

# **Business Report for the 20th Year**

**Nobelpharma Co., Ltd.**

[From January 1, 2022 to December 31, 2022]

# **Business Report**

[From January 1, 2022 to December 31, 2022]

## **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 policies and code of conduct are indicated below. Since 2020, the management policy, behavioral standards, and request to line managers (Attachment) have been partially changed (underlined) to reflect the fact that working from home is now routine.

#### **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 From the calm inland sea to the raging open sea

- We recognize that 2023 will be the year when our company leaves the calm inland sea behind to row out into the raging open sea. In 2023, generic versions of our existing major products will enter the market. We expect our extensive internal and external pipelines to generate new drug sales, but although promising, this too is fraught with difficulty, and rough waves await us. Marketing overseas is no easy

matter. Both internal and external executives and employees are prepared to pull together and “grin and bear it” as we strive to surmount these waves.

- In order to ride these rough waves, we will need to reduce baggage above the waterline and lower our center of gravity. This is truly a case of 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”) as defined in our Code of Conduct.

#### 1.2.2 Overseas development/overseas sales

- In March 2022, we received approval for a new drug for the treatment of facial angiofibroma associated with tuberous sclerosis (RAPALIMUS® Gel) in the United States, and we released it to the market under the trade name of HYFTOR™ in August 2022. HYFTOR™ is our first product to be approved overseas. It was supported by the SAKIGAKE fast-track review system in Japan.
- We plan to obtain approval and launch the product in Europe in 2023. In China, we plan to obtain approval in 2023 and launch the product in 2024.
- We are promoting and preparing development of TITANBRIDGE® (NPC-17) and RETYMPA® (NPC-18) in Europe and the United States and NOBELZIN® (NPC-02) and MELATOBEL® (NPC-15) in China as our product lineup to follow RAPALIMUS® Gel.

#### 1.2.3 Production

- Insufficient manufacturing capacity for MELATOBEL® Granules has continued to limit our shipment volume, causing major problems for patients and medical institutions and a significant hurdle to doing business. In addition, although NOBELZIN® Granules was listed in the NHI price list in May 2021, the release was delayed until February 2023 for the same reason, leading to a similar situation. Elsewhere, there were obstacles to arranging for investigational products. The main cause of these problems is considered to be our business form as a company that outsources all manufacturing, but we do not plan to change our policy of not possessing any manufacturing plants. With this as our premise, we will make further efforts to strengthen our production system.
- We have begun investing in seed discovery through Nobelpharma Financial Co., Ltd., our company’s wholly owned subsidiary.

#### 1.2.4 Human Resources

- Work from home (WFH), which started in March 2020, has become routine.
- The average attendance rate was 12.7%, up from 5.4% in 2021 (both as of December). The average overtime hours and rate of leave taking were favorable at 2.0 hours and 75.0%.
- The number of employees in Japan increased by 12 from 370 in 2021 to 382 in 2022 (both as of the end of December). The main changes were a decrease of 11 people mainly owing to the return of employees who had been on loan to the Sales & Marketing Division, along with an increase of 12 people in the Research & Development Division / Project Planning & Development Division, and an increase of 11 people in the Supply Chain & Manufacturing Division. If we consider the time lag between joining and leaving the company, total personnel expenses remained at almost the same level (3,575 million yen compared to 3,552 million yen the preceding year, excluding 980 million yen allocated to the retroactive portion of the Managing Director and CEO’s retirement benefit).
- The average age is 53.2 and the average length of service is 5.2 years.
- We are promoting optimization of the Sales & Marketing Division’s personnel.
- We now have 37 overseas employees in the United States, 12 in China, and 12 in Europe (as of December 2022).
- Although we plan to maintain the Work from Home system, we are taking the following measures because of concerns about lack of communication and weakening of the sense of belonging to the company.

- Corporate executive meetings will be held as in-person meetings. 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.
- 1on1 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.

