

Business Report for the 21st Year

Nobelpharma Co., Ltd.

[From January 1, 2023 to December 31, 2023]

Business Report

(From January 1, 2023 to December 31, 2023)

1. Nobelpharma

1.1 Corporate Mission, Policies, Code of Conduct

Corporate Mission

The company conducts its business activities under its corporate mission, “to contribute to society by providing critical but neglected pharmaceuticals and medical devices”.

Although sales and profits are important management indices that should be pursued, the company considers them to be a means for executing the corporate mission and the result of executing the corporate mission.

The management policy, behavioral standards, and request to line managers (Attachment) are indicated below. The management policy, behavioral standards, and request to line managers (Attachment) were partially changed (underlined) in January 2023 to reflect the fact that working from home has been routine since 2020. In over 20 years in business, we have seen changes in our personnel lineup, but all the while we have consciously maintained a commitment to upholding this corporate mission.

Policies

1. General

- 1) Give priority to legal and ethical compliance in the course of business--never prioritize loyalty to company over morals.
- 2) Share our Mission, Policies and Code of Conduct among all stakeholders (employees, shareholders, officers)
 - * They cannot be shared unless they can repeatedly be invoked on a regular basis.
- 3) Pursue evolution of the Company, yet becoming larger is not our main goal
- 4) Aim to be a company that lasts 100 years while protecting its mission
- 5) Ensure transparency and disclosure
- 6) Launch business overseas

2. Personnel

- 1) Value employees and families, and respect self-development
- 2) Employ the principle of “select few*,” and create an environment where they can enjoy working
 - * The “select few” are those who have knowledge and experience, think for themselves and act on their own, and are passionately devoted to working.
 - * The select few are recognized irrespective of gender, age, nationality, religion, or preference
 - * Each member of the select few has an independent character and treats others with respect
- 3) Value suggestions and opinions from employees

3. Products

- 1) Pursue high-quality products and data
- 2) Ensure post-marketing safety
- 3) Search for product seeds externally

4. Capital

- 1) Profits are a result of and means of achieving the Mission
- 2) Focus on higher return on sales/profits per employee
- 3) Keep in mind the disadvantages of failure--not the assumption of success--when making investment decisions

- 4) Profits are distributed to shareholders (dividends*), employees, and internal reserves
 - * dividends: 1/3 of profits after tax
 - * employees: not to exceed dividends
- 5) Invest asset only with a principal guarantee

Code of Conduct

1. Principle:
When in doubt, the patient benefit takes priority
2. Our Challenges:
 - 1) YMWS: “**Yatte** **Minakucha** **Wakaranai**, shikashi **Songiri** wo tamerauna” = You never know how it will turn out unless you try, but do not hesitate to cut losses”
 - 2) ZY: “**Zenrei** ga nainara **Yattemiru**” = Even if there is no precedent, be the first to try it
3. Speed:
 - 1) Never forget patients are waiting
 - 2) Be unafraid to buy time
 - 3) Without worrying about possible delays, set a challenging deadline (day, month, and year) intuitively to begin with, and do not give up easily, but persist in attempting to realize and achieve it
 - * Stay away from “approximately/around” and “early/late ~,” etc.
 - * Loose deadlines focused on immediate concerns are not the smart way. Decide on a concrete goal in advance.
 - * “Wait-and-see” is a waste of time
 - 4) If problems or mistakes occur, prevent their expansion first before preventing reoccurrence
 - 5) Speedy decisions by managers who have authority over ○ million-yen projects
 - * For the time being, ○ million = 10 million for Division Manager; 3 million for Department/Branch Manager/PM/PL
4. Cost/Efficiency:
 - 1) Never take or lead to wasteful actions
 - 2) Zero overtime work, working from home, and using up accumulated leave are considered optimal
 - 3) Consider patient needs, scientific rationality and laws/regulations when pursuing higher quality in products/data
 - 4) As a general rule, competitive quotes should be obtained from at least △ companies for projects valued at ○ million yen or more, and in certain cases, multiple purchases should be made
 - * For the time being, ○ = 1, and △ = 2 (for from 1 million yen to less than 3 million yen) or 3 (for 3 million yen or more)
5. Communications/Relationship:
 - 1) Embrace inter-departmental advice and cooperation—hiding in silos is a symptom of “Big Company” Disease
 - 2) Courageously state the opinion you think is correct, and do not choose your words while trying to gauge your superior’s reaction
 - 3) Confidently entrust tasks to subordinates, but never leave them unmanaged
 - 4) Hear anyone out--never interrupt in the middle
 - 5) Start with the conclusion/result when explaining/responding
 - 6) Greetings may seem small, but they are important

1.2 Noteworthy Points in 2022

1.2.1. Domestic sales

- As a result of various factors, actual sales fell far short of our sales plan (23,100 million yen vs. 29,800 million yen). One big reason for this was that our plan erred on the timing for the launch for a generic version of our key product NOBELZIN®. Later, market share for our NOBELZIN® Family rallied with the launch of the AG (authorized generic), and we plan to connect this momentum to the new drug ZINTUS®.
- We set a very ambitious target for MELATOBEL® (4,300 million yen), which we consequently fell short of (2,900 million yen), but adoption of this product at the front lines of medicine is still proceeding smoothly. We think that this also reflects the fruits of our collaboration with the Medipal Group.
- The 3 sales department, 12 area system we had maintained until FY 2023 has changed to a 2 sales department, 8 area system effective FY 2024. Moreover, in FY 2024, we have made a big shift in MRs' information provision activities by dividing them into 2 parts: [1] information provision activities mediated by MRs (PUSH products) and [2] information provision activities that are not mediated by MRs (PULL products). PUSH products concentrated on activities targeting key doctors, while PULL products deploy information provision activities efficiently with most of the activities being conducted by SCs (special coordinators).

1.2.2. Overseas development/overseas sales

- US sales of NPC-12G (Japanese product name RAPALIMUS® Gel), a new drug for the treatment of facial angiofibroma accompanying tuberous sclerosis, showed disappointing growth following the 2022 launch. If our US subsidiary were to go into the red, it would have an adverse effect upon the entire Group. Therefore, the Japanese head office has begun to support its subsidiary in increasing sales and cutting expenses aiming a radical improvement since January 2024.
- RAPALIMUS® Gel was approved in China in March 2023, in the EU in May 2023, and in England in September 2023, and it went on sale (commissioned sale) in England and Germany in October and in China in December. The Chinese trademark for this drug is 纤洛丽 ("Xian Luo Li"), and the trademark in the EU and US is HYFTOR.
- We are promoting and preparing for development of TITANBRIDGE® (NPC-17) and RETYMPA® (NPC-18) in the EU and US and NOBELZIN® (NPC-02), MELATOBEL® (NPC-15), and JEMINA® (NPC-16) in China as our product lineup to follow RAPALIMUS® Gel. In February 2024, NPC-02 was approved for Wilson's disease in China.

