# Pharmaceuticals Business

**Nippon Shinyaku brings to market on average at least one new product a year by not only undertaking in-house drug discovery based on our R&D capabilities built up since the founding of the Company in 1919 but also introducing in-license products and undertaking PLCM. We also proactively take on challenges in fields that other companies avoid and move forward with research and development of original treatments to create unique pharmaceuticals required by patients suffering from disease and their families and to be a company that is trusted by society.**

## R&D


The R&D Division is responsible for the creation of new value for pharmaceuticals, which is the most important part of an R&D-oriented pharmaceutical company. With originality as our keyword, we are committed to working on themes and approaches that other companies avoid, and this has led to the development of small molecule drugs for pulmonary hypertension and the creation of nucleic acid drugs, an original modality. In order to fulfill our issue of materiality of realizing a healthy future by creating innovation, we will work to expand the application of nucleic acid drugs, research new modalities, and search for new drug discovery targets and compounds by utilizing AI.

In selecting themes, we place importance on scientific validity and business potential in addition to originality. In the area of intractable and rare diseases, one of our focal areas, patients are few and clinical trials must be conducted on a global scale. Obtaining approval in the U.S. is not an easy task, as the approval review process changes depending on the R&D status of other companies and the circumstances surrounding the disease, and more stringent scientific backing is often required. However, as we believe the high safety and efficacy of the compounds we discover are important and will lead to early approval, we will continue our uncompromising dedication to drug discovery.

The center of our concerns is always what we can do for patients. We will also achieve patient centricity in clinical trials by trying to make patient participation easier and pursuing what they most want to be addressed. I want to make Nippon Shinyaku a pharmaceutical company that attracts attention for its science-based drug development. To achieve this goal, we will select the best modalities to treat diseases and explore their potential so that we can contribute to people's health through original, world-class products.

## Feedback from a Patient

### A future in which all patients have the freedom to choose their own treatment

**Tamotsu Takeda** Representative Director Japan Muscular Dystrophy Association

I have no memory of ever being able to stand and walk on my own since I was an infant. Back then, there was no awareness of my intractable disease, and we did not know its cause or how to treat it. Later, I was diagnosed with spinal muscular atrophy (SMA) by a muscular dystrophy specialist, but I had become alienated from medical care and rehabilitation after learning that there was no known cause or treatment for my disease.

SMA is a progressive, intractable disease that reduces the number of things one can do alone with each passing day, but I have recently learned that there is a treatment. With the advancement of medicine, I feel that the day is close when intractable diseases, previously said to have no treatment, become treatable. I believe that someday soon I will be able to keep doing tomorrow the things I can still do today, and even more activities like eating ramen by myself, playing sports, and enjoying life.

In order to make this future possible, it is important for all patients to have the freedom to choose their own treatments. I and everyone from the Japan Muscular Dystrophy Association hope that pharmaceutical companies, physicians, and patients will be able to share treatment information with each other so that patients can choose the treatment that is right for them.

I hope that everyone at Nippon Shinyaku will continue to make further efforts in development and mutual collaboration to meet the needs of patients and deliver treatments, so that together we can envision a brighter future.

**Materiality** Realizing a healthy future by creating innovation

| Main Activities | FY2022 Activities | Issues and FY2023 Strategies |
|---|---|---|
| • Promoting drug discovery utilizing nucleic acid medicines, new modalities, and new targets and methods<br>• Promoting drug discovery research and clinical trials based on Patient Centricity | • Enhanced technologies related to small molecules and nucleic acids and introduced data-driven drug discovery<br>• Ventured into new drug discovery modalities, including gene therapy<br>• Established a drug discovery center in Boston, the heart of the drug discovery ecosystem<br>• Strengthened human resource development initiatives in each department | • Diversifying in-house drug discovery by increasing access to the world's most advanced drug discovery innovations and increasing opportunities for partnering<br>• Planning and implementing IP strategies that support drug discovery utilizing a wider range of new modalities |

**Materiality** Strengthening efforts to protect the global environment

| Main Activities | FY2022 Activities | Issues and FY2023 Strategies |
|---|---|---|
| • Promoting animal welfare-friendly initiatives | • Implemented humane animal research and environmental maintenance with consideration of animal welfare<br>• Conducted introductory and continuing education to raise animal welfare awareness | • Maintaining an animal research environment that is up-to-date and promoting humane animal research based on the 3Rs. |

**Materiality** Resolving social issues and coexisting with the community

| Main Activities | FY2022 Activities | Issues and FY2023 Strategies |
|---|---|---|
| • Disseminating scientific findings through academic papers and conferences for the development of the scientific field | • Contributed to the development of related science fields by presenting scientific findings through academic papers or conferences<br>• Protected and utilized scientific findings (inventions) through intellectual property | • Publishing scientific findings through academic papers and conferences<br>• Continuing to protect and utilize scientific findings (inventions) through intellectual property |

# Pharmaceuticals Business

## Delivering Our Unique Products Globally

Nippon Shinyaku has excellent R&D capabilities which have produced products such as the small molecule drug Uptravi and the nucleic acid drug Viltepso. We are also working on new modalities, including gene therapy, to increase the number of diseases that can be treated. We will continuously improve our drug discovery capabilities by combining them with data-driven drug discovery, our current focus. This will promote the creation of new research themes and promote in-house drug discovery, centered around our focal areas and fields. Furthermore, in addition to PLCM to increase product value by expanding the range of indications and developing new dosage forms for existing products and products under development, we are enriching our pipeline through in-licensing of products from other companies and open innovation activities.

