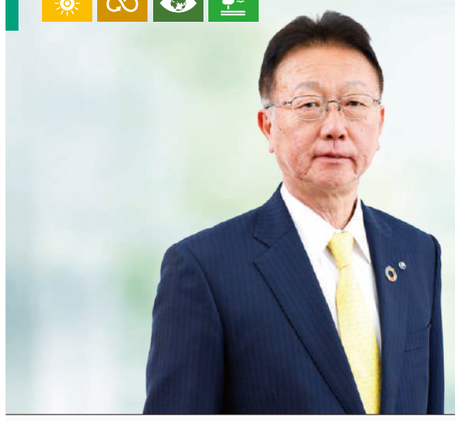
Material issues and related SDGs

Realizing a healthy future by creating innovation

Strengthening efforts to protect the global environment

Strengths

- Competencies in sales and products that have built strong relationships of trust with many food manufacturers since our establishment in 1961
- R&D capabilities and quality control system that make use of advanced technologies and unique know-how cultivated in the Pharmaceuticals Business
- Supply chain management through a strong network of suppliers in Japan and overseas



We aim to grow in both the B2C and B2B businesses and transform into a highly profitable structure during the period of the 7th Five-Year Medium-Term Management Plan

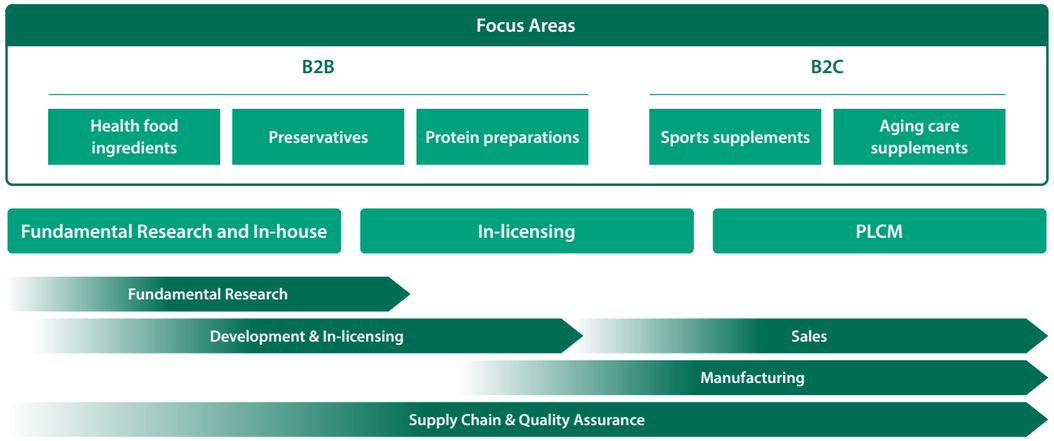
Hitoshi Ishizawa
Director, Functional Food

Nippon Shinyaku's Functional Foods business was launched in 1961 as the second pillar of sales after the Pharmaceuticals Business. The originality of the Functional Foods business is that in addition to B2B businesses such as protein preparations, health food ingredients, and quality stable preservatives, we are also developing B2C businesses for sports supplements and aging care supplements. We are aware that our department plays an important role at Nippon Shinyaku, a prescription medicine manufacturer. With a high level of morale, we engage in our daily work highly aware of product safety and with a strong sense of mission to contribute to people's health and vibrant diets. We intend to utilize the technologies we have cultivated in the pharmaceutical industry for basic research and clinical trials, and will further strengthen our presence in the healthcare field.

In fiscal 2023, the final year of the 6th Five-Year Medium-Term Management Plan, we achieved the targets for revenue and operating profit. Both the B2B and B2C businesses grew significantly, while the B2C business, sports supplements and aging care supplements, in particular, achieved robust results. As a result, we made steady progress toward the 7th Medium-Term Management Plan. However, given that the number of new health food ingredient products launched fell short of the plan, and the profit margin fluctuated greatly due to external factors such as the COVID-19 pandemic and Russia's invasion of Ukraine, we believe that continuous launch of new products and a shift to a stable and highly profitable structure will be issues for the future. During the period of the 7th Medium-Term Management Plan, we will review our business portfolio to improve capital efficiency and make intensive investments in our focus areas.