1.2.3. Production

- We deeply regretted the supply shortage of MELATOBEL® Granules and NOBELZIN® Granules in 2022, which greatly inconvenienced the patients and everyone at the medical institutions. In response, we constructed a solid system for providing a stable supply of both products by increasing our production facilities, etc., in 2023. On the other hand, sales conditions were such that this resulted in overproduction, and the following loss on abandonment is expected.

MELATOBEL® Granules: 542 million yen (2024)

NOBELZIN® Granules: 182 million yen (2025)

- Based on the occurrence of these kinds of situations, we have reconstructed our internal system to more accurately forecast the demand-supply balance.
- Moreover, full-fledged export of products overseas began in 2023, and we have constructed a system for supplying each of the US, EU, and China smoothly. As a result, we realized a stable supply for all of our products both within Japan and overseas in 2023.

- As for the 4 new products for which we expect to obtain approval in 2024, we plan to exercise strict management to maintain a stable supply and ensure appropriate levels of inventory.

1.2.4. Medical Division

- The Medical Division was newly established in April of 2023, and the following form the foundation of its activities.
 - (1) Post-marketing drug development: promoting and supporting clinical research through investigator-initiated trials and joint research
 - (2) Promotion of Patient Centricity: conducting patient hearings and creating SOPs for interactions with patients
 - (3) Creating medical plans based on Patient Insights and Doctor's Insights
 - (4) Considering clinical research on HYFTOR in collaboration with NPA

1.2.5. Human Resources

- The number of employees in Japan decreased by 6 from 382 in 2022 to 376 in 2023 (both as of the end of December). Total personnel expenses decreased slightly from 3,552 million yen (including personnel expenses for R&D and excluding 980 million yen allocated to the retroactive portion of the Managing Director and CEO's retirement benefit) to 3,401 million yen.
- The average overtime hours and rate of leave taking were favorable at 2.25 hours per month and 78.3%.
- The average age is 53.7 and the average length of service is 5.8 years.
- We are promoting optimization of the Sales & Marketing Division's personnel.
- We now have 34 overseas employees in the US, 12 in China, and 16 in the EU (as of the end of December 2023).
- With the downgrading of COVID-19 to a Category V infectious disease, the remote work system that was initiated in March 2020 will be maintained, but we will continue to take the following measures introduced last year to promote communication and increase consciousness of being a member of the company. Additionally, targets for the frequency of physically reporting to work at the company were set for each department in November 2023. As a result, the average attendance rate was 20.7%, up from 12.7% in 2022 (both as of December).
 - Management conferences and meetings of executive officers are live in-person events. Executive Officers and General Managers must be physically present at the meetings (mandatory).
 - An all-employees meeting will be held at least once a year, and everyone must be physically present (mandatory).
 - All-employees meetings will be held at the division unit level at least once a year, and everyone must be physically present (mandatory).
 - The Board of Directors meetings and shareholders' meetings will be held as in-person meetings.
 - 1 on 1 meetings will continue to be held, and it is recommended that they sometimes be held in person.
 - Evaluation interviews will be held in person (mandatory).
 - In recruitment, at least the final interview will be held in person, and the initial recruitment interview will be held in person if possible.
 - Training for new employees will be conducted in person (mandatory).
 - If there are new employees, in-person lunch meetings should be held at the division and department levels, etc. (mandatory).
 - The head office will hold a buffet-style home party once a month.
 - Quarterly explanatory meetings will continue to be held online.

- We will introduce a system that allows employees to build relationships with other employees freely, outside of work, through a mixture of online and in-person involvement in hobbies, sports, and interests. Financial support to cover the cost of activities will be considered.

	mil yen		Year-on-year (%)	% to total sales	
	2022	2023		2022	2023
Sales *	21,204	19,027	89.7%	100.0%	100.0%
Cost of goods sold	2,698	3,455	128.0%	12.7%	18.2%
Gross profit	18,506	15,572	84.1%	87.3%	81.8%
SG&A expense *	14,706	12,925	87.9%	69.4%	67.9%
Personnel expenses *	3,634	2,365	65.1%	17.1%	12.4%
R&D expenses *	5,892	5,479	93.0%	27.8%	28.8%
Operating income	3,799	2,646	69.7%	17.9%	13.9%
Non-operating income/expenses	149	162	108.9%	0.7%	0.9%
Ordinary income	3,948	2,809	71.1%	18.6%	14.8%
Extraordinary income/loss	-30	-	-	0.0%	-
Net income before tax	3,918	2,809	71.7%	18.5%	14.8%
Income taxes	1,217	730	60.0%	5.7%	3.8%
Net income	2,701	2,078	76.9%	12.7%	10.9%
Net income per employee ('000 yen)	7,070	5,527			
Retained earnings brought forward					
Beginning balance	8,868	10,979			
Dividend	590	396			
Net income	2,701	2,078			
Ending balance	10,979	12,661			

1.3. Progress and Results of Operations

* Personnel expenses and R&D expenses are major items included in SG&A expenses.

* Personnel expenses did not include those of R&D, and R&D expenses included personnel expenses of R&D.

With the launch of generic versions of key products during the term (FY 2023), etc., total sales decreased to 15,572 million yen (down 2,933 million yen year-on-year), but thanks to decreases in the personnel expenses component of the SG&A expense, as well as a decrease in development expenses owing to an overhaul of the R&D project plan, we were able to secure ordinary income of 2,809 million yen (down 1,139 million yen year-on-year).

The details are as follows.

Total sales came to 19,027 million yen (YoY 89.7%). The NOBELZIN® family (NOBELZIN®, NOBELZIN® Granules, NOBELZIN® AG) and dysmenorrhea (LEP) family (LUNABELL® LD, LUNABELL® ULD, JEMINA® and FREWELL®) posted sales of 9,396 million yen and 4,605 million yen, respectively, accounting for 49.6% and 24.3%, respectively, of total product sales. Overseas export sales came to 157 million yen.

The cost of goods sold was 3,455 million yen including valuation loss of 923 million yen for products and raw materials (YoY 128.0%), accounting for 18.2% of total sales. Selling, general and administrative expenses totaled 12,925 million yen (YoY 87.9%), accounting for 67.9% of total sales. The main components were personnel expenses of 2,365 million yen (YoY 65.1%), accounting for 12.4% of total sales; R&D expenses of 5,479 million yen (YoY 93.0%), accounting for 28.8% of total sales; sales promotion expenses of 1,394 million yen (YoY 90.6%); and outsourcing expenses of 1,726 million yen (YoY 99.0%). Sales promotion expenses mainly included 881 million yen in sales commissions, etc. (YoY 97.9%) on NOBELZIN® and JEMINA® to ASKA Pharmaceutical Co., Ltd., etc.