Through these R&D activities, based on the concept of patient centricity, we will continually deliver unique new drugs to patients in disease areas with unmet treatment needs. To this end, we have developed an organizational structure that is capable of conducting R&D on a global basis.

## Progress of the Medium-term Management Plan and FY2022 Overview

### Expanding the pipeline in our focal areas

In March 2022, we obtained manufacturing and marketing approval for MonoVer (code no.: NS-32, generic name: ferric derisomaltose), an iron deficiency anemia treatment in-licensed from Pharmacosmos A/S in 2016, and it launched in March 2023.

Uptravi (code no.: NS-304, generic name: selexipag), a pulmonary arterial hypertension (PAH) treatment launched in 2016, is in a Phase II trial for pediatric indications. In addition, a late-stage Phase II clinical trial is underway to add arteriosclerosis obliterans to the indications for Uptravi.

A global Phase III clinical trial is underway for Viltepso (code no.: NS-065/NCNP-01, generic name: viltolarsen), a Duchenne muscular dystrophy (DMD) treatment launched in Japan and the U.S. in 2020.

In December 2022, Chugai Pharmaceutical Co., Ltd. obtained approval for an additional indication of chronic lymphocytic leukemia for humanized anti-CD20 monoclonal antibody Gazyva (code no.: GA101, generic name: obinutuzumab), and in June 2022, we initiated a Phase III clinical trial for lupus nephritis in collaboration with them. In addition, in March 2023 we initiated a Phase III clinical trial for pediatric nephrotic syndrome in collaboration with Chugai.

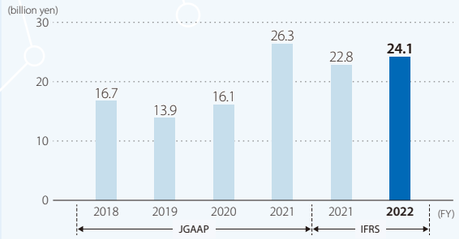
In 2019, we entered into an exclusive distribution agreement in Japan with UCB S.A. (formerly Zogenix, Inc.) for Fintepla Oral Solution 2.2 mg/mL (code no.: ZX008, generic name: fenfluramine hydrochloride), a treatment for epileptic seizures associated with Dravet syndrome. In September 2022, UCB S.A. obtained approval for manufacturing and marketing, and Nippon Shinyaku began distribution of the product in November 2022.

NS-161 and NS-025 are now in Phase I clinical trials in Japan for inflammatory and urological diseases, respectively.

### Promoting licensing activities

In February 2023, we entered into an exclusive partnership for the Japan distribution of CAP-1002 for the expected indication of DMD with U.S. company Capricor Therapeutics Inc. This agreement follows the exclusive partnership for U.S. distribution we entered with them in January 2022. CAP-1002 is comprised of human allogeneic cardiosphere-derived cells and is expected to be effective in a wide range of DMD patients, regardless of the type of genetic mutation. Capricor Therapeutics Inc. is currently conducting a Phase III clinical trial in the U.S.

**Research and development expenses**




## Pipeline (As of August 10, 2023)

Nippon Shinyaku's latest pipeline
WEB https://www.nippon-shinyaku.co.jp/english/ir/financial/develop.php

### Japan

| Code no. (generic name) | Origin | Development | Indications | Phase | NDA filing | Launch |
|---|---|---|---|---|---|---|
| **NS-065/NCNP-01** (Viltolarsen) | Co-development: National Center of Neurology and Psychiatry | Nippon Shinyaku | Duchenne muscular dystrophy | III: Underway | | |
| **NS-87** (daunorubicin/cytarabine) | Licensed-in from: Jazz Pharmaceuticals plc | Nippon Shinyaku | High-risk acute myeloid leukemia | III | | |
| **ZX008** (Fenfluramine hydrochloride) | Distribution partnership UCB S.A. (formerly Zogenix, Inc.) | UCB S.A (formerly Zogenix, Inc.) | Lennox-Gastaut syndrome | III | | |
| **ZX008** (Fenfluramine hydrochloride) | Distribution partnership: UCB S.A. (formerly Zogenix, Inc.) | UCB S.A (formerly Zogenix, Inc.) | CDKL5 deficiency disorder | III | | |
| **GA101** (Obinutuzumab) | Licensed-in from: Chugai Pharmaceutical Co., Ltd. | Co-development: Chugai Pharmaceutical Co., Ltd. | Lupus nephritis | III | | |
| **GA101** (Obinutuzumab) | Licensed-in from: Chugai Pharmaceutical Co., Ltd. | Co-development: Chugai Pharmaceutical Co., Ltd. | Pediatric nephrotic syndrome | III | | |
| **NS-304** (Selexipag) | Nippon Shinyaku | Nippon Shinyaku | Arteriosclerosis obliterans | II | | |
| **NS-304** (Selexipag) | Nippon Shinyaku | Co-development: Janssen Pharmaceutical K.K. | Pediatric pulmonary arterial hypertension | II | | |
| **NS-580** | Nippon Shinyaku | Nippon Shinyaku | Endometriosis | II | | |
| **NS-580** | Nippon Shinyaku | Nippon Shinyaku | Chronic prostatitis / Chronic pelvic pain syndrome | II | | |
| **NS-089/NCNP-02** (brogidirsen) | Co-development: National Center of Neurology and Psychiatry | Nippon Shinyaku | Duchenne muscular dystrophy | I/II In preparation | | |
| **NS-229** | Nippon Shinyaku | Nippon Shinyaku | Eosinophilic granulomatosis with polyangiitis | I/II In preparation | | |
| **NS-401** (tagraxofusp) | Licensed-in from: The Menarini Group | Nippon Shinyaku | Blastic plasmacytoid dendritic cell neoplasm | I/II | | |
| **NS-050/NCNP-03** | Co-development: National Center of Neurology and Psychiatry | Nippon Shinyaku | Duchenne muscular dystrophy | I/II In preparation | | |
| **NS-917** (radgocitabine) | Licensed-in from: Delta-Fly Pharma, Inc. | Nippon Shinyaku | Relapsed/refractory acute myeloid leukemia | I | | |
| **NS-161** | Nippon Shinyaku | Nippon Shinyaku | Inflammatory diseases | I | | |
| **NS-025** | Nippon Shinyaku | Nippon Shinyaku | Urological diseases | I | | |