In addition, in order to realize a fundamental transformation of operations using digital technology, we will build a platform that can efficiently promote the development of new products that balance both taste and shelf life, while striving to improve customer value in the quality stable preservatives business. Nippon Shinyaku's Functional Foods business will continue to provide products that contribute to improving people's health and dietary quality, and will achieve further growth and evolution.

Functional Food Division Business Model



Helping to Solve Social Issues Related to Food

As the aging accelerates, the extension of healthy life expectancy has become a social issue, and governments are working to reduce medical costs by promoting self-care. The Functional Food Division is working to improve people's quality of life and resolve social issues by developing and providing products that are easily accessible for all people, not only with higher nutritional value but also in terms of price. These include protein-fortified foods to improve health and extend healthy life expectancy, and products suited for complete and balanced nutrition such as concentrated liquid foods used in medical institutions and care facilities for the elderly.

In addition, in order to contribute to the realization of a sustainable society, such as by reducing food loss by extending the shelf life, we are promoting initiatives for food safety and security. Furthermore, to help resolve social issues related to food for all generations, i.e., the problems of skipping breakfast among young people, frailty and sarcopenia due to undernutrition among the elderly, and skinniness among women, we will continue our activities with the aim of improving access to nutrition through the development of products and the promotion of dietary education in collaboration with local governments and educational institutions.

Business Model and Business Areas of the Functional Food Division

Business model

The Functional Food Division has an R&D Division and a Quality Assurance Division, and develops and provides high-quality, original products by leveraging our advanced technological capabilities as a prescription medicine manufacturer. To this end, we are working to expand our business based on the three pillars of promoting basic research and developing our own products, introducing products that meet user needs, and PLCM.

In terms of business development, we are mainly engaged in two businesses: the B2B business, which provides functional food ingredients to processed food manufacturers, and the B2C business, which provides supplements that improve the health and quality of life of consumers. Currently, we serve only Japan, but we will explore expansion into overseas markets with a focus on Asia in the future.

Contributing to People's Health through the Creation of Products and Services with Unique Characteristics

Functional Food Business

Business areas

In the B2B business, we are developing the following three main product areas.

(1) Health food ingredients: Products that improve health and quality of life in the healthcare field
(2) Quality stable preservatives: Products that contribute to food safety and security and food loss reduction in the field of processed foods
(3) Protein preparations: Products that enhance and stabilize quality in the field of processed foods, and are used as ingredients for sports nutrition and nutritional medical foods.

In the B2C business, we are developing two product areas as supplements made by a prescription medicine manufacturer.

(1) Sports supplements: Highly unique supplements that improve performance during exercise, from top athletes to sports enthusiasts
(2) Aging care supplements: Highly unique supplements that are pioneers in aging care by improving health and quality of life

R&D

As an R&D-led new drug manufacturer, we deliver products with high originality and functionality to the world, and we have established an R&D base in Kyoto to produce them. Focusing on the three categories of health food ingredients, quality stable preservatives, and protein preparations, we are promoting the development of products and materials, basic research that forms the basis for these products, and the improvement of customer experience using DX. Our aim is to contribute to improving people's health and quality of life in the healthcare field, food safety and security in the processed food field, and food loss reduction.

Initiatives to enhance quality

As the Functional Food Business of a prescription medicine manufacturer, we place the highest priority on the safety and security of our products, and we are continuously improving our management system to enhance quality. We are strengthening relationships with suppliers who are manufacturers of raw materials and stepping up cooperation with product manufacturing contractors. Additionally, as part of our efforts to bolster our internal systems, we regularly hold meetings of internal committees to share information on quality, respond to quality problems and complaints, and formulate measures to prevent recurrence. In addition, we hold monthly training on compliance, risk management, and other issues for all employees of the Functional Food Division to improve their knowledge of relevant laws and regulations related to food advertising and labeling.