The major decrease in personnel expenses was owing to lump-sum allocation of 980 million yen to the retroactive portion of the Managing Director and CEO's retirement benefit in the previous fiscal year.

Outsourcing expenses mainly included 320 million yen for business management services and indirect department operations outsourcing to Hisanaga & Co. Ltd., 188 million yen as the commission for safety information processing support operations, etc. by CMIC, 151 million yen to Mebix, Inc., for specific clinical research, and 100 million yen for royalties on Medichat, etc. by Medipal Holdings Corporation.

As a result, operating income was 2,646 million yen (YoY 69.7%), and it accounted for 13.9% of total sales.

Ordinary income was 2,809 million yen (YoY 71.1%), accounting for 14.8% of total sales, after recording non-operating income of 296 million yen including subsidy income of 137 million yen, interest income of 64 million yen from loans to subsidiaries, and currency exchange profit of 51 million, with non-operating expenses of 134 million yen including payment interest of 45 million yen, loss on revaluation of investments in securities of 66 million yen, and bond interest expenses of 9 million yen.

With income taxes of 730 million yen, net income was 2,078 million yen (YoY 76.9%), accounting for 10.9% of total sales, and net income per employee was 5 million yen (previous year: 7 million yen).

Retained earnings brought forward as of December 31, 2023 were 12,661 million yen, with the beginning balance of retained earnings brought forward of 10,979 million yen and a dividend payment of 396 million yen.

Foreign subsidiaries (reference)

Results in FY 2023*	mil yen				
	Nobelpharma America LLC	Plusultra pharma GmbH	Plusultra pharma UK Limited	Jiangsu Nobelpharma Co., Ltd.	Total
Sales	1,124	33	-	34	1,191
Operating income	-1,046	-292	-143	-199	-1,680
Current income	-1,109	-292	-143	-197	-1,741
Retained earnings	-4,803	-743	-333	-502	-6,380

* Figures for overseas subsidiaries were converted at the exchange rate for the local currency as of the end of 2023.

Overseas subsidiaries in China, the EU, and England were able to obtain approval for “HYFTOR” in 2023 after the North American subsidiary in the preceding year, and 2023 became the year in which our company began full-scale overseas sales, which has been its goal since its founding.

Results for US sales came to 1,124 million yen (preceding year's sales: 129 million yen), however, falling substantially short of initial expectations.

The US company is now working upon improvement measures with the head office in Japan to deal with this situation as soon as possible.

Other bases had operating losses, as launch in the latter half of the year made it impossible to achieve sales that exceeded expenses, but from FY 2024 forward, they are expected to secure profits year after year, as described in the Mid-Term Five Year Plan.

1.4. Domestic sales

The table below shows sales by product in 2023 on a wholesale price (NHI price) basis.

Area	Brand Name	Launch	Indication	Sales (on a wholesale price (NHI price) basis) (Yen in millions)		Year-on-year (%)
				2022	2023	
Obstetrics and Gynecology Family	LUNABELL® LD	July 2008 September 2013	Dysmenorrhea	2,721	2,060	80.9
	LUNABELL® ULD					
	JEMINA®	October 2018	Dysmenorrhea	3,880	3,938	101.5
	FREWELL® LD FREWELL® ULD	December 2018	Dysmenorrhea	4,835	4,094	93.3
Subtotal				11,436	10,091	88.2
Pediatric Family	NOBELBAR®	December 2008	Neonatal convulsion, status epilepticus	119	112	94.2
	INDACIN®	January 2013	Patent ductus arteriosus of prematurity	44	34	78.6
	COSMEGEN®	January 2013	Wilms' tumor, choriocarcinoma, pediatric solid malignant tumor, etc.	26	31	120.6
	Respia®	December 2014	Apnea of prematurity	215	212	98.4
	Melatobel®	June 2021	Sleep-onset difficulty associated with neurodevelopmental disorder in children	1,939	2,878	148.4
Subtotal				2,342	3,267	139.5
NOBELZIN® Family	NOBELZIN®	April 2008 March 2017	(Wilson's disease), hypozincemia	15,358	13,227	86.1
Subtotal				15,358	13,227	86.1
Neurosurgery Family	Fostoin®	January 2012	Status epilepticus, prevention of postoperative seizures, etc.	914	914	100.0
	Alabel®	September 2013	Diagnosis of malignant glioma	295	318	107.8
Subtotal				1,209	1,232	101.9
Respiratory Family	Unitalc®	December 2013 March 2022	Prevention of recurrent malignant pleural effusion Secondary intractable pneumothorax that is difficult to treat with surgery	79	83	104.9
	RAPALIMUS®	December 2014 September 2021	Lymphangioliomyomatosis Refractory lymphatic disease (lymphatic malformation, lymphangiomatosis, Gorham's disease, lymphangiectasia)	576	709	123.0
Subtotal				656	792	120.8
Otolaryngology Family	TITANBRIDGE®	July 2018	Adductor spasmodic dysphonia	7	21	294.6
	RETYMPA®	December 2019	Tympanic perforation	100	104	103.5
Subtotal				107	125	116.2
Other Drug Families	ZANOSAR®	February 2015	Gastroenteropancreatic neuroendocrine tumor	256	201	78.6
	RAPALIMUS® Gel	June 2018	Skin lesions associated with tuberous sclerosis	377	372	98.8
Subtotal				633	574	90.6
Total				31,741	29,308	92.3

FY 2023 was a year in which the launch of the generic version of key product NOBELZIN® in August had a major effect on results. As for MELATOBEL®, another key product, the spreading effect to areas where efforts were made to develop bases centered around pediatric specialists created a situation in which it was possible to deliver MELATOBEL® to many patients. Moreover, a team system was introduced for sales activity in FY 2022, and it became well established in FY 2023. MR activities, owing in part to the “reform of doctors’ work styles”, have shifted further from real face-to-face meetings to online meetings, and consequently, we are now in an era of rapid and efficient utilization of digital (DX) technologies. Sales amounted to 29.31 billion yen in FY 2023 (YoY 92.3%), compared with the sales target of 31.75 billion yen (on a wholesale price (NHI price) basis). The reason why we did not reach our sales target was that sales switched from the original NOBELZIN® to the generic version that was introduced to the market in August 2023. In FY 2024, we plan to launch 4 new products (including additional indications). Our activities will aim to introduce the new products to the market early on and promote the further growth of MELATOBEL®.