### Overseas

| Code no. (generic name) | Origin | Development | Indications | Phase | NDA filing | Launch |
|---|---|---|---|---|---|---|
| **NS-065/NCNP-01** (Viltolarsen) | Co-development: National Center of Neurology and Psychiatry | Nippon Shinyaku | Duchenne muscular dystrophy | III: Underway | | |
| **CAP-1002** | Partnership: Capricor Therapeutics Inc. | Capricor Therapeutics Inc. | Duchenne muscular dystrophy | III | | |
| **NS-018** (ilginatinib) | Nippon Shinyaku | Nippon Shinyaku | Myelofibrosis | II | | |
| **NS-089/NCNP-02** (brogidirsen) | Co-development: National Center of Neurology and Psychiatry | Nippon Shinyaku | Duchenne muscular dystrophy | I/II In preparation | | |
| **NS-229** | Nippon Shinyaku | Nippon Shinyaku | Eosinophilic granulomatosis with polyangiitis | I/II In preparation | | |
| **NS-050/NCNP-03** | Co-development: National Center of Neurology and Psychiatry | Nippon Shinyaku | Duchenne muscular dystrophy | I/II In preparation | | |

# Pharmaceuticals Business

## FY2023 Initiatives and Strategy

In the area of intractable and rare diseases, in addition to the DMD treatments to follow Viltepso (NS-089/NCNP-02, NS-050/NCNP-03, and NS-051/NCNP-04), we will develop NS-229 and NS-161 for inflammatory diseases.

As for Nippon Shinyaku's focal areas and fields, in hematologic malignancies, we will promote the development of a treatment for high-risk acute myeloid leukemia (NS-87) and for myelofibrosis (NS-018). In gynecology, we will promote the development of a treatment for endometriosis (NS-580), and in urology, we are developing NS-025.

As for licensing activities, we will promote the introduction of unique products and developments that complement our R&D activities and expand our R&D pipeline.

## Value Creation Initiatives

### In-house drug discovery initiatives

In recent years, the use of new drug discovery modalities has increased in the field of drug discovery research. In addition to small molecule drugs and nucleic acid drugs, Nippon Shinyaku is also working on new modalities including gene therapies. To assist in our endeavors, we have strengthened collaboration with academic institutions and other external parties. We will increase our access to the world's most advanced drug discovery technologies not only in Japan but also through our overseas drug discovery centers, analyze the attributes and potential of various drug discovery modalities and select the modalities we consider optimal for specific diseases and mechanisms. In addition, we are accelerating R&D through data-driven drug discovery and promoting the strategic creation of new drug discovery themes.

Enriching the pipeline with in-house drug discovery, in-licensing, and PLCM

### Promoting PLCM strategies

Due in part to depletion of drug discovery targets, the cost and duration of new drug development continues to increase, adding to the difficulty of drug discovery each year. In addition, the external environment is changing dramatically as NHI drug prices are revised annually. Against this backdrop, pharmaceutical companies are finding it ever more important to secure profitability via initiatives to maximize product value. Nippon Shinyaku works to maximize the value of existing products such as Uptravi by utilizing comprehensive analysis technologies and large-scale data to proactively expand the range of indications and develop new dosage forms. We also engage in strategic PLCM planning for drug candidates still in development, based on these compounds' distinguishing features.

### Enriching the pipeline through in-licensing

In addition to in-house drug discovery, Nippon Shinyaku actively utilizes in-licensed products and development articles to enrich its pipeline. In the past, we have collaborated with many partner companies in a wide range of fields, and we have been first to meet the challenge of conducting research in areas where other companies are not involved. Through in-licensing, we will develop and market products of new value in cooperation with our partners and, as with our pharmaceuticals discovered in-house, we will continue to provide unique new drugs in Japan and internationally in disease areas with unmet treatment needs.

Promoting Research on Nucleic Acid Drugs

## Human resource development in R&D

The R&D Division has defined the type of human resources it seeks in employees who are committed to successful drug discovery research, and is working on a training program to cultivate them. Drug discovery is challenging and requires numerous processes and a lot of time. Cross-divisional teamwork is essential to steadily reach market launch and further speed up the process. Through the training program, we aim to create an organization that values cooperation and altruism, while developing individuals and the R&D Division as a whole so that they lead us to a high rate of drug discovery success.

