Realizing a Healthy Future by Creating Innovation

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

R&D

We will drive forward R&D by giving our all in thinking about patients, while continuing to expand our pipeline, primarily through the three pillars of in-house drug discovery, in-licensing, and PLCM.

Keiichi Kuwano
Director, Research & Development

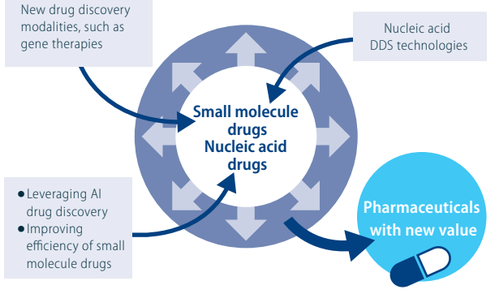
At Nippon Shinyaku, we value our uniqueness and conduct research and development based on our determination to deliver new drugs through our own efforts to patients in need, even if they are few in number. In recent years, we have launched products focused on the field of intractable and rare diseases, including Uptravi, a treatment for pulmonary hypertension (PH) and Viltepso, a treatment for Duchenne muscular dystrophy (DMD). In FY2024, as a part of our measures to maximize the value of Uptravi, we started sales of a pediatric formulation. The pill used for the Uptravi pediatric formulation has a small diameter of 3 mm that makes it easy to swallow, but this also makes it difficult to handle. To address this, we developed a dedicated pill case that makes it easier for patients and medical professionals to manage and count the pills. This is another example of our uniqueness and how we are dedicated to addressing the needs of patients. In the future, we will continue to focus on the three areas of hematology, intractable and rare diseases, and urology and gynecology as we continuously expand our pipeline through in-house drug discovery, in-licensing, and PLCM.

With regard to in-house drug discovery, we will develop drugs with effects and characteristics superior to existing treatments, emphasizing the concept of contributing to the "ways of life" of patients. In terms of nucleic acid drugs, we will add the central nervous system area to our target diseases as we seek further possibilities. We will also introduce new drug discovery technologies and modalities through open innovation, and develop nucleic acid drug delivery systems and gene expression enhancing nucleic acids. For PLCM, in addition to improving formulations, we develop drugs for secondary indications in parallel to checking the efficacy in humans for the first indication in order to maximize the value of the drug at an early stage.

Speeding up global development is essential to delivering pharmaceuticals to patients around the world. To do this, we established a new management department dedicated to global development and a new department to promote the prioritization of projects and optimization of resource allocation. We are improving our capabilities for negotiating with authorities in various countries as we seek to increase the possibility of fast approval, and we are also making efforts to ensure robust clinical study planning. By pursuing these initiatives, we will speed up development and increase the probability of success as we aim to realize our vision for 2035: "Creating various types of new ways of life for each person around the world."

Pursuing Uniqueness in R&D

We have developed new drugs by leveraging the two different fundamental technologies and drug discovery modalities of small molecule drugs, which include the Uptravi PH treatment, and nucleic acid drugs, which include the Viltepso DMD treatment. We will utilize these strengths to continue research for both modalities in the future, and we will also take on the challenge of finding new drug discovery modalities, such as gene therapies. By leveraging cutting-edge technologies such as AI, we will enhance our unique drug discovery capabilities. Furthermore, we will use open innovation that actively incorporates advanced technologies and ideas from both Japan and overseas to make our R&D even more unique and enable us to quickly develop innovative pharmaceuticals that meet the needs of patients.



Nippon Shinyaku's drug discovery base

Nippon Shinyaku's drug discovery base consists of two main technologies; nucleic acid drugs and small molecule drugs. We conduct research to generate new drugs by leveraging the unique characteristics of each.

Nucleic acid drugs can treat the root causes of diseases by directly acting on genetic information. We have researched nucleic acid drugs continuously for a long time and overcome many difficulties, the result of which was our launch of Viltepso, a treatment for DMD that was Japan's first nucleic acid drug. By applying the fundamental technologies of the nucleic acid sequence design that we built during this process, we will optimize sequence design as appropriate for new drug discovery targets. We are currently focusing R&D on the field of DMD, but we will also expand to other areas, such as the central nervous system.

Small molecule drugs are a widely used method where a synthesized compound binds to the target molecule to regulate its function. Nippon Shinyaku is building a unique compound library and strengthening our hit compound search system to drive forward efficient development of new small molecule drugs. We have established intractable and rare diseases and hematology as focus areas, and we promote PLCM by developing multiple other indications in parallel to the primary indication from the initial stages of development.

In the future, we also aim to develop Nucleic acid–Small molecule Conjugates that leverage the unique characteristics of our nucleic acid drugs and small molecule drugs. Using these fundamental technologies, we generate new drugs that meet the needs of patients while building and maintaining a high-level drug discovery research system.