1.5. Research and Development (Japan and overseas)

Domestic Development

Among the 4 products for which approval applications were filed in FY 2023 (NPC-12, NPC-25, NPC-09, and NPC-26), RAPALIMUS (NPC-12, for intractable vascular tumor and intractable vascular malformation), on which we worked jointly with Gifu University, was approved in January 2024. Moreover, we expect to receive approval in March 2024 for all of the following: zinc histidine hydrate (NPC-25) for the indication of hypozincemia, aceneuramic acid (NPC-09) for the indication of progressive muscle weakness in GNE myopathy, and sargramostim (NPC-26) for the indication of autoimmune pulmonary alveolar proteinosis. On the other hand, development has been discontinued for NPC-06, a drug for acute phase herpes zoster pain, as a life cycle management product, because it was not possible to verify a significant difference from placebo in the phase III study. Moreover, in the Phase II joint study conducted in Japan and the United States on NPC-21 for CMV infection, the expected results were not obtained for the primary endpoint. However, since results indicating that a certain degree of efficacy could be expected for the secondary endpoint have been obtained, we plan to formulate our future development plan by May 2024 while confirming the opinions of experts and the regulatory authorities.

What is more, we decided upon development themes for 3 new products (NPC-29, NPC-30, and NPC-31) by January 2024, and we are conducting clinical studies in collaboration with various partners, as well as preparing for next-phase studies. While reflecting upon the reasons why we did not succeed in the aforementioned efforts, we aim to proceed with development carefully and rapidly.

Overseas Development

RAPALIMUS® Gel (NPC-12G) was approved first in the US in March 2022 and then in China in March 2023, in the EU in May 2023, and in England in September 2023. Moreover, NPC-02 (Japanese product name: NOBELZIN®) was approved in China in February 2024 for the indication of Wilson’s disease. In addition, an application for approval of NPC-15 (Japanese product name: MELATOBEL®) in China for the indication of sleep-onset difficulty associated with neurodevelopmental disorder in children was submitted in January 2024.

The table below summarizes the development stage, expected NDA and market size classification in the three categories of A. New Drugs and Medical Devices, B. Life Cycle Management (LCM) and C. Overseas Development in the development pipeline as of March 1, 2024. Overseas Development as of

March 1, 2023. Many are drugs based on new concepts that originated in Japan. Market size classification is as follows:

- I: Potential primary sources of revenue (sales of over 3 billion yen)
- II: Short term approval and marginal profit are expected; however, they are not likely to be a primary source of revenue.
- III: Projects originating in academia, such as business-university collaboration, where short term approval is expected. Lower development cost with promising public subsidies. Difficult to estimate sales due to innovative concepts.
- IV: Similar to III but relatively long time required for approval.

A. New Drugs and Medical Devices (including global simultaneous development products)

	Compound	Indication	Licensor	Development stage	Estimated approval	Classification
1	NPC-25 Zinc histidine hydrate	hypozyncemia	In-house	Application pending	March 2024	I
2	NPC-09 Aceneuramic acid	Progressive muscle weakness in GNE myopathy	In-house	Application pending	March 2024	II
3	NPC-26 Sargramostim	Autoimmune Pulmonary alveolar proteinosis	Partner Therapeutics Inc.	Application pending	March 2024	II
4	NPC-22 Scopolamin	Hypersalivation	Kitasato University	In preparation for PII/III	March 2027	I
5	NPC-21 Anti-CMV antibody	CMV infection	Evec Inc.	PII	TBD	I
6	NPC-29 Ubiquinol	Multiple system atrophy	University of Tokyo	PII	TBD	I
7	NPC-30 (GAIA-102) High-activity NK-like cells	Neuroblastoma	Gaia BioMedicine Inc. Kyushu University	PI	TBD	III
8	NPC-31 P092 maleate	Prion disease	Gifu University	In preparation for PI	TBD	III

B. Life Cycle Management (LCM) (including global simultaneous development products)

	Compound	Indication	Licensor	Development stage	Estimated approval	Classification
1	NPC-12 RAPALIMUS®	Intractable vascular tumor/ vascular malformation (new indication)	Gifu University	Already approved	Jan 2024	II
2	NPC-06 Fostoin®	Neurology area (new indication)	Pfizer Inc.	PIII	March 2026	II
3	NPC-18 RETYMPA®	Regeneration of external auditory canal (new indication)	Kaken Pharmaceutical	PIII	March 2026	IV
4	NPC-12 RAPALIMUS®	Epilepsy with focal cortical dysplasia type II (new indication)	Showa University	PIII	June 2026	IV
5	NPC-12 RAPALIMUS®	Pendred syndrome (new indication)	Keio University	PII	TBD	III

6	NPC-12 RAPALIMUS®	Primary immunodeficiency syndrome (new indication)	Tokyo Medical and Dental University	PII	TBD	IV
7	NPC-12 RAPALIMUS®	Systemic sclerosis (new indication)	Oita University	PI/II	TBD	IV
8	NPC-12G RAPALIMUS® Gel	Skin lesions due to vascular abnormality (new indication)	Wakayama Medical University	In preparation for PIII (Global joint study)	TBD	I
9	NPC-15 Melatobel®	Mild cognitive impairment / mild sleep-onset difficulty in dementia (new indication)	In-house	PII	TBD	I
10	NPC-15 Melatobel®	Xeroderma pigmentosum (new indication)	Kobe University	PII	TBD	IV
11	NPC-26 Sargramostim	Pulmonary non-tuberculous mycobacteriosis (new indication)	Niigata University	PII	TBD	I

C. Overseas Development

	Compound	Indication	Licensors	Development stage	Estimated approval	Classification
1	NPC-12G (RAPALIMUS® Gel)	Angiofibroma	-	EU: Already approved England: Already approved	May 2023 September 2023	I
				China: Already approved	March 2023	
2	NPC-02 (NOBELZIN®)	Wilson's disease	-	China: Already approved	February 2024	II
3	NPC-15 (MELATOBEL®)	Sleep-onset difficulty associated with neurodevelopmental disorder in children	-	China: Filed	January 2025	I
4	NPC-17 Thyroid cartilage fixation device (TITANBRIDGE®)	Adductor spasmodic dysphonia	-	US: Clinical trial in preparation	TBD	III
				Europe: CE marking in process	April 2025	
5	NPC-16 (JEMINA®)	Dysmenorrhea	-	China: in preparation for PIII	June 2028	I
6	NPC-18 (RETYMPA®)	Tympanic perforation	MEEI/ Harvard/ NY University	US: PII	TBD	III

1.6. Funding and Major Lenders

In 2023, the Company borrowed 1,350 million yen, and repaid 523 million yen to financial institutions.