We believe that it is important to always maintain a passion for drug discovery and a sense of care for patients and their families who are waiting for medicines in order to unrelentingly follow through with the R&D of pharmaceuticals. Which is why the R&D Division has also initiated activities related to patient centricity, through which we will conduct R&D that incorporates the perspectives of patients and their families, leading to the type of drug discovery that patients truly want.

### Basic approach to animal welfare

We have established internal regulations in accordance with relevant laws and regulations, and established an Animal Research Committee to examine if all animal research is carried out with appropriate consideration based on the principles of the 3Rs (Replacement [with alternative methods], Reduction [of the number of animals used], and Refinement [to reduce pain and discomfort suffered by animals]). As for our animal research implementation system, we periodically conduct self-inspections, and we have also been accredited by a third-party organization. We maintain an appropriate breeding environment for animals used in our experiments in consideration of animal welfare. In addition, as part of our efforts to protect the global environment, for the preservation of biodiversity, experiments using genetically modified animals are conducted in compliance with the Cartagena Act. Furthermore, waste generated by our animal research is disposed of by contractors licensed by the government.

## Voice

### Unraveling new pathological mechanisms of rare hereditary diseases during overseas study

Using Nippon Shinyaku's support for overseas study, I studied at a lab in the U.S. for two and a half years, from April 2019 to October 2021. The lab where I studied is working to unravel new pathological mechanisms of rare hereditary diseases using cutting-edge genome editing technology, and the purpose of my overseas study was to gain this expertise. Since returning to Japan, I am applying the techniques I learned to drafting new drug discovery themes. In addition, as I was studying in the Texas Medical Center, one of the largest medical research complexes in the U.S., I was able to build a network of contacts with many researchers there through joint research and seminars, and learn about diverse values. I would like to make use of these connections and perspectives in my work in the future.

**Tatsuhiko Arakawa**
Proposal Strategy Section
Strategic Planning and
Research Department

## Topics Holding of the R&D Conference

The R&D Conference is held every year to share the progress and results of R&D with all members of the R&D Division and link them to daily R&D activities and activities for maximizing product value. In FY2023, we held the 11th R&D Conference in July. Due to the impact of the COVID-19 pandemic, the last few conferences were held online, but this time, for the first time in four years, the meeting was held in a hybrid format, with a face-to-face meeting in the auditorium of the head office in addition to the online meeting. Lively discussions took place with many internal and external directors participating.

At the conference, business development activities in the U.S. at NS Pharma were presented in real time from the U.S. News, products under development and exploratory themes were reported, and the progress and results of items in each phase were shared. New and unprecedented initiatives in R&D were also presented, and all topics attracted a great deal of interest from the participants, and some discussions had to be cut off prematurely in the hall due to the time constraints. Through discussions at the R&D Conference, we will pursue the creation of new value and continuously bring new drugs to the market.

# Pharmaceuticals Business

## Initiatives Related to Intellectual Property

Nippon Shinyaku 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 our corporate value. We also respect third-party IP rights, practicing thorough IP-related risk management including ownership investigations.

### R&D activities and intellectual property

At Nippon Shinyaku, 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 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 in an internal committee consisting of multiple department managers.

### Understanding and analyzing intellectual property

With the basic attitude of respecting third-party IP rights, the Nippon Shinyaku Group regularly conducts ownership investigations regarding its products. We also conduct patent trend analysis in specific technical fields and IP analysis of competitors. 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.

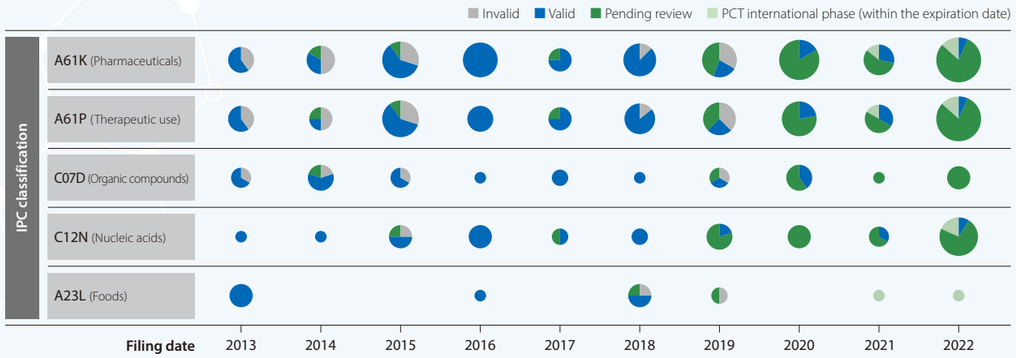
### Building our reputation and brand based on trademarks

The Nippon Shinyaku Group determines 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.

### Patent application trends

Our number of patent applications for pharmaceuticals and their uses has been increasing since 2019. This is especially clear in the field of nucleic acids, and we will protect the future business of Nippon Shinyaku in terms of intellectual property by ensuring that we protect the rights to the results of our efforts in our focal fields through patents. In addition, as research findings that can be patented stably emerge, mainly in our focal areas, we will continue to file patent applications for them in a timely manner, and acquire and utilize patent rights to protect our future business.

