Glossary of Terms

Healthcare and Medicines	**Acute Myeloid Leukemia (AML)**	A disorder marked by an abnormal proliferation of immature myeloid cells. Normal hematopoietic function is impaired by unlimitedly proliferation of leukemia cells in the bone marrow, causing a variety of symptoms that include infectious disease and bleeding.
	Chronic Thromboembolic Pulmonary Hypertension (CTEPH)	A disorder whereby organized thrombi cause a occlusion in the artery leading from the heart to the lungs (pulmonary artery), leading to abnormally high blood pressure in the pulmonary artery. Clinical symptoms include shortness of breath during exertion.
	Dravet Syndrome	A rare, devastating and life-long form of epilepsy that generally begins in infancy or early childhood and is marked by frequent, treatment-resistant seizures, frequent resulting hospitalizations and medical emergencies, significant developmental and motor and behavioral impairments. Dravet Syndrome has been designated as an intractable disease by the Ministry of Health, Labour and Welfare, and there are estimated to be about 3,000 patients living with this disease in Japan.
	Duchenne Muscular Dystrophy (DMD)	A hereditary muscular disorder whereby dystrophin gene abnormalities cause a loss of dystrophin proteins, which protect muscle cell membranes. It is the most frequently occurring type of muscular dystrophy, occurring in one of every 3,500 newborn boys. It is identified by symptoms such as a tendency to fall and inability to walk quickly in children aged 2 to 5, with muscular atrophy and muscle strength deterioration following. Patients become unable to walk on their own before their early teens, require the use of a wheelchair, and generally die in their 20s or 30s from respiratory failure or heart failure.
	Exon Skipping	Restoring the open reading frame of amino acids via medications that use antisense oligonucleotides to remove (skip) certain parts of the mRNA region (exon) that are translated into proteins. This has the effect of generating functional proteins.
	Iron Deficiency Anemia	Anemia caused by iron deficiency and reduction of hemoglobin synthesis associated with excessive menstruation, post-partum hemorrhage in women, gastrointestinal bleeding, and poor absorption of iron through the intestinal tract and other relevant diseases. In addition to symptoms such as palpitations, shortness of breath, and easy fatigue due to anemia and spoon nails due to iron deficiency are also observed.
	Modality	A drug discovery method for therapies such as low-molecular weight compounds, peptide (medium molecule weight) drugs, and nuclear acid drugs.
	Myelodysplastic Syndromes (MDS)	Intractable diseases that carry a poor prognosis and very often lead to leukemia. The main symptoms are general fatigue caused by anemia, an increased susceptibility to infections due to a decrease in white blood cells, and bleeding tendency as a result of a decrease in platelet count.
	Nucleic Acid Drugs	Drugs that consist of nucleic acids, which make up genes, and target genes that cause of disease. These nucleic drugs work by either stopping or regulating the production of proteins from those genes. Referred to by many as next-generation drugs, they show promise for treating diseases that are difficult to treat with traditional low-molecular drugs.
	Pulmonary Arterial Hypertension (PAH)	A life-threatening disorder characterized by abnormally high blood pressure in the artery leading from the heart to the lungs. PAH has a variety of symptoms that begin with minor shortness of breath and fatigue during everyday activity, then restricted physical activities, eventually leading to death due to right ventricular failure.
Other	**Drug Price**	The price of a pharmaceutical paid to an insurance pharmacy or medical institution providing services covered by health insurance. What category a pharmaceutical can be used for as part of medical care, as well as prices, are determined by the Health, Labor and Welfare Minister.
	Patient Centricity	This is a concept which involves always putting the patient at the center, providing responses that are focused on the patient, and ultimately respecting the individual judgement of the patient to the maximum extent.
	PLCM	An abbreviation of Product Life Cycle Management. With new pharmaceutical development having become increasingly challenging, this is a means of improving the value of existing products by adding additional indications and dosage forms.
	Priority Review Voucher	A voucher issued by the FDA in the U.S. to incentivize new drug development for rare conditions affecting children (including tropical diseases), priority review vouchers grant the right to have a new drug designated for priority review at the time of application approval. These rights can also be traded.
	PRTR System	An abbreviation of Pollutant Release and Transfer Register. A PRTR is a system for tracking, aggregating, and publishing data about the extent to which various toxic chemical substances are released into the environment and are transferred off-site as part of waste, as well as the origin of these substances.

IR FAQ

Q1 Please explain President Nakai's three commitments in detail.

We aim to achieve further growth for the Company through three commitments: 1. Continue to launch at least one unique product each year on average, 2. Generate at least 50% of consolidated sales from overseas, and 3. Target at least 100% gains in sales and operating profit compared to FY2020.