As a result, as of the end of December 2023, the balance of loans payable and bonds was 10,010 million yen, and the balance of cash and deposits was 8,638 million yen.

As of December 31, 2023, the status of borrowing is as follows:

Loans payable

Mizuho Bank, Ltd.	4,450 million yen
Sumitomo Mitsui Banking Corporation	850 million yen
MUFG Bank, Ltd.	1,150 million yen
Resona Bank, Ltd.	400 million yen
The Bank of Yokohama, Ltd.	100 million yen
The Shoko Chukin Bank, Ltd.	812 million yen
The Tokyo Shinkin Bank	100 million yen
Japan Finance Corporation	47 million yen
Total	7,909 million yen
Japan Agency for Medical Research and Development	551 million yen

Corporate bond

2nd straight bond	Osaka Soda Co., Ltd.	500 million yen (maturity date: Dec. 2024)
7th straight bond	Resona Bank, Ltd.	300 million yen (maturity date: May 2026)
8th straight bond	Resona Bank, Ltd.	150 million yen (maturity date: Mar. 2027)
9th straight bond	Sumitomo Mitsui Banking Corporation	500 million yen (maturity date: Mar. 2027)
10th straight bond	Resona Bank, Ltd.	100 million yen (maturity date: Mar. 2028)
Total		1,550 million yen

1.7. Financial Results, Assets, 2023 Forecast, and Development Schedule

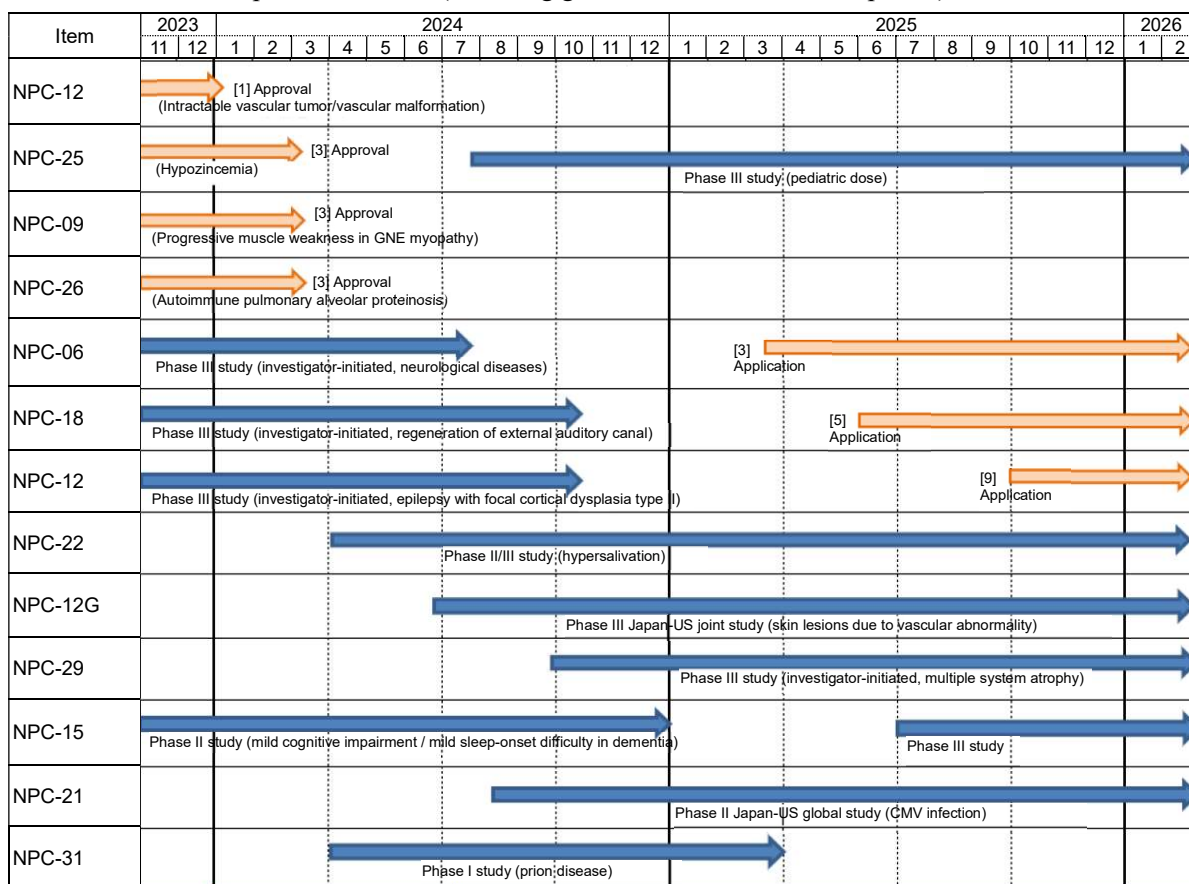
The Company's financial results, assets and next year forecasts are as follows:

In the current term (FY 2024), there are some factors that will augment earnings, such as a major increase in shipments of key product MELATOBEL® and launch of 4 new products. However, we expect both income and profits to decrease, reflecting the major impact of the launch of the generic version of NOBELZIN® in 2023. Among overseas subsidiaries, those in the US and EU are expected to show a profit in the next term. In the US, we are preparing to take action if necessary while monitoring the risk of a downturn in sales. In China, the aim is to turn a profit in 2025, including lump-sum payments accompanying sales contracts.

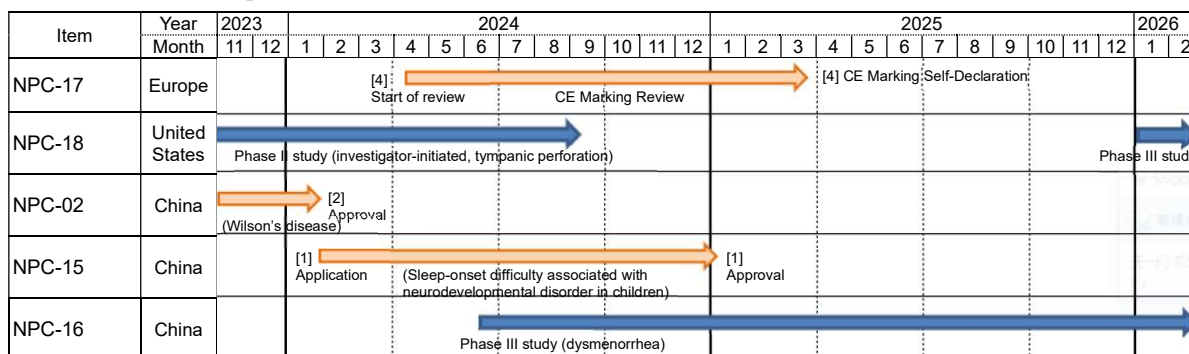
Mil yen except for *	2020 (Results) 18th year	2021 (Results) 19th year	2022 (Results) 20th year	2023 (Results) 21st year	2024 (Estimate) 22nd year
Sales	16,929	20,741	21,204	19,027	15,943
Ordinary income	3,466	4,747	3,948	2,809	-1,056
Net income	2,511	3,551	2,701	2,078	-585
* Net income per share	185,000	262,000	199,000	153,000	-43,000
Total assets	18,574	23,008	27,679	28,806	26,280
Net assets	7,052	10,094	12,205	13,887	13,717
* Equity ratio	38.0%	43.9%	44.1%	48.2%	52.2%
* Net assets per share	521,000	746,000	902,000	1,026,000	1,014,000