**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.

# Medical Affairs

**Materiality** | **Realizing a healthy future by creating innovation**

| Main Activities | FY2022 Activities | Issues and FY2023 Strategies |
|---|---|---|
| • Providing information to medical institutions and implementing disease awareness-raising activities for patients and their families<br>• Promoting social understanding of diseases | • Pulmonary hypertension: Held co-sponsored seminars for medical professionals and public lectures for patients and their families<br>• Muscular dystrophy: Held public lectures online and patient networking events utilizing the metaverse | • Promoting patients' understanding of their diseases<br>• Planning events with a focus on patients<br>• Continuing to hold public lectures and events for diseases such as pulmonary hypertension and muscular dystrophy |

**Materiality** | **Resolving social issues and coexisting with the community**

| Main Activities | FY2022 Activities | Issues and FY2023 Strategies |
|---|---|---|
| • Disseminating scientific findings through academic papers and conferences for the development of the scientific field | • Took initiatives that included non-clinical research, clinical research, database research, and registry research as evidence generating activities in disease areas related to the pharmaceuticals handled by the Group<br>• Published paper on research findings related to anemia | • Responding to changes in the environment surrounding research<br>• Presenting research findings at academic conferences and disseminating information through papers<br>• Fulfilling unmet medical needs through new research |

## Increasing Benefits for Patients by Disseminating Information

The mission of Medical Affairs is to engage in medical and scientific exchanges with key external experts using advanced, cutting-edge scientific knowledge to identify unmet medical needs*, generate scientific evidence to fulfill them, and disseminate information to medical professionals and patients in order to deliver the optimal medical care for all patients. At Medical Affairs, the goal is to optimize the value of the pharmaceuticals handled by the Group and contribute to increasing benefits for patients.

* Unmet medical needs (UMNs): Refers to medical needs that are not adequately satisfied for medical professionals and patients. Examples include needs for diseases for which no effective treatments have yet been found and needs for new therapeutic drugs or treatment methods.

## Progress of the Medium-term Management Plan and FY2022 Overview

In FY2022, in its evidence generating activities, Nippon Shinyaku worked on initiatives in non-clinical research, clinical research, database research, and registry research, and published a paper on its findings in database research. In term of patient support activities, it held online public lectures on pulmonary hypertension, and online public lectures and patient networking events on muscular dystrophy. In FY2023, with respect to its evidence generating activities, the Company is pushing ahead with preparations for new research on hematological malignancies, pulmonary hypertension, Duchenne muscular dystrophy, and anemia. In regard to its patient support activities, it plans to continue with its public lectures and networking events on pulmonary hypertension and muscular dystrophy. Nippon Shinyaku will act to make contributions to the healthcare field beyond the provision of pharmaceuticals in cooperation with medical science liaisons (MSLs)* who are responsible for medical affairs activities in medical institutions.

* Medical Science Liaison (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.

## Value Creation Initiatives and Strategy

In recent years, the environment around healthcare has been changing significantly due to rapid advances in digital technologies. Nippon Shinyaku will also consider making use of these technologies to solve medical issues and generate evidence that bring benefits for patients. For example, the Company would like to take on the challenge of contributing to better healthcare with a focus on digital healthcare using the latest technologies, including wearable devices and applications, artificial intelligence (AI), and big data analysis to improve the effectiveness of medical and healthcare.

# Resource Procurement, Production & Assurance


The tasks of the Resource Procurement, Production & Assurance Division are wide-ranging. We single-handedly manage defensive operations spanning everything from raw material procurement to production planning, manufacturing, delivery, product and data quality assurance, safety information collection and assessment, and approval application and maintenance. A single misstep on our part at any point would prohibit us from fulfilling our most important duty—stable product supply. Accordingly, each day I am keenly aware of the importance of complying with laws and regulations, assessing risk, controlling inventory, and managing our suppliers. In addition to implementing the expected credit checks and due diligence, we also place importance on interpersonal communication in management. We hold weekly online meetings with the Odawara Central Factory and other relevant divisions. We also share information and engage in technical cooperation with affiliated companies. Through these means, we build better relationships. We in the Resource Procurement, Production & Assurance Division are frequently aided by such excellent relationships. For example, at the start of the COVID-19 pandemic when there was a shortage of sterile filters for injection production, the Raw Materials Procurement Department was able to successfully procure such filters from the United States through affiliated companies.

As Nippon Shinyaku seeks greater expansion globally, building a global supply system is a massive challenge. Issues such as environmental considerations as well as differences in regulations and business practices in supply destination countries require the prior gathering of sufficient information. In addition, even with raw materials that are within legal limits, there can be slight differences in quality between lots. We are thus also launching initiatives to promote the digitalization of information, avoid human error, and enhance stable product supply, such as integrating and analyzing data on quality and manufacturability.