### 1.3. Progress and Results of Operations

	mil yen		Year-on-year (%)	% to total sales	
	2021	2022		2021	2022
Sales *	20,741	21,204	-	100.0%	100.0%
Cost of goods sold	2,076	2,698	129.9%	10.0%	12.7%
Gross profit	18,664	18,506	99.1%	90.0%	87.3%
SG&A expense *	14,130	14,706	-	68.1%	69.4%
Personnel expenses *	2,754	3,634	132.0%	13.3%	17.1%
R&D expenses *	4,636	5,892	127.1%	22.4%	27.8%
Operating income	4,534	3,799	83.8%	21.9%	17.9%
Non-operating income/expenses	212	149	70.1%	1.0%	0.7%
Ordinary income	4,747	3,948	83.2%	22.9%	18.6%
Extraordinary income/loss	-9	-30	-	-	-
Net income before tax	4,738	3,918	82.7%	22.8%	18.5%
Income taxes	1,187	1,217	102.5%	5.7%	5.7%
Net income	3,551	2,701	76.1%	17.1%	12.7%
Net income per employee ('000 yen)	9,597	7,070			
Retained earnings brought forward					
Beginning balance	5,825	8,868			
Dividend	508	590			
Net income	3,551	2,701			
Ending balance	8,868	10,979			

\* 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.

#### Foreign subsidiaries (reference)

Results in FY 2022	mil yen		
	Nobelpharma America LLC	Plusultra pharma GmbH	Jiangsu Nobelpharma Co., Ltd.
Current income (*)	-1,798	-296	-187

\* Current income of foreign subsidiaries is obtained by converting the local currency, using the exchange rate as of the end of 2022.

Total sales in 2022 were 21,204 million yen, up \_\_\_\_% year-on-year. NOBELZIN® and dysmenorrhea (LEP) family (LUNABELL® LD, LUNABELL® ULD, JEMINA® and FREWELL®) posted sales of 10,939 million yen and 5,479 million yen, respectively, accounting for 53.7% and 26.9%, respectively, of total product sales.

The cost of goods sold was 2,698 million yen, up 29.9% year-on-year, accounting for 12.7% of total sales. Selling, general and administrative expenses totaled 14,706 million yen, an increase of \_\_\_\_% year-on-year, accounting for 69.4% of total sales, mainly including personnel expenses of 3,634 million yen, up 32.0% year-on-year and accounting for 17.1% of total sales, R&D expenses of 5,892 million yen, up 27.1% year-on-year and accounting for 27.8% of total sales, sales promotion expenses of 1,641 million yen (up \_\_\_\_% year-on-year), and outsourcing expenses of 1,743 million yen (up 21.6% year-on-year). Sales promotion expenses mainly included 903 million yen of sales commission, etc. on NOBELZIN® and JEMINA® to ASKA Pharmaceutical Co., Ltd., etc.

Note that sales commissions to MEDICEO CORPORATION and SHIKOKU YAKUGYO Co., Ltd. for NOBELZIN®, JEMINA®, and MELATOBEL® (2,334 million yen this year), which had been recorded as sales promotion commissions until the previous fiscal year, are deducted from the sales because the “Revenue Recognition Accounting Standards” were applied, starting this fiscal year.

Outsourcing expenses mainly included 295 million yen for business management services and indirect department operations outsourcing to Hisanaga & Co. Ltd., 216 million yen for safety information processing support operation, etc. by CMIC, 115 million yen for royalties on Medichat, etc. by Medipal Holdings Corporation, and 70 million yen for initial establishment of EDC, etc. to Fujitsu Japan. The direction for continuation of Medichat use is under consideration.

As a result, operating income was 3,799 million yen, up 83.8% year-on-year, and it accounted for 17.9% of total sales.

Ordinary income was 3,948 million yen, up 83.2% year-on-year, accounting for 18.6% of total sales, after recording non-operating income of 266 million yen including subsidy income of 248 million yen, with non-operating expenses of 117 million yen including currency exchange losses of 61 million yen, payment interest of 39 million yen, and bond interest expenses of 8 million yen.

With income taxes of 1,217 million yen, net income was 2,701 million yen, up 76.1% year-on-year, accounting for 12.7% of total sales, and net income per employee was 7 million yen (2021: 9 million yen).

Retained earnings brought forward as of December 31, 2022 were 10,979 million yen, with the beginning balance of retained earnings brought forward of 8,868 million yen and a dividend payment of 590 million yen.

\* The “Revenue Recognition Accounting Standards” (Corporate Accounting Standards No. 29, March 31, 2020), etc. have been applied from the beginning of the current fiscal year, and the major management indices, etc. for the current fiscal year reflect application of these accounting standards, etc.

For this reason, the ratio to the previous year is not described for the above selling, general and administrative expenses.