Continuously tackling the challenges of new drug discovery modalities

Behind the success of our Uptravi PH treatment and Viltepso DMD treatment was our determination to continuously tackle the challenges of creating new treatment concepts and using new drug discovery modalities.

Although new drug discovery modalities have great potential, they also include cases where they will be used to treat human diseases for the first time. As a result, special care is required to confirm safety and efficacy, which means it takes time to turn them into actual drugs. By selecting new drug modalities that are unique and highly compatible with our proprietary technologies, and also making use of outside technologies, we will generate new, high-quality pharmaceuticals in a speedy manner to deliver effective treatments to patients as quickly as possible. In this way, we aim to realize our vision.

Realizing a Healthy Future by Creating Innovation

R&D

Open innovation

We established Innovation Research Partnering (IRP) in Cambridge, Massachusetts in the U.S. This area is home to an agglomeration of start-ups and biotech companies that lead the world in drug discovery R&D, as well as academic institutions such as Harvard University and the Massachusetts Institute of Technology. Through networking activities that leverage these geographical advantages, we will be able to access leading-edge technology information and seeds directly and at an early stage. By implementing these technologies or seeds that we find during IRP information collection and networking activities and combining them with our strong proprietary technologies, we aim to develop pharmaceuticals speedily based on new drug discovery technologies.

We will also collaborate with academic institutions that conduct leading-edge research both in Japan and overseas from the creation stage of new treatment concepts to discover, foster, and develop consistent platform technologies and generate First-in-Class pharmaceuticals that are globally renowned.

Through such open innovation strategies, we aim to expand our pipeline continuously by creating new drugs and new technologies that have the potential to become future pillars of Nippon Shinyaku.

Building where Innovation Research Partnering is located

Initiatives to Speed up R&D

In the 7th Medium-Term Management Plan, we set out "speeding up R&D" as one of the ways to strengthen our management foundation.

In drug discovery research, we are shortening the time from the drafting of a research theme to the start of clinical study, and building a system that enables us to launch at least one in-house product a year. To help us do this, we established a new Drug Discovery Strategy Department to manage drug discovery research comprehensively and promote transformation. This is speeding up research by optimizing drug discovery processes and standard schedules and conducting thorough progress management.

We also operate a drug discovery integrated database that leverages an AI engine that we developed ourselves to generate research themes and respond to issues faster and more efficiently. Furthermore, when searching for lead compounds and evaluating safety for each research theme, we are leveraging AI engines that have been optimized for each issue, which is helping to accelerate the progress of the research themes.

As for delays in clinical development, one of the issues that came to light during the 6th Medium-Term Management Plan, we are working to strengthen project management, pursue the possibility of early approval, and perform robust schedule planning. Specifically, we established systems to prioritize projects and optimize resource allocation. We also implemented project management tools that can be used across the organization, from research laboratories to the clinical development departments of our U.S. subsidiary, which enable us to manage the progress of clinical trials and implement them according to plan. We are also using such tools to share know-how about global development to facilitate early detection of issues that might cause delays and promote proactive actions. In addition, we are shortening the transition periods between development phases by taking measures such as bringing forward preparation for POC exams and organizing the processes of development step meetings. In this way, we will speed up clinical development and increase the probability of success.

Increasing the efficiency and speed of drug discovery research

Building a system capable of launching at least one in-house product a year

Resource allocation and project prioritization to decide how much of our limited resources should be invested in which areas

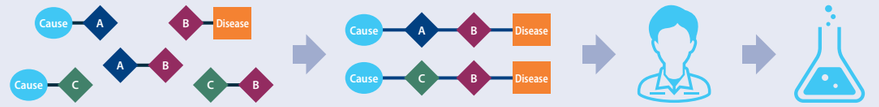
Create a well-balance R&D pipeline portfolio through investments that have been prioritized (success probability, profitability, focus areas, business value, etc.)

Systems and initiatives for launching at least one in-house product a year

- Establish new decision-making meetings of the collegial system to ensure rapid information sharing, issue response, and thorough progress management
- All researchers draft a proposal
- Shorten times by organizing and optimizing drug discovery processes

Promotion of efficient R&D by leveraging AI

(Image)



Huge amounts of information about diseases, symptoms, genes, etc. in academic papers and databases

Collection of information and preparation of inferences using AI

Confirmation and verification of inferences by researchers

Earlier start of R&D activities

Speeding up clinical development

Strengthening project management

- Strict progress check across management
- Improve negotiation skills with overseas authorities by hiring qualified medical doctors
- Building a clinical development system that can respond flexibly and globally
- Use of project management tools
- Review of development step meetings, bringing forward preparation for POC exams

Pursuing the possibility of early approval

- Promote biomarker search from early stage
- Efforts to reach consensus with authorities