**Materiality** | **Realizing a healthy future by creating innovation**

| Main Activities | FY2022 Activities | Issues and FY2023 Strategies |
|---|---|---|
| **Supply chain**<br>• Establishing a global sales and supply system to provide pharmaceuticals and functional foods to the world<br>• Strengthening the stable supply system of products through risk management | • Surveyed suppliers on supply chain and CSR matters with the aim of sustainable and stable procurement<br>• Achieved a 100% risk assessment implementation rate regarding Nippon Shinyaku products, APIs, formulations, and important raw materials (149/149 items)<br>• Began construction of a nucleic acid API purification plant at the Odawara Central Factory | • Sharing the Nippon Shinyaku Sustainable Procurement Policy throughout the Group and with business partners<br>• Enhancing stable product supply by increasing demand forecasting precision using AI and other digital technologies<br>• Completing construction of the nucleic acid API purification plant at the Odawara Central Factory and making preparations for its operation |
| **Reliability assurance**<br>• Establishing a mechanism for supplying safe and high-quality products, including new drugs such as nucleic acid medicine | • Implemented thorough plant management regarding products and built a reliability assurance system for marketing in China | Implementing integrated safety information management from the development stage and thorough plant management regarding products |

## Aiming for Stable Product Supply and the Construction of a Global Supply System

We are working to manufacture pharmaceuticals under new modalities to provide medicines and new treatments for diseases for which there are no therapeutic agents yet, such as nucleic acid drugs in addition to conventional pharmaceuticals. In order to deliver these to patients not only in Japan but around the world, it will be necessary to build a global supply system able to comply with each location's regulations, environment, and customs. Amid an uncertain social landscape, the environment around pharmaceuticals is turning more challenging. However, by implementing solid quality assurance and stable product supply under all conditions, and by providing appropriate safety and other product information, we will deliver peace of mind and confidence to patients and all of our stakeholders.

## Progress of the Medium-term Management Plan and FY2022 Overview

In FY2022, we leveraged our experience building a pharmaceutical supply system for the United States to further the creation of a supply chain and reliability assurance system for the Chinese market. In addition, in order to respond to the increase in demand for nucleic acid drugs that will accompany further global expansion, we worked to enhance our supply system. For example, we began construction of a plant to handle a portion (the purification) of the nucleic acid manufacturing process at our Odawara Central Factory. We also added second suppliers for nucleic acid APIs, formulations, and raw materials.

## Value Creation Initiatives and Strategy

In FY2023, we will continue to enhance our supply systems for the United States and Chinese markets and, with an eye toward expansion into new territories, work to gather necessary information and build required systems. In addition, in accordance with completion of construction on the nucleic acid API purification plant at the Odawara Central Factory, we will begin manufacturing pharmaceuticals that belong to new modalities.

We will further enhance the reliability assurance systems we have built, continue to provide appropriate information to society and patients, and work to secure even further reliability.

## Building a Supply Chain that Can Support Stable Product Supply

A pharmaceutical supply chain which involves suppliers from multiple countries and regions faces the risks of natural disasters, infectious diseases, and geopolitical strife, the challenges involved in providing a stable supply of generics increased further in FY2022. Believing that avoiding the various supply chain risks and maintaining a stable product supply is our greatest challenge, the Nippon Shinyaku Group is promoting the following three strategies in order to increase its pharmaceutical supply chain capabilities.

### 1. Constructing a nucleic acid API purification plant at the Odawara Central Factory

We aim to complete this new nucleic acid purification plant in December 2023. We are positioning this facility as an investment to further build up our manufacturing technologies and to establish a strong global supply system.

## Voice

**Satoshi Asano**
SC Management Section
Supply Chain Management Department

### Realizing Stable Product Supply for Patients Around the World

Viltepso, released as Japan's first antisense oligonucleotide, is also the first product that Nippon Shinyaku has marketed itself in the United States. Unlike with the domestic products with which Nippon Shinyaku has accumulated an abundance of data and knowhow, we have had almost no experience marketing products ourselves overseas. The demand for such products cannot be accurately perceived or predicted based on what we have learned through our products in Japan alone. We engage in periodic meetings with the supply chain division of NS Pharma, a local Group company, to share detailed information on topics such as the state of sales domestically and overseas, future prospects, and production and shipping schedules, and in turn develop plans that enable the stable provision of Viltepso both in Japan and internationally. Going forward, Nippon Shinyaku will strive to build a global supply chain that is even stronger and more optimized so that we may deliver our unique, high-quality pharmaceuticals quickly and stably to patients not just in Japan or the United States but around the world.

## Pharmaceuticals Business

**2. Building a risk management system to dynamically manage potential supply chain risks**

Having a detailed grasp of our supply chain will help Nippon Shinyaku to manage risks. We are striving to maintain an accurate awareness of the stable supply and BCP* initiatives our suppliers engage in by conducting written surveys of suppliers involved in all APIs and formulations. Through a risk-based approach rooted in the results of these surveys as well as quality information and business records, we are taking thorough steps to reduce risks.

* BCP: An abbreviation of "business continuity plan."

**3. Promoting the DX of our supply chain**

At the Odawara Central Factory, we are moving forward with preparations to create a connected factory by creating a vial inspection system utilizing AI image recognition and connecting manufacturing facilities via IoT for improved quality and preventative maintenance. We are also investigating predictive modeling utilizing AI to detect environmental changes and other threats which could impact stable product supply and aid in highly accurate demand prediction.

Through these three strategies, we will reduce pharmaceutical supply risks and at the same time increase our competitiveness, propelling us further in our transition to a resilient supply chain.

### Reliability Assurance Initiatives

The Production & Assurance Division handles compliance with relevant laws and ordinances as well as tasks spanning the entire pharmaceutical life cycle, from the R&D stage through to product launch and beyond. Taking charge of product quality assurance, data reliability maintenance, safety information management, pharmaceutical applications, and post-manufacture and marketing surveys and medicine consultations, we strive to ensure the effectiveness and safety of pharmaceuticals.