#### 1.4. Domestic sales

The table below shows sales by product in 2022 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 (%)
				2021	2022	
Obstetrics and Gynecology Family	LUNABELL® LD LUNABELL® ULD	Jul 2008 Sep 2013	Dysmenorrhea	2,983	2,721	91.2
	JEMINA®	Oct 2018	Dysmenorrhea	3,259	3,880	119.1
	FREWELL® LD FREWELL® ULD	Dec 2018	Dysmenorrhea	4,190	4,835	115.4
Subtotal				10,432	11,436	109.6
Pediatric Family	NOBELBAR®	Dec 2008	Neonatal seizures, status epilepticus	110	119	107.6
	INDACIN®	Jan 2013	Patent ductus arteriosus of prematurity	45	44	98.0
	COSMEGEN®	Jan 2013	Wilms' tumor, choriocarcinoma, pediatric solid malignant tumor, etc.	21	26	120.6
	Respia®	Dec 2014	Apnea of prematurity	226	215	95.3
	Melatobel®	Jun 2021	Sleep-onset difficulty associated with neurodevelopmental disorder in children	1,163	1,939	166.7
Subtotal				1,566	2,342	149.6
NOBELZIN® Family	NOBELZIN®	Apr 2008 Mar 2017	Wilson's disease, hypozincemia	14,751	15,358	104.1
Subtotal				14,751	15,358	104.1
Neurosurgery Family	Fostoin®	Jan 2012	Status epilepticus, prevention of postoperative seizures, etc.	933	914	97.9
	GLIADEL®	January 2013	Malignant glioma	782	627	80.3
	Alabel®	September 2013	Diagnosis of malignant glioma	314	295	94.0
Subtotal				2,029	1,836	90.5
Respiratory Family	Unitalc®	Dec 2013 Mar 2022	Prevention of recurrent malignant pleural effusion Secondary intractable pneumothorax that is difficult to treat with surgery	74	79	107.6
	RAPALIMUS®	Dec 2014 September 2021	Lymphangioleiomyomatosis Refractory lymphatic disease (lymphatic malformation, lymphangiomas, Gorham's disease, lymphangiectasia)	372	576	154.7
Subtotal				446	656	146.9
Otolaryngology Family	TITANBRIDGE®	Jul 2018	Adductor spasmodic dysphonia	25	7	29.1
	RETYMPA®	Dec 2019	Tympanic perforation	89	100	112.4
Subtotal				114	107	94.4
Other Drug Families	ZANOSAR®	Feb 2015	Gastroenteropancreatic neuroendocrine tumor	329	256	77.9
	RAPALIMUS® Gel	Jun 2018	Skin lesions associated with tuberous sclerosis	361	377	104.4
Subtotal				690	633	91.8
Total				30,027	32,368	107.8

The fiscal year 2022 was a year when MR activities were invested into products with additional indications (RAPALIMUS® Tablets, UNITALC®) in addition to the three main products (NOBELZIN®, JEMINA®, MELATOBEL®). With the lifting of restrictions on the distribution of existing major product MELATOBEL® in October of 2022, it has become possible to carry out full-scale MR activities. Also, in



FY 2022, because of the effects of COVID-19 and changes in the medical environment, we introduced a team system for MR activities to reduce the number of MRs. MR activities 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 32.36 billion yen in FY 2022, up 7.8% year-on-year, compared with the sales target of 33.68 billion yen (on a wholesale price (NHI price) basis). The biggest reasons why the sales target was not achieved were that there was a supply restriction on prescriptions of MELATOBEL® from June 2021 to September 2022, and MR information activities could not be carried out. This no longer applies in FY 2023, as the supply restriction on MELATOBEL® was lifted in October 2022. Because the MRs were unable to disseminate information on MELATOBEL® for about one year, we will shift to a system in which half of the weight of MR information activities will focus on MELATOBEL® in FY 2023. In addition, we will implement new efforts to enable new products to penetrate the market quickly in the future.

### 1.5. Research and Development (Japan and overseas)

We have been working on the development of malaria vaccines for 8 years, but we have decided to abandon development because production of an investigational new drug has not proceeded as expected.