Review of the 6th Five-Year Medium-Term Management Plan and Remaining Issues

As a result of implementing the R&D and sales strategies for functional foods set forth in the 6th Medium-Term Management Plan, both the B2B and B2C businesses of the Functional Foods Division grew significantly. Actual sales were 23.1 billion yen compared to the sales target of 17.0 billion yen in the final year (FY2023), achieving the quantitative target.

Going forward, in order to establish a high-revenue structure, we will further enhance profitability by reviewing our business portfolio and intensively investing in our focus areas, and we will also work to increase capital efficiency by improving cash conversion cycles.

Strategies and Future Initiatives to Achieve the 7th Five-Year Medium-Term Management Plan

Measures to expand our lineup of healthcare products

In the B2C business, we are promoting the development of highly unique sports supplements for the rapidly growing market, i.e., supplements that can be taken according to the situation, such as before, during, and after exercise, with a focus on protein supplement foods, which are growing as mainstay sports supplements. In addition, we are developing aging care supplements adaptable to changes in the market, such as the further progress of an aging society and Femtech. By expanding these products through appropriate promotions, we will contribute to the health of more people.

In the B2B business, we will expand our lineup of functional materials that improve people's health, targeting frailty and lifestyle-related diseases by developing new health food ingredients through basic research and introduction, and promoting PLCM to maximize the value of existing health food ingredients. In protein preparations, we will continue to develop protein materials suitable for diet, sports, and health products.

Providing new solutions to reduce food loss

The development of quality-stable preservatives that achieve both great taste and shelf life will lead to the reduction of food loss and play an important role in the realization of a sustainable society. Nippon Shinyaku has earned the trust of many customers in the field of quality stable preservatives and has grown to have one of the top market shares in the industry. In addition to providing products, we will also provide solutions that utilize digital technology to dramatically improve the value of the customer experience. The membership website released in June 2023 provides information and materials required by product development personnel at business partners in a timely manner. Looking ahead, we will strongly support product development by building a system that can instantly identify bacteria that cause food spoilage and provide effective shelf life measures. Through these new initiatives, we will earn the trust of our business partners.

Major Supplement Products

NIPPON SHINYAKU PEOPLE

Developing AI that contributes to the product development of processed food manufacturers

In order to contribute to the reduction of food loss, I am developing an AI that analyzes the bacteria that cause food spoilage and formulates measures to prevent it. This AI combines Raman spectroscopy and machine learning, and I have been conducting basic research after having enrolled in graduate school (doctoral program for working professionals) in order to establish the technology. I presented the results at the 12th International Conference on Predictive Modelling in Food, and received many voices of interest and expectation. Furthermore, in order to efficiently acquire Raman spectra, I developed and introduced an instrument in collaboration with an optical equipment manufacturer. With the completion of this AI, we will be able to strongly support the product development of processed food manufacturers in terms of speed and quality, and contribute to the reduction of food loss. In the future, I hope to implement it in society to tackle and resolve all issues related to food spoilage.

Takashi Yamamoto Food Science Laboratories, Functional Food Division

Strengthening Patient Support and Advocacy Activities Based on Patient Centricity

Pharmaceuticals Business: Sales

Material issues and related SDGs

Realizing a healthy future by creating innovation

Strengths

- Pursue specialization by focusing on the fields of pulmonary hypertension, pediatric neurology, and hematology and undertake a wide range of information provision activities that straddle fields
- MR's strong problem-solving skills, the result of a team system and in-house certification
- Assign product marketers with field specialization who can propose treatments and raise disease awareness in a manner appropriate for the unique aspects of the area

Nippon Shinyaku promotes investments in digital technology and human resources and efficiently provides information through MR activities

Shouzou Sano
Managing Director, Sales and Marketing

As work style reforms for doctors have moved forward, there have been dramatic changes in how sales staff provide information. Because of the COVID-19 pandemic, MR activities at workplaces were limited, and an omnichannel approach, which integrates digital and face-to-face methods, became the norm. At Nippon Shinyaku, we have introduced Veeva CRM* for the life science industry. Considering the high open rate of 50%–70% for Approved Email through Veeva, we think it is possible to conduct high-quality MR activities that leverage digital technology.