“Accounting Standards for Revenue Recognition” (Accounting Standards for Corporations No. 29; March 31, 2020), etc., were applied starting at the beginning of the previous fiscal year (FY 2022).

A. Domestic Development Schedule (including global simultaneous development)



B. Overseas Development Schedule



1.8. Status of reexamination, pharmaceutical risk management plan, and quality control

Reexamination: We are handling reexamination for 3 products: JEMINA®, NOBELZIN® (low zinc), and ALABEL®. We received the results of the reexamination of JEMINA® (Category 1) in October. We applied for reexamination of NOBELZIN® (low zinc) in April, and in November we received the results of the GPSP on-site inspection and the compliance document inspection (“Pass”). The application for reexamination of ALABEL® was submitted in June.

Safety control: 4,138 adverse events were collected among Japanese cases (2022: 3,615 events) and 1,193 among overseas cases (2022: 2,336 events). Package insert precautions were revised for the

following 9 products: FOSTOIN®, NOBELBAR®, ALABEL®, RAPALIMUS® Tablets, RETYMPA®, ZANOSAR®, NOBELZIN®, INDACIN®, and JEMINA®.

Post-marketing surveys: The conditions for approval of ZANOSAR® (all-cases survey) were lifted in May. Case fixation has been completed for 2024 reexamination items RESPIA®, RAPALIMUS® Tablets, and ZANOSAR®, as well as for treatment outcome evaluation item TITANBRIDGE®.

Quality: A total of 160 quality information cases (complaints) were collected (2022: 142), and appropriate action was taken to investigate the cause and make improvements. Periodic GMP inspections were performed at 16 manufacturing sites, and changes in approval documents and licenses/certificates were handled appropriately.

Overseas expansion: The NPA PV system audit by the internal audit department was conducted while promoting the strengthening of the system as the global head of safety management. In addition, we upgraded the PV system in association with the launch of RAPALIMUS® Gel in the EU and China, following the US.

1.9. Status of Compliance

To “prevent legal and regulatory violations from occurring, and in the unlikely event that one does occur, [to] prevent it from expanding in scope”, we conduct the following activities: monitoring, information collection through the in-house whistle-blowing system, investigation of whistle-blowing cases and planning of corrective action, training on laws and regulations, etc., consultation on whether situations constitute violations of laws or regulations, and issuing of compliance reports. We are striving to make the system as accessible to employees as possible by giving the highest priority to protection of the whistle-blower in the handling of whistle-blowing cases. As new efforts, we also confirmed the compliance systems of new manufacturing subcontractors and began holding periodic meetings with the compliance divisions of subsidiaries in foreign countries.

In order to further accommodate the concept of risk-based quality assurance, the Clinical Quality Assurance Department is promoting more efficient and effective regulatory auditing methods. We will establish a system for PV audits in compliance with global PV regulations, improve staff education and training, reliably conduct PV audits based on the global audit plan, and establish audit functions to ensure the quality of computer systems related to GCP and PV functions.

Provision of sales information: Promotional materials, etc. are subjected to preliminary checks and approval, and sales information provision activities are monitored. We will explore a risk-based management system so that we can handle the annually increasing volume of materials.

1.10. Status of Administrative Departments

Management Planning: We will reexamine the system so that we can respond to emergencies resulting from the expansion of our business into new lines and the diversification of our operations. Moreover, regarding the generic versions of NOBELZIN® Tablets 25 mg and 50 mg for the treatment of Wilson’s disease (copper absorption inhibitor) and hypozincemia, we filed suit with Tokyo District Court on April 17, 2023 to demand an injunction against Sawai Pharmaceutical Co., Ltd., which obtained marketing approval on February 15, 2023, for infringement of patents held by Nobelpharma (Patent No. 6716464, Patent No. 6768984).

Accounting and Finance: We strive to quickly grasp our financial status, make appropriate management decisions on ever-changing situations, and increase the accuracy of accounting. In addition, we will focus on grasping and managing the revenue and financial condition of overseas bases.

DX Promotion: We will promote business reform through the application of digital technology while supporting business expansion from the IT side. We will also improve the IT environment of our overseas

bases and strengthen their cooperation with Japan. In 2023, we improved our information security related rules and implemented user education through e-learning. We also are continually making efforts to strengthen our system security.

Intellectual Property: Introduction of academia-initiated drug discovery stage projects is increasing, and we will build a strategic portfolio in cooperation with academic personnel in charge of intellectual property. In addition, we are striving to create a good intellectual property portfolio by ensuring that a Freedom to Operate (FTO) infringement search is conducted for each project. We also place importance on the enhancement of intellectual property education and are working to raise levels of understanding of intellectual property throughout the company through e-learning and invitation of external lecturers.

Public Relations: We will provide various kinds of information to establish our corporate branding inside and outside the company. We will also establish a website with information for children living with intractable diseases and carry out activities that are close to patients and parents.

We set the targets for the mid-long term future vision of sales and profit as an immovable high goal named North Star. In 2019, the numerical targets in 2023 as North Star in the 2019-23 mid-term business plan were sales of 50 billion yen and ordinary income of 10 billion yen. In 2023, we unfortunately failed to reach the numerical target for 2023 set as the “North Star”, but we will continue to aim for the North Star.