Improving probability of success

- Robust clinical study planning
- Strengthening of POC exams planning
- Prioritization of clinical trial projects
- Consider partnering after obtaining POC
- Thoroughness of timing of study planning
- Establishment of a system to promote health technology assessment (HTA) and clinical development in parallel

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Development pipeline (As of August 7, 2025)

Global development product ★Orphan drug ●Rare pediatric disease

*Launched in Japan and U.S. in 2020

	Phase1	Phase2	Phase3	Application filed
Intractable and rare diseases	●NS-050/NCNP-03 Duchenne muscular dystrophy ★●ATSN-101 GUCY2D gene mutation type of Leber congenital amaurosis ★●RGX-111 Mucopolysaccharidosis type I ★●NS-089/NCNP-02 Duchenne muscular dystrophy ★NS-229 Eosinophilic granulomatosis with polyangiitis		★NS-065/NCNP-01* Duchenne muscular dystrophy ★●CAP-1002 Duchenne muscular dystrophy ★ZX008 CDKL5 deficiency disorder GA101 • Lupus nephritis • Pediatric idiopathic nephrotic syndrome • Systemic lupus erythematosus without nephropathy	★●CAP-1002 Duchenne muscular dystrophy Cardiomyopathy ★●RGX-121 Mucopolysaccharidosis type II
Hematological malignancies	★NS-917 Relapsed/refractory acute myeloid leukemia		★LY3527727 • Mantle cell lymphoma • Chronic lymphocytic leukemia	★NS-401 Blastic plasmacytoid dendritic cell neoplasm
Circulatory and metabolic system	NS-863 Circulatory and metabolic system diseases	NS-304 Arteriosclerosis obliterans		
Urology and gynecology	NS-025 Urological diseases	NS-580 • Chronic prostatitis / Chronic pelvic pain syndrome • Endometriosis		

All researchers draft a proposal

At Nippon Shinyaku, we encourage everyone to make draft proposals, based on our policy under which the Discovery and Drug Efficacy Department fosters a culture where it becomes a matter of course for everyone to draft new research themes. Drafting a new research theme is the starting point of drug discovery, and if this process is neglected then it will not be possible to expand the R&D pipeline. "All researchers draft a proposal makes draft proposals" is an initiative that encourages all researchers at the Discovery and Drug Efficacy Department to take on the challenge of generating an idea once a year, instead of leaving everything only to the specialist researchers in charge of drafting work. Although of course there are differences between researchers in terms of age group, skill, and experience, everyone has the same determination to help patients in need and deliver drugs through their own efforts, which is the foundation of drug discovery.

To help researchers even with limited experience to put this determination into practice, we have established a department to manage the process from drafting to theme promotion in order to support idea generation. We have also established a framework that leads naturally to completion of the draft proposal by providing a list of the items that require consideration when drafting a proposal, which the researcher then fills in. It is thanks to our diverse human resources that we can generate diverse ideas as we pursue uniqueness, and through this friendly competition with each other, we aim to produce new drugs that are globally renowned.

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. 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 practice thorough IP-related risk management by conducting third-party 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 multiple patents. 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.

Understanding and analyzing intellectual properties

We conduct patent trend analysis and IP analysis of competitors in technical fields believed to be important for us over the medium to long term. In addition to early stage IP risk management, we can use this information in our R&D strategy and business strategies. Furthermore, the Group analyzes IP protecting its products and their surroundings to create opportunities for in-house R&D and business expansion, including strategic licensing.

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.

Medical Affairs

The mission of Medical Affairs is to identify unmet medical needs, generate medical and scientific evidence related to these needs, and communicate the information to medical professionals and patients. To deliver the most appropriate healthcare to all patients, we aim to optimize the medical value of our in-house pharmaceuticals to help improve patient benefits. To do this, we conduct exchanges with medical experts and patient organizations, and also hold various surveys, which help us to identify issues related to target diseases, such as the status of existing treatments and diagnoses, and collect information about our products that cannot be obtained from clinical trials alone. We formulate medical plans based on the collected information, and conduct evidence generation and disease awareness activities according to these plans.

*Unmet medical needs: These are medical needs that are not being met satisfactorily from the viewpoint of medical professionals or patients. For example, diseases that lack effective treatments, or the need for new therapeutic agents or treatments.

For patients

We are conducting various types of research, including non-clinical research, clinical research, database research, and registry research for our in-house pharmaceuticals as activities to generate evidence for treatment optimization. We have published numerous results from such research in conference presentations and academic papers. We have also collaborated with patient organizations to hold public seminars on hematological malignancies and muscular dystrophy, and plan other initiatives, such as gathering the opinions of patients and communicating them to society. In the future, we will continue to stay focused on patients and conduct pharmaceutical development that incorporates their opinions.