One of Nippon Shinyaku's strengths is our human resources. In order to make greater use of this strength, MRs continually receive training so that they can provide the best information, and this includes monthly training and role playing that incorporates AI for such scenarios as meetings with doctors. Furthermore, there is a team system for MRs, which makes it possible for the product marketing personnel with specialized knowledge, the Chairman and President at times, and even me to exchange information with doctors and promote strategic activities using our unified capabilities.

Unfortunately, it was not possible to achieve our revenue target included in the 6th Medium-Term Management Plan. Despite steady progress in introducing new products, problems related to managing multiple products, such as provision of information being skewed toward only certain products, have come to light. It is necessary, therefore, not only to strengthen investment in digital technology and human resource development but also construct an efficient information provision system.

In the 7th Medium-Term Management Plan, we are focusing on quickly expanding sales and maximizing the value of new products. We will work closely with the R&D Division in each phase of a product's life cycle, starting before product approval and continuing after launch, and implement initiatives to get product value to take root. Furthermore, we aim to become number one in our fields of specialization, and strengthen relationships with partner companies toward the acquisition of in-licencing products partnerships.

Having learned about patient support programs in the U.S., I launched the support program "Sherpa" for patients with pulmonary arterial hypertension. As physicians have limited time, nurses working only on the program listen to patients' worries regarding treatment and life and provide that information to physicians as feedback. Through these initiatives, the percentage of patients who stop taking Uptravi has fallen to 6% from 30%. Patient centricity-based activities are initiatives tied to solutions to social issues through engagement with patients, doctors, and similar parties and should be valued.

* CRM (Customer Relationship Management): This is a system for building good relations with customers by collecting and using customer information.

Overview of and Remaining Issues Related to the 6th Five-Year Medium-Term Management Plan

Channels for exchanging information with medical professionals, which is indispensable for spreading pharmaceuticals in a market, are rapidly growing more diverse. Even at Nippon Shinyaku, there has been a certain level of support for strengthening the provision of information and solutions to issues through digital technology by establishing a new department within the Sales and Marketing Division. On the other hand, diseases that our products target require specialized knowledge, and many physicians want more direct dialogue for treatment proposals tailored to each patient. As for remaining issues, we are working to coordinate and integrate digital technology into MR activities and provide healthcare workplaces with the best information.

Initiatives Focused on Strategy to Implement the 7th Five-Year Medium-Term Management Plan

Promoting the provision of information through digital technology

At a time of dramatic changes in the healthcare environment, it is important to make proper use of each information provision channel, which are geared toward a particular work style and preference of medical professionals, in order to continue to quickly meet healthcare workplace needs. In addition to creating and distributing quality digital content, we will tie this to the timely and prompt provision of information, and one such measure is to assign a digital MR for each product. We will also create a system that ensures the accurate delivery of information that doctors truly want through the timely analysis of satisfaction with our contact with medical professionals and content of our communications. Furthermore, we will raise the quality of our information provision activities via both face-to-face and digital channels even higher by introducing role playing that incorporates generative AI into human resource education, raising the level of specialized knowledge of Sales and Marketing Division members, including MRs, and similar activities.

Initiatives for disease awareness: providing information through customer journey map

We will move forward with building a system based on a patient centricity-focused approach so that each patient has equal access to information regardless of the stage of their patient journey. We not only support patients moving through the treatment process with such initiatives as creating and expanding websites and material for patients, expanding operation of the patient support program in the pulmonary hypertension field, and examining the introduction of the program into other fields but will also contribute to greater patient knowledge and understanding of their disease by continuing to issue educational material and holding events.

NIPPON SHINYAKU PEOPLE

Introducing e-only MRs who support the physician work style reforms

So that we can deliver information indispensable for treating intractable and rare diseases to medical professionals as quickly as possible, I have completed preparations to introduce e-only MRs who make use of digital technology when we obtain approval for a new AML drug. When a person is diagnosed with AML, it is important that they immediately start treatment, and there is a need to quickly deliver information on the proper use of such medicines. In addition, there is a need among medical professionals to create an environment in which desired information can be easily obtained when wanted as work style reforms for doctors were fully launched in April 2024. We are aiming to be a trusted treatment partner by accurately understanding the needs of these medical professionals and quickly delivering required information through all channels, including MRs.