Q2 How does the Company plan to generate at least 50% of consolidated sales from overseas?

Viltepso, a therapy for Duchenne muscular dystrophy (DMD), was launched in Japan and the U.S. in FY2020. To bring the drug to more places around the world, we are now taking steps aimed at gaining early approval in China, Europe, and other regions. Going forward, we will develop a pipeline for exon-skipping drugs that follow Viltepso and other globally developed drugs, and plan to increase the percentage of sales from overseas operations to at least 50% by 2030.

Q3 What are the factors that caused your forecast for FY2023 to fall short of the numerical targets of the 6th Five-Year Medium-term Management Plan?

The main reasons why the forecast for FY2023 fell short of the numerical targets of the 6th Five-Year Medium-term Management Plan are that the launch of Viltepso in the U.S. was delayed due to COVID-19 and that product sales in Japan decreased due to the introduction of off-year price revisions by MHLW.

On the other hand, we believe that long-term growth is possible through the development of new modalities, such as gene therapy, and pipeline items outside the DMD field, in addition to the nucleic acid drug group and cell therapy drug currently under development.

Q4 Please tell us about how you will overcome Uptravi's patent cliff.

The patent for Uptravi is expected to expire in October 2026 in the U.S. and April 2027 in the rest of the world. The patent expiration is expected to reduce both sales of Uptravi in Japan and overseas royalty income, but sales and profit growth are considered possible due to Viltepso's growth, nucleic acid drugs for DMD in development, CAP-1002, a DMD cell therapy, and the global launch of in-house developed products such as NS-580 and NS-018.

Q5 How do you plan to roll out nucleic acid drugs?

To provide drugs to as many DMD patients as possible, we are working to develop nuclear acid drugs beyond Viltepso. In addition, we are proceeding with research on peptide-conjugated nucleic acids, stereocontrolled nucleic acids, and novel sequence nucleic acids as next-generation antisense nucleic acids. In addition to DMD, we are also working on the development of NS-035 for patients with Fukuyama congenital muscular dystrophy.

Q6 What pipeline items are you focusing on going forward?

In the area of DMD, we are working on the development of nucleic acid drugs NS-089, NS-050, NS-051, exon 45 and exon 55 skipping drugs as follow-ons to Viltepso, and we believe that together these nucleic acid drugs will be able to treat about 40% of all DMD patients. In addition, the cell therapy drug CAP-1002, for which we entered into a distribution agreement with Capricor Therapeutics in the U.S. in January 2022, and in Japan in February 2023, is expected to enable us to treat DMD patients who have difficulty walking, which represents approximately half of them.

In addition, we are developing NS-018, a treatment for myelofibrosis, NS-580, a treatment for endometriosis, and NS-025, a treatment for urological diseases and other in-house products. We plan to carry out development of in-house products on a global basis.

Q7 What are your plans regarding corporate mergers and acquisitions (M&A)?

We will be constantly gathering and analyzing information about companies and venture firms in Japan and overseas, and will be thinking about possibilities for strategic partnerships (business and capital alliances) and M&A.

Q8 What steps are you taking with regard to sustainability?

To further promote sustainability within the Nippon Shinyaku Group, the "basic CSR policy" was revised to and became the "Nippon Shinyaku sustainability policy." Based on our business philosophy, we clearly state that we view addressing social issues as an important business issue and aim to realize a sustainable society. In addition, the Sustainability Committee, which is chaired by the President, reviews progress made toward establishing sustainability plans and achieving materiality targets, as well as progress made in carrying out initiatives involving issues of materiality, and reports and makes suggestions to the Board of Directors. The Board of Directors deliberates on and makes decisions about important matters.

Declaration of Authenticity

Takanori Edamitsu
Director, Business Management & Sustainability

Nippon Shinyaku has released integrated reports since 2012, with Integrated Report 2023 being the 12th release. The Company recently established "Helping People Lead Healthier, Happier Lives" as the foundation of its business, and along the way to achieving sustainable growth, has developed innovative new drugs and functional foods that provide new value.

In our Integrated Report 2023, we redefined our stakeholders in terms of our business model and the value creation process based on it, looking to make it easier to understand who they are and Nippon Shinyaku's strengths. In addition, by linking issues of materiality to our business, we have tried to clearly show the path to solving these issues.

As the Director in charge of overseeing the production of this report, I attest to the legitimacy of the report production process and the accuracy of the information contained herein.

I hope that this Integrated Report 2023 will help you better understand our company. We will continue to refine this report and strive to make it a valuable resource for communication with our stakeholders.

August 2023