North Star	Target
Sales	50 billion yen
Ordinary income	10 billion yen

2. Current Status of the Company

2.1. Shares (as of December 31, 2023)

[1] Number of shares authorized		50,000 shares
[2] Number of shares issued	Ordinary share	13,525 shares
	Number of shareholders	3
[3] Status of Major Shareholders		
Hisanaga & Co., Ltd. (ordinary shares)		10,000 shares (73.9%)
Medipal Holdings Corporation (ordinary shares)		2,705 shares (20.0%)
Inabata & Co., Ltd. (ordinary shares)		820 shares (6.1%)

2.2. Share Warrant

2.2.1. Share warrant that is issued to and held by the Company’s executive officers as consideration for execution of their duties

Not applicable

2.2.2. Share warrant that is issued to and held by the Company’s employees as consideration for execution of their duties

Not applicable

2.2.3. Share warrant in issue

Not applicable

2.3. Corporate Executives

2.3.1. Management Reshuffle

(1) Directors and Company Auditors

As of March 28, 2024, the status of full-time and part-time directors is as follows:

Managing Director & CEO:	Jin Shiomura	
Director (part-time):	Nobukuni Taneya	(Outside Director, arara Inc.)
Director (part-time):	Takahisa Iizuka	(Executive Officer, Deputy General Manager of Business Development Division, MEDIPAL HOLDINGS CORPORATION)
Director (part-time):	Koichi Noda	(Executive Officer, General Manager, Financial Management Office, Inabata & Co., Ltd.)
Director (part-time):	Toshio Miyata	(M.D., Ph.D., President, Mih Clinic)
Director (part-time):	Georg Holländer	(Head of Department of Pediatrics, University of Oxford)
Director (part-time):	Takashi Kobayashi	(Representative Director, BioResource Innovation Hub in Kobe)
Audit & Supervisory Board Member (part-time):	Tomoyasu Toyoda	(Company Auditor, MEDIPAL HOLDINGS CORPORATION)
Audit & Supervisory Board Member (part-time):	Yasuhiro Kaga	(former Member of the Board of Directors, Managing Executive Officer of Mitsubishi UFJ Securities Holdings Co., Ltd.)

(2) Executive Officers

As of April 1, 2024, the status of executive officers and directors is as follows:

Vice President	Shigeki Shimasaki	(Head of Research & Development Division)
Senior Executive Officer	Arata Tabata	(Head of Business Development & Project Planning Division/External Relations Department Supervisor)
Senior Executive Officer	Hitoshi Yokoyama	(Head of Sales & Marketing Division)
Executive Officer	Toshiaki Okamura	(Head of Regulatory Affairs Division/Head of External Relations Department)
Executive Officer	Yoshihide Yamamoto	(Head of President Office)
Executive Officer	Kenji Shimizu	(Deputy Head of Research & Development Division/Head of Clinical Development Department 2)
Executive Officer	Yoshiki Yagi	(Deputy Head of Research & Development Division)
Executive Officer	Hitoshi Hasegawa	(Head of PMS Regulatory Compliance & Assurance Division/General Marketing Compliance Officer)
Executive Officer	Masanori Osakabe	(Deputy Head of Research & Development Division/Head of International Clinical Development Department/Head of Medical Device Development)
Executive Officer	Yoshiki Kida	(President & CEO, Nobelpharma America, LLC)
Executive Officer	Makoto Shiragami	(Head of Compliance Division/Head of Compliance Promotion Department)

Executive Officer	Masayoshi Onozaki	(Head of Global Business Development Division)
Executive Officer	Tetsuro Noguchi	(Head of Supply Chain & Manufacturing Division)
Executive Officer	Eijiro Akatsu	(Head of Administrative Affairs & Corporate Planning Division)
Executive Officer	Sachiko Ezoe	(Head of Medical Division)
Executive Officer	Hiromi Okatake	(Head of Legal/IP Management Department)
Executive Director	Masato Iwamoto	(General Manager of Supply Chain Management Department)
Executive Director	Atsunori Iwao	(General Manager of Quality Assurance Department/Quality Assurance Officer)
Executive Director	Masatomi Nemoto	(General Manager of Pharmacovigilance Department/Safety Management Officer)
Executive Director	Yasuo Suga	(Deputy Head of Sales and Marketing Division/Product Marketing Development 1 Supervisor)
Executive Director	Tsutomu Iwasa	(General Manager of West Japan Sales Department)
Executive Director	Yasuo Satake	(General Manager of Sales HR Development Department)
Executive Director	Takahiro Yamasaki	(President & CEO, Plusultra pharma GmbH)
Executive Director	Yumi Imai	(General Manager of PMS Regulatory Compliance Department)
Executive Director	Nobuyuki Sato	(General Manager of Digital Transformation Department)
Executive Director	Toru Yokoyama	(General Manager of Central/East Japan Sales Department)
Executive Director	Yukio Urasaki	(Head of BD/Project Planning & Development Division)
Executive Director	Yoshinobu Takahashi	(Deputy Head of Sales and Marketing Division/Product Marketing Development 2 Supervisor)
Executive Director	Rongzhe Jiang	(General Manager, Jiangsu Nobelpharma Co., Ltd.)
Executive Director	Hideki Matsuoka	(General Manager of HR & General Affairs Department)

2.3.2. Remuneration paid to directors and company auditors

Classification	Headcount	Amount paid
Directors	7	15,601,000 yen
Company auditor	2	3,300,000 yen
Total	9	18,901,000 yen

2.4. Matters related to accounting auditor

2.4.1. Name of accounting auditor

Deloitte Touche Tohmatsu LLC

2.4.2. Amount of remuneration, etc. for accounting auditor

Amount of remuneration, etc. for accounting auditor in the current business year: 16 million yen

(Note) This is remuneration, etc. for business stipulated by Article 2, Paragraph 1 of the Certified Public Accountants Act (Law No. 103 of 1948) and compensation for audit certification under the Companies Act.

2.4.3. Reasons that company auditor approves remuneration, etc. for the accounting auditor

The company auditor obtained necessary documents and received reports from the relevant department of the Company and the accounting auditor, and confirmed and verified the details of the accounting auditor's audit plan, the status of the execution of duties by the accounting auditor and calculation basis of estimated remuneration. As a result, the company auditor determined that the amount of remuneration, etc. for the accounting auditor was appropriate and approved it in accordance with Article 399, Paragraph 1 of the Companies Act.

2.4.4. Policy on decision to dismiss or not to reappoint accounting auditor

When the accounting auditor meets any of the items of Article 340, Paragraph 1 of the Companies Act, and when it is deemed to be difficult to carry out an adequate audit due to events that damage the accounting auditor's quality and independence, the company auditor may determine the details of a proposal on dismissal or refusal of reappointment of an accounting auditor to be submitted to a general meeting of shareholders.

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Revised on January 19, 2023 (underlined parts)

September 1 Postscript (commentary)

July 16, 2019

Managing Director and CEO

Request to Line Managers

Commentary We have many employees who have joined us mid-career and those with management experience have been appointed as line managers; accordingly, manager education has not been adequately provided. In 2019, when the company was evolving to a new stage, I thought it would be a good idea to offer some guidelines as to what line managers should be mindful of.