Keiya Kato
Hematology Product Marketing Group, Hematology Product Marketing Department, Sales and Marketing Planning Division

Strengthening Patient Support and Advocacy Activities Based on Patient Centricity

Pharmaceuticals Business: Medical affairs

Material issues and related SDGs

Realizing a healthy future by creating innovation

Strengths

- Generate medical and scientific evidence related to unmet medical needs and communicate that evidence to medical professionals in order to deliver optimal healthcare to all patients
- Conduct medical and scientific exchanges with key external experts that make use of advanced and latest scientific knowledge, etc.
- Involved in medical affairs from early development stage
- Conduct thorough life cycle management from application to around time of approval

Overview of and Remaining Issues Related to 6th Five-Year Medium-Term Management Plan

As for medical affairs, we are developing an action plan from a patient centricity-based perspective. Because we consider it important for patients to promote greater understanding of diseases, we held various events. For example, at a metaverse public seminar on muscular dystrophy, we not only gave lectures but also conducted other activities, such as holding recreation activities and hosting an artwork exhibition. In addition, we discussed important points regarding daily life during online public lectures on pulmonary hypertension and discussed "cancer treatment and taste disorders" as daily topics for patients during the AYA week 2024 public lectures. Although the number of participating patients has increased every year, there are still many patients who are not aware of these events. We will therefore work so that even more patients can attend these events.

Furthermore, we are conducting various types of research, including non-clinical research, clinical research, database research, and registry research, in order to generate evidence in disease fields related to our products. As for database research, we conducted joint research using real-world data in order to clarify "the percentage of Japanese with anemia, the state of treatment, and medical costs, quality of life (QOL), and productivity loss for anemia patients." The results of this research were published in an academic journal in FY2023. We also posted a press release regarding this on the Company's website. In Japan, results from the research have drawn attention because there are insufficient reports on the impact that anemia has on society. We hope that this research provides an opportunity to get anemia recognized as a social issue and to change perceptions of the condition. As for the creation of evidence, we are aware that we still have insufficient experience and results and will steadily acquire experience piece by piece.

Metaverse event

Strategy and Future Initiatives to Achieve 7th Five-Year Medium-Term Management Plan

We will use digital technology to solve medical issues and generate evidence.

For example, we would like to take on the challenge of contributing to better healthcare by focusing on digital health that uses wearable devices, apps, artificial intelligence (AI), and other cutting-edge technology. Furthermore, through our evidence generating activities, we will not only move forward with research on hematological malignancies, pulmonary hypertension, Duchenne muscular dystrophy, and anemia that is already underway but also prepare for new research. We also aim to create from unmet medical needs ascertained by medical science liaisons (MSL)* and others evidence that is linked to patient benefits and provide that information.

* Medical Science Liaisons (MSL): Refers to employees belonging to an organization which is independent of the Sales and Marketing Division whose main role is to engage in exchanges with key external experts in the fields of medicine and science.

Maintaining a Safe and High-quality Supply of Products

Pharmaceuticals Business: Resource Procurement, Production, and Assurance

Material issues and related SDGs

Realizing a healthy future by creating innovation

Strengths

- Promotes DX and grows to include manufacturing sites that can handle global demand for pharmaceuticals with new modalities, such as nucleic acid
- Unified supply chain-related departments that extend from raw material procurement to postmarketing surveillance and robust, stable supply system that promotes risk management
- Resource Procurement, Production & Assurance Division that is involved from early development stage and contributes to development of pharmaceuticals

Through strong lateral collaboration as the division responsible for pharmaceutical safety and security, we fulfill the basic mission of a pharmaceutical company

Hitomi Kimura
Director, Resource Procurement, Production & Assurance

In February 2024, we were able to complete construction of the nucleic acid API purification plant at the Odawara Central Factory, which was scheduled to be completed during the period of the 6th Five-Year Medium-Term Management Plan. Through the 7th Five-Year Medium-Term Management Plan, we will steadily work to establish the production process. This is not only the first time we will conduct API purification at the Odawara Central Factory, but also our first attempt at commercial production of middle molecule drugs. We will continue to work together to tackle this issue.