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 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

	Compound	Indication	Licensor	Development stage	Estimated approval	Classification
1	NPC-26 Sargramostim	Autoimmune pulmonary alveolar proteinosis	Partner Therapeutics Inc.	Preparation for filing	Jan 2024	II
2	NPC-09 Aceneuramic acid	Progressive muscle weakness in GNE myopathy	In-house	Preparation for filing	Jan 2024	II
3	NPC-25	hypozincemia	In-house	PIII/ Preparation for filing	Jan 2024	I
4	NPC-21 Anti-CMV antibody	CMV infection	Evec Inc.	PII	Dec 2027	I
5	NPC-22 Scopolamin	Hypersalivation	Kitasato University	PI/II	Sep 2026	IV
6	NPC-28 Cultured periosteal cells	Jawbone regeneration	Niigata University Kohjin Bio Co., Ltd.	Non-clinical	TBD	IV
7	GAIA-102	Neuroblastoma	Gaia BioMedicine Inc. Kyushu University	PI	TBD	III
8	P092	Prion disease	Gifu University	Non-clinical	TBD	III
9	Anti-S100A8/A9 antibody	Inflammatory disease	Okayama University	Non-clinical	TBD	IV

## B. Life Cycle Management (LCM)

	Compound	Indication	Licensor	Development stage	Estimated approval	Classification
1	NPC-12 RAPALIMUS®	Intractable vascular tumor/vascular malformation (new indication)	Gifu University	Preparation for filing	Jan 2024	II
2	NPC-06 Fostoin®	Pain associated with herpes zoster (new indication)	Pfizer Inc.	PIII	September 2024	I
3	NPC-18	Regeneration of external auditory canal	Kaken Pharmaceutical	PIII	TBD	IV
4	NPC-12 RAPALIMUS®	Pendred syndrome (new indication)	Keio University	PII	TBD	III
5	NPC-12 RAPALIMUS®	Epilepsy with focal cortical dysplasia type II (new indication)	Showa University	PII	TBD	IV
6	NPC-12 RAPALIMUS®	Primary immunodeficiency syndrome (new indication)	Tokyo Medical and Dental University	PII	TBD	IV
7	NPC-12G RAPALIMUS®	Intractable vascular tumor/vascular malformation (new indication)	Wakayama Medical University	PII	TBD	IV
8	NPC-15	Xeroderma pigmentosum	Kobe University	PII	TBD	IV
9	NPC-26 Sargramostim	Pulmonary non-tuberculous mycobacteriosis (new indication)	Niigata University	PII	TBD	I

## C. Overseas Development

	Compound	Indication	Licensor	Development stage	Estimated approval	Classification
1	NPC-12G (RAPALIMUS® Gel)	Angiofibroma	-	Europe: Filed	Apr 2023	I
				China: Filed	June 2023	
2	NPC-17 Thyroid cartilage fixation device (TITANBRIDGE®)	Adductor spasmodic dysphonia	-	US: Clinical trial in preparation	TBD	III
				Europe: CE marking in process	November 2023	
3	NPC-18 (RETYMPA®)	Tympanic perforation	MEEI/ Harvard/ NY University	US: PII	TBD	III
4	NPC-02 (NOBELZIN®)	Wilson's disease	-	China: Filed	Dec 2023	II
5	NPC-15 (MELATOBEL®)	Sleep-onset difficulty associated with neurodevelopmental disorder in children	-	China: Preparation for filing	April 2024	I

## 1.6. Funding and Major Lenders

In 2022, the Company borrowed 2,500 million yen, and repaid and redeemed 903 million yen to financial institutions.

As a result, as of the end of December 2022, the balance of loans payable and bonds was 9,183 million yen, and the balance of cash and deposits was 8,403 million yen.

As of December 31, 2022, the status of borrowing is as follows:

### Loans payable

Mizuho Bank, Ltd.	3,300 million yen
Sumitomo Mitsui Banking Corporation	850 million yen
MUFG Bank, Ltd.	1,260 million yen
Resona Bank, Ltd.	400 million yen
The Bank of Yokohama, Ltd.	100 million yen
The Shoko Chukin Bank, Ltd.	860 million yen
The Tokyo Shinkin Bank	250 million yen
Japan Finance Corporation	62 million yen
Total	7,082 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: Dec 2024)
7th straight bond	Resona Bank, Ltd.	300 million yen (Maturity: May 2026)
8th straight bond	Resona Bank, Ltd.	150 million yen (Maturity: Mar 2027)
9th straight bond	Sumitomo Mitsui Banking Corporation	500 million yen (Maturity: Mar 2027)
10th straight bond	Resona Bank, Ltd.	100 million yen (Maturity: 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 coming fiscal year, we plan to increase sales, with the driving force provided by MELATOBEL® and our other existing major products, but because we expect to continue to accelerate research and development and make substantial R&D investments, as we did last year, we anticipate increased revenue but decreased profits.