Just let me clarify that these guidelines are not meant to make an alibi or an excuse after something wrong happens, as is often the case in organizations these days. In order for a company of a certain size to operate functionally, it is necessary to maintain good human relationships, and for this reason we have created this. In addition, it is also a commandment to myself. However, please note that we are not necessarily saying that you have no qualification as line manager just because you cannot carry out these guidelines. The general aim is to encourage you to be conscious of and work towards these guidelines.

1. Review the Corporate Mission, Management Policies, and Code of Conduct periodically, to understand and take them deeply to heart.

Commentary The Corporate Mission is the meaning of our company to exist in society, or the life of the company, if you will. Talk about it from time to time with valued customers, contractors, business partners, and even with your family and personal friends outside the company. Then please internalize it and make it a part of you.

2. Be aware that your behavior is always being observed. The most unacceptable behaviors are those that appear to mix work and private matters.

Commentary The point is the “appearance” of mixing work with private matters. Even if you have no intention of mixing work with private affairs, the behavior is not acceptable as long as any member of the company perceives it as such. Keep in mind that even the littlest things tend to be taken as mixing.

3. It is when a job is tough (such as apologizing to a customer) that the manager should take the lead. Staff members respect courageous managers.

Commentary It is not just apologies to customers; making important decisions is also tough. Everyone has something they are not good at. It may be hard but showing your staff that you will not run away from any tough jobs is also an important duty of a line manager.

4. Do not create an impression of favoritism, such as having lunch/going out for drinks with a specific staff member (or even a group of staff members).

Commentary The point is creating “wrong impression.” Even if there is no intention, some staff members may take it as an act of favoritism. This is not to say that lunches with staff members are absolutely out of the question. They are OK as long as they do not give the impression of favoritism. On the other hand, let me point out to staff members that it is a common sense, in my opinion, to accept friendly gathering invitations from line managers “once in a while.”

5. Inviting a staff member of the opposite gender out for one-on-one lunch/drinks is not acceptable. Staff find it difficult to refuse, so it could be construed as harassment.

Commentary Such invitations are unacceptable. As staff are in the weaker position, they might be smiling outside and angry inside.

“Don’t straighten your cap under a plum tree (Don’t do anything that could be misconstrued, because when you raise your hand it might look as if you are trying to steal the plums.)” Of course, as long as it is not one-on-one, such invitations should be fine every now and then.

6. Do not hesitate to make amends for your wrongs (Analects of Confucius).

Commentary What this means is that everyone makes mistakes and acknowledging one’s own mistakes can be hard, yet we should have the courage to do just that. Words of Confucius from more than 2,000 years ago are convincing. The Analects of Confucius contain universal wisdom.

7. Do not point out other’s mistakes, nor boast of your own achievements (Nakane Tori).

Commentary Criticizing others and boasting about yourself can make you feel good. That is why we tend to do so without thinking. However, if we take these words to heart, it will curb such behavior. If you are not conscious of it, you will become mediocre person who has lost sight of the purpose of life. Staff will not respect someone like that.

Nakane Tori was a scholar from Japanese Edo Period who turned his back on fame and fortune to pursue a life of seclusion. This injunction was posted on the wall for all his students to see.

8. Managers should greet out loud when you come into or leave the office. Also, if the manager is quick with harmless jokes, the workplace becomes brighter. Puns are just fine.

Commentary Workplaces that have smile and laughter will raise efficiency and lower stress. I would ask line managers to take the lead in this regard. Greetings are something that shows “I have no hostility toward you.” Conversely, without greetings, the other person may feel bitterness in you.

9. Even in online meetings, it is a good idea for the manager to take the initiative to greet participants and break the ice with a joke. You should also call on people by name to encourage those who usually do not speak up to do so. Then be sure to listen to everyone’s opinions.

Commentary It is difficult for subordinates to speak up even if they have an opinion. The manager or moderator should exercise care to ensure that everyone participates.

To subordinates, I would say that it is common sense to show your face and participate in online meetings. Consider it your duty as a member of society.

10. Have one-on-one communication with your staff regularly and repeatedly under no influence of alcohol. The purpose of such talks is to listen to what your staff want to say.

Commentary It may be difficult, but the “regularly and repeatedly” is the important point. Talks over drinks are not very effective. In these one-on-one communications, if your staff member does 60% of the talking, it is successful. Be careful not to make it your one-man show.

11. Do it in private when giving lectures or in public when giving compliments.

Commentary This is advice that we all remember hearing at some point. Yet we tend to do just the opposite. Try to keep this in mind all the time.

12. There is nothing good to result by a heavy-handed order. The harsher the message, the more carefully you should express it.

Commentary In the pre-war Japanese army, high-handed orders and obedience through violence were commonplace. It is clear what the results have been.

13. Never reject a staff member's proposal on the spot. Listen first, then if necessary, leave a day or two before saying no.

Commentary It takes courage for staff to bring proposals to their managers. More often than not, they come forward with it after giving serious thoughts. Having more knowledge and experience than staff, line managers may think the proposals from staff are not so good. Even so, if you reject them on the spot, they will lose motivation. Conversely, if their proposals are given even a little praise, your staff will try even harder and come up with better proposals. It is also often the case that proposals that seem insignificant at first glance turn out to have some good points upon reflection.

14. There are times when you must give your staff instructions that are against their intent. At such times, strive to gain their understanding by carefully explaining the background and objective of your instructions. However, if they are still not convinced even after you have carefully explained three times, you may carry through with the instructions.

Commentary This is related to No. 12 above. People who understand and are convinced will show better performance. You may find it onerous, but if you make the effort to convince them, it will be more efficient in the end. If they still do not understand after explaining three times, you should direct them to do as you ask. That is not being high-handed.

15. If a staff member does not improve even after giving guidance five times, there is a strong chance that such member is not suited to that work. Making such staff understand this and recommending to transfer may be a thoughtful thing to do.

Commentary There is no guarantee that the current work is the best for the staff. Nor is there any guarantee that their current manager is the best for them. Even the company may not be the best fit for them. They might demonstrate their strengths better somewhere else. You should not give up easily, but if you have guided them carefully five times and they still have not improved, recommendation for a change will also be a kind consideration for them. However, the key point here is "having that staff understand," and you must not transfer them blindly.

16. Do not buy or sell the shares of related parties, either listed or unlisted.

Commentary This is an extra point. More than 3,600 companies in Japan have their shares listed on the stock exchange, so if you want to invest in shares, you should do so in companies that are not related to your work, either directly or indirectly. Even just being suspected of conducting insider trading can be troublesome. This is another of those "don't tie your shoelaces in a watermelon patch (lest you be thought of as a watermelon thief)" lessons.

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