The Resource Procurement, Production & Assurance Division, which I manage, is responsible for our basic mission as a pharmaceutical company—that is, to ensure efficacy and safety and to provide a stable supply of high-quality pharmaceuticals. At the weekly meeting of department managers, there is an exchange of opinions regarding issues and what should be done next, which makes it possible to conduct work with a mutual understanding of others' work. One of the division's strengths is the strong lateral collaboration between departments.

Our division is responsible for raw material procurement and production planning and plays an important role in supporting the Sales and Marketing Division and R&D Division. In the past, production plans were closely linked to the planner because they were based on that person's experience, but we have built a system that automatically proposes highly precise production plans using AI and statistic models, and are moving forward with more appropriate inventory management by adhering to newly set risk-based, safe inventory standards. At the Odawara Central Factory, we are also moving forward with examining the use of AI for the visual inspection of vials, and will work to further increase its accuracy for actual use.

An issue is our lack of experience in overseas markets. If we export our pharmaceuticals for rare diseases, it will be necessary to strengthen our local information gathering capabilities in order to respond to strict regulations of each country and cultural differences between countries. When supplying products overseas, it is also important to collaborate with affiliated companies throughout the whole supply chain and reliability assurance system. Furthermore, I would like to reinforce meetings with related departments and the mutual dispatch of workers and increase experience in order to overcome language and cultural barriers. As the department responsible for pharmaceutical safety and security, we will do all that we can to provide patients worldwide with a stable supply of high-quality, unique pharmaceuticals.

Maintaining a Safe and High-quality Supply of Products

Pharmaceuticals Business: Resource Procurement, Production, and Assurance

Overview of and Remaining Issues Related to 6th Five-Year Medium-Term Management Plan

Spreading our sustainable procurement policy

As one part of our efforts to actively promote sustainable procurement, we reworked our Responsible Procurement Guidelines into a Sustainable Procurement Policy and requested that key business partners know this policy and cooperate with procurement activities based on this policy. In FY2023, we revised this policy to make it consistent with related policies and registered partnership construction statements in order to create coprosperity with suppliers.

We will work to further spread our Sustainable Procurement Policy by introducing this policy throughout the Nippon Shinyaku Group and formulating a supplier code of conduct that reflects this policy and undertaking activities to educate and obtain the consent from business partners.

Increasing demand forecast precision using digital technology

Through the 6th Five-Year Medium-Term Management Plan, we not only achieved highly precise demand forecasts using advanced statistical models based on actual past sales data and AI systems but also the automation of production planning operations by combining this with existing ERP system functions. We also set risk-based safe inventory criteria and built an operable system.

We will conduct inventory management that balances stable supply and appropriate inventory volume by verifying the system and quickly reflecting changes in demand in production plans.

Construction of the Odawara nucleic acid API purification plant

It was proposed that we construct a nucleic acid API purification plant within the Central Factory in order to provide a stable supply of nucleic acid drugs. After obtaining in-house approval in June 2021, we completed construction in February 2024 as planned after about thirty months of planning and building.

Construction of a reliability assurance system

For the Production & Assurance Division, work is progressing smoothly, which has entailed ensuring the maintenance and management of production and marketing approval for our various products in Japan and establishing a reliability assurance system for sales of Viltepso in the U.S. and Gaslon N tablets 2mg in China. As for post-manufacture and marketing surveys, we started our first database survey and are making progress as planned.

Strategy and Future Initiatives to Implement 7th Five-Year Medium-Term Management Plan

Develop and strengthen global supply chain

In order to develop and strengthen our global supply chain, we will undertake the following activities related to procurement, production, and logistics in order to establish a competitive supply system while keeping stable supply and cost management in mind.

1. Reinforcing sustainable procurement initiatives and reducing procurement costs

The Sustainable Procurement Policy has been adopted as the group-wide procurement policy and is being introduced throughout the Nippon Shinyaku Group. We will formulate a Supplier Code of Conduct, which reflects this policy, and are moving forward with informing and gaining the approval of key business partners. In addition to coordinating and evaluating various types of surveys, including CSR procurement and stable supply surveys, and examining appropriate feedback methods for business partners, we are investigating ways to efficiently and effectively conduct supplier due diligence and environmental response surveys in partnership with key departments.