In addition, through solid coordination between the various reliability assurance divisions under the general marketing supervisor, QA manager, and safety manager, we ensure compliance with the terms of approvals; maintain and manage pharmaceutical manufacturing and marketing licenses; and implement compliance with the GQP*1, GVP*2, and GPSP*3 ministerial ordinances. Through these means, we aim to further enhance our manufacturing and marketing systems to ensure product quality, effectiveness, and safety.

Additionally, in accordance with the global supply of products, we continuously revise our structure and procedures to ensure compliance with the regulations of new countries whose markets we are entering. In FY2022, we worked with a local subsidiary to build a reliability assurance system in China. In FY2023, we will be working steadily on operations to ensure product reliability in the United States and China. We will also be further developing our systems with an eye on future moves.

*1 GQP: An abbreviation of Good Quality Practice. A standard for the quality management of, among others, pharmaceuticals, quasi-drugs, cosmetics, and regenerative medicine products. Conformity to this standard is one of the requirements of pharmaceutical manufacturing and marketing licenses.

*2 GVP: An abbreviation of Good Vigilance Practice. A standard for post-manufacture and marketing safety management of pharmaceuticals, quasi-drugs, cosmetics, medical devices, in vitro diagnostic products, and regenerative medicine products. Conformity to this standard is one of the requirements of pharmaceutical manufacturing and marketing licenses.

*3 GPSP: An abbreviation of Good Post-marketing Study Practice. A standard for post-manufacture and marketing surveys and testing.

### Voice

**Shohei Nakagawara**
Quality Assurance Section
Quality Assurance Department
Regulatory Affairs, Pharmacovigilance and Quality Assurance Division

#### Globalizing the Work of Quality Assurance in Line with Each Country's Regulations and Requirements

When we engage in quality assurance, we strive to ensure that customers can take our products with peace of mind, focusing on appropriately maintaining and managing quality so that pharmaceuticals have the expected safety and work effectively. We have built a pharmaceutical quality system based on our quality policy. Under this system, we appropriately manage and supervise manufacturing facilities, assess product quality, and also engage in communication with regulatory authorities. As we globalize our pharmaceutical distribution, we need quality management which is in conformance with each country's regulations and requirements. Accordingly, we are gathering information about these so that we may respond swiftly even in the event of a quality issue at a factory, and so that we can ensure a stable product supply. Among our efforts in this area, our experience building our own marketing system in the United States for Viltepso was of great use when we created a reliability assurance system in China. Going forward, we will continue to strive to deliver our high-quality, unique pharmaceuticals to patients around the world.

## Sales

### Aiming to be a trusted treatment partner with high-quality information and integrity

**Shouzou Sano**
Managing Director, Sales and Marketing

The primary mission of our Sales and Marketing Division is to "deliver our unique products to as many patients suffering from illness as possible, as quickly as possible." To this end, we aim to become a treatment partner trusted by doctors and patients through providing high-quality information based on the spirit of patient centricity.

The Sales and Marketing Division also bears a great deal of responsibility in fulfilling President Nakai's three commitments. To achieve the continued launch of at least one unique product each year on average, it is essential to introduce in-licensed products and undertake PLCM. Demonstrating Nippon Shinyaku's relevance in our focal areas and fields and proving the strength of our marketing will lead to successful in-licensing.

Another role of medical representatives (MRs) is to grasp the needs of medical professionals and patients from their daily activities to obtain leads for PLCM. Concentrating on intractable and rare diseases, one of our focal areas, we help patients access early diagnosis and appropriate treatment by providing up-to-date information through ongoing communication, and collaborating with medical professionals in hospitals and clinics.

We are sometimes recognized by people outside the Company for the high integrity of our employees. Our work in Sales and Marketing is based on integrity, and without that integrity, and without knowledge, we cannot achieve results. Through the introduction of an in-house certification exam program and a team system for MR activities, we are striving to build a highly cohesive organization where we can grow through friendly internal rivalry. We must further hone our expertise and improve our marketing capabilities toward the critical goal of global expansion. Each Sales and Marketing team member will keep the spirit of patient centricity in mind and continue to fulfill our roles and responsibilities.

**Materiality** | **Realizing a healthy future by creating innovation**

| Main Activities | FY2022 Activities | Issues and FY2023 Strategies |
|---|---|---|
| • Promoting treatment, diagnosis, medication guidance, and life improvement through the use of digital technologies<br>• Providing information to medical institutions and implementing disease awareness-raising activities for patients and their families | • Promoted medication guidance through "Sherpa," a support program for patients with pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension<br>• Provided information by combining MR activities with digital services (our owned site and third-party services) according to the following sequence of phases: disease recognition → diagnosis → treatment → continued medication<br>• Provided information on our disease awareness and product information websites created for patients | • Familiarizing physicians with the value of "Sherpa" (high patient satisfaction)<br>• Providing information using digital technology<br>• Combining MR and digital activities<br>• Providing information digitally using customer journey maps<br>• Considering and implementing marketing automation |

# Pharmaceuticals Business

## Earn the Trust of Physicians by Providing High-Quality Information

The Sales and Marketing Division is committed to its mission to deliver our unique products to as many patients as possible, as quickly as possible based on the concept of patient centricity, where the patient is at the center of thoughts and actions in medical care. To achieve this mission, we will establish a system that enables us to accurately provide medical professionals involved in patient care with the information they need when they need it. We aim to become a treatment partner trusted by medical professionals by training MR as well as digital human resources and providing high-quality information through a combination of MR and digital activities.