Furthermore, we will continue to work to reduce raw material procurement costs for nucleic acid drugs and key products through such activities as changing and adding suppliers and revising unit purchase price.

2. Developing and invigorating Odawara Central Factory's global supply system

To provide a stable supply of a therapy for Duchenne muscular dystrophy, a growth driver for Nippon Shinyaku, we are working to strengthen our global supply system by ensuring the launch of production at our nucleic acid API purification plant.

Furthermore, we are promoting the manufacturing of oral solid doses and aiming to establish a highly reliable supply chain for the whole product lifecycle by accumulating proprietary production technology and accelerating the launch of pharmaceuticals through the smooth shift to commercial production, in order to contribute to greater value of existing buildings, including the building for highly active solid formulations, and shorter development time for in-house products.

To generate sustainable growth, we are also working to increase productivity through such activities as automating operations that make use of digital technology and leveraging data, and to maximize throughput for the whole plant and create a highly competitive production system.

3. Creating a global supply chain system for new modalities

With an eye toward expanding the regenerative medicine products business internationally, we will build a supply chain system that meets the regulations of each country and region in order to offer a stable supply of our drugs and expand new sales areas beyond Japan, the U.S, and China. Along with this response to new modalities, we will increase the competitiveness of our supply chain by establishing an end-to-end cold chain, which includes low-temperature production and storage, and reinforcing quality and inventory control system.

Building a system that can handle regulations in a wide range of countries

The Production & Assurance Division strives to ensure the quality, efficacy, and safety of products by appropriately conducting various operations, including ensuring the reliability of application data, pharmaceutical applications and the maintenance of approvals, ensuring product quality, managing safety information, conducting post-manufacture and marketing surveys, and handling consultations regarding medicines, at all stages from R&D to product launch and beyond. As for future initiatives, we will deliver safe, high-quality products to patients worldwide in partnership with supply chain members by building a system to handle not only domestic laws and regulations* but also regulations in the various countries we sell products.

*Domestic laws and regulations
Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices: Law related to such issues as ensuring the quality, efficacy, and safety of pharmaceuticals, medical devices, etc.
GQP ministerial ordinance: Ministerial ordinance related to quality management standards for pharmaceuticals, quasi-drugs, cosmetics and regenerative medicine products
GVP ministerial ordinance: Ministerial ordinance related to post-manufacture and marketing safety management standards for pharmaceuticals, quasi-drugs, cosmetics, medical devices, in vitro diagnostics, and regenerative medicine products
GPSP ministerial ordinance: Ministerial ordinance related to conducting post-manufacture and marketing surveys and tests of pharmaceuticals

Establishing a reliability assurance system for new modalities, including biopharmaceuticals

To address diseases for which there are no effective traditional small molecule drugs, we are working to develop drugs with new modalities. We will create a system to ensure the reliability for these modalities, too.

Using post-marketing safety information

We will develop plans that make more meaningful use of post-manufacture and marketing survey, which are conducted as one of our post-marketing safety measures, and make the results public through academic papers, etc., in a timely manner. This will be used to increase product value and promote proper use.

NIPPON SHINYAKU PEOPLE

Partnerships that are growing more complex due to globalization

I am responsible for the packaging process at the Odawara Central Factory's Production Department, and we are promoting factory automation in order to reduce the number of required workers. Recently, we have examined using AI to automate the visual inspection of vials. For vials that contain freeze-dried preparations, we rely on people to conduct visual inspections because there are numerous inspection points and complex decision criteria. It would be best, however, to automate the process because the work takes a lot of time and places a heavy burden on workers. With the idea that it may be possible to automate the inspection process using AI, we started tests using various AI engines and were ultimately able to determine good and defective vials using an AI model that we developed. We are now moving forward with an examination of installing this automated inspection equipment.

Toru Ichikawa
Product Section 1, Production Department, Odawara Central Factory