## Progress of the Medium-term Management Plan and FY2022 Overview

In FY2022, we focused our activities on our most important strategic products, Uptravi in the area of pulmonary hypertension and Viltepso in the area of pediatric neurology, both of which were discovered and developed in-house. Since providing information to specialists alone is not enough to deliver drugs to potential patients, we also conducted disease awareness and medical coordination activities geared toward non-specialists to ensure that patients receive optimal treatment as soon as possible.

As for new products, in 2022, in the area of pediatric neurology, we launched Fintepla for the treatment of epileptic seizures in patients with Dravet syndrome, a disease designated as intractable by the Japanese government. This is the first new drug for the treatment of Dravet syndrome in ten years and has been eagerly awaited by many patients. In March 2023, in the area of gynecology, we launched MonoVer for the treatment of iron deficiency anemia. Many patients with anemia suffer in silence as they believe that their illness is common. Left with no treatment option, they choose to simply accept the disease. Since both drugs meet the needs of patients and have a significant role to play in fulfilling our social mission, we will achieve early market penetration in FY2023.

In the area of pulmonary hypertension, we launched the patient support program "Sherpa" in April 2022. "Sherpa" provides regular support by telephone to patients by nurses who have received specialized training in the program. We have received comments such as, "It is such a relief to have someone who understands my situation listen to me talk about my problems and anxieties," and "I'm very grateful to be able to get accurate answers for the questions I have between appointments about the disease and the medications." We will continue to provide the program for patients in FY2023.

MRs and aPMs Focused on Specialty Products Collaborate

## Developing human resources to strengthen information provision activities

### MR human resources

In order to implement high-quality information provision activities by MRs, we have continued training in problem-solution based detailing since FY2021, in which MRs communicate the benefits that our products bring to physicians and patients based on an understanding of each patient's background, values, and treatment issues. In FY2023, we will promote further improvement of problem-solution based detailing by focusing on training for sales office managers, who are the main actors in OJT, and role-playing drills.

In addition, each branch office has an area product marketing (aPM) personnel who serves as the main area marketing contact. aPM personnel are focused on specialty products, while MRs oversee all products, so that a synergistic effect can be achieved by accompanying MRs and aPMs.

### Digital human resources

In FY2023, we established the Digital Solutions Department to expand and further strengthen our digital operations. This department will, in collaboration with the Product Marketing Department at the head office, produce and distribute digital content to strengthen information provision activities utilizing digital technology. Digital content will be expanded and enhanced to meet challenges and objectives, ranging from disease awareness for the purpose of market expansion, to evidence supporting the selection of Nippon Shinyaku's pharmaceutical products, and measures to prevent side effects ensuring proper use of drugs. By analyzing the delivery data and implementing the PDCA cycle, we will promote the use of digital content so that medical professionals can obtain the information they need, when they need it.

We have also established a system that allows MRs to use iPads equipped with all our digital content to deliver information, and we are working on a system that enables high-quality information provision by combining MR activities with digital content.

## Disease Awareness Initiatives

Among Nippon Shinyaku's focal areas, intractable and rare diseases present a particular need for providing information to medical professionals and patients, as there is often insufficient information about patients, symptoms to watch out for, and treatment methods. In addition to enhancing digital content for MRs to exchange information face-to-face with medical professionals and strengthening information provision activities, we are focusing on providing information through digital media such as websites. We will approach patients in need of treatment through disease awareness efforts to ensure that necessary medications reach those who need them as soon as possible.

In addition, the area-specific aPM personnel assigned to each branch office work with MRs to promote disease awareness initiatives suited to regional characteristics and conditions. We believe that providing medical professionals with specialized information in their areas of expertise, accurately identifying problems that patients face based on information collected on a case-by-case basis, and promoting initiatives to solve these problems will lead to patient centricity. We aim to become a trusted presence by working together as a united Sales and Marketing Division team and taking the correct approach to the problems faced by medical professionals and patients.

Implementing high-quality information sharing activities

**Amount of digital content on Nippon Shinyaku's owned websites**

| | FY2022 results | FY2023 target |
|---|---|---|
| Page content | 63 | 73 |
| Brochure content | 10 | 57 |
| Video content | 80 | 82 |
| Total | 153 | 212 |

## Voice

### Uplifting as many patients needing treatment as possible

In my work in the Product Marketing Department, I try to deliver the right information to patients. I have been involved in planning and managing a support program for patients taking medications. The anxiety patients feel during treatment can cause them to give up taking their medications, so we set up a program that can support them in continuing their treatment.

Sometimes patients tell me that they are grateful for this program for helping them through their loneliness and anxiety regarding their treatment. Moments like these make me newly aware of my mission, and I will continue to uplift as many patients as possible by conveying the importance of going through treatment and the value of Nippon Shinyaku's products.

**Erina Kouno**
FerrCare Product Marketing Group, Primary Care Product Marketing Department
Sales and Marketing Planning Division
Sales and Marketing Division