Mil yen except for *	2019 (Actual results) 17th year	2020 (Actual results) 18th year	2021 (Actual results) 19th year	2022 (Actual results) 20th year	2023 (Forecasts) 21st year
Sales	13,403	16,929	20,741	21,204	23,972
Ordinary income	2,951	3,466	4,747	3,948	3,816
Net income	2,370	2,511	3,551	2,701	1,861
* Net income per share	175,000 yen	185,000 yen	262,000 yen	199,000 yen	137,000 yen
Total assets	14,138	18,574	23,008	27,679	29,064
Net assets	5,330	7,052	10,094	12,205	13,520
* Equity ratio	37.7 %	38.0 %	43.9 %	44.1 %	46.5 %
* Net assets per share	394,000 yen	521,000 yen	746,000 yen	902,000 yen	1 million yen

The "Revenue Recognition Accounting Standards" (Corporate Accounting Standards No. 29, March 31, 2020), etc. have been applied from the beginning of the current fiscal year, and the major management indices, etc. for the current fiscal year reflect the application of these accounting standards, etc.



Post-marketing surveillance: Patient registration for all-case surveillance of RAPALIMUS® Gel was completed in March.

Quality: A total of 142 quality information cases (complaints) were collected, and appropriate action was taken to investigate the cause and make improvements. Regarding the TITANBRIDGE® breakage incident, we recalled the product in March and performed monitoring of patients as well as analysis and evaluation of risk. Shipments of products were resumed on September 5. The quintennial QMS inspection of TITANBRIDGE® was conducted by PMDA in September.

Overseas expansion: The Global PV system audit by the internal audit department took place over 3 days in May as part of the establishment and 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 United States.

### **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., and consultation on whether situations constitute violations of laws or regulations. 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.

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.

Accounting and Finance: We will complete the introduction of the new accounting system so that we can 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 addition, security enhancement measures are being implemented to prepare for various risks such as cyber attacks.

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 2022, we will unfortunately fail to reach the numerical target for 2023 set as the North Star in the 2022-26 mid-term business plan, 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, 2022)

(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 24, 2023, the status of full-time and part-time directors is as follows:

Managing Director & CEO: Jin Shiomura

Director (part-time): Isamu Sojyo (former Executive Managing Director of Japan Intellectual Property Association)

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	(President, Mih Clinic)
Director (part-time):	Georg Holländer	(Head of Department of Pediatrics, University of Oxford)
Audit & Supervisory Board Member (part-time):	Yoshitaka Kishi	(former full-time member of Audit & Supervisory Committee, DIA RIX CORPORATION)
Audit & Supervisory Board Member (part-time):	Tomoyasu Toyoda	(Company Auditor, MEDIPAL HOLDINGS CORPORATION)
Audit & Supervisory Board Member (part-time):	<u>Yasuhiro Kaga</u>	(former Member of the Board of Directors, Managing Executive Officer of Mitsubishi UFJ Securities Holdings)

## (2) Executive Officers

As of April 1, 2023, 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 Bio Business Division/External Relations)
Senior Executive Officer	Hitoshi Yokoyama	(Head of Sales & Marketing Division)
Executive Officer	Kozo Hayase	(Head of Administrative Affairs & Corporate Planning Division/Overseas Subsidiaries)
Executive Officer	Kenji Shimizu	(Deputy Head of Research & Development Division, General Manager of Clinical Development Department 2)
Executive Officer	Yoshiki Yagi	(Head of Project Planning & Development Division/Deputy Head of Bio Business Division)
Executive Officer	Toshiaki Okamura	(Head of Regulatory Affairs Division/General Manager of External Relations Department)
Executive Officer	Yoshihide Yamamoto	(Head of President Office)
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/General Manager of International Clinical Development Department)
Executive Officer	Yoshiki Kida	(President & CEO, Nobelpharma America, LLC)
Executive Officer	Makoto Shiragami	(Head of Compliance Division/General Manager of Compliance Promotion Department)
Executive Officer	Yukio Urasaki	(Head of Business Development Division)
Executive Officer	Masayoshi Onozaki	(Head of Global Business Development Division)

Executive Officer	<u>Tetsuro Noguchi</u>	(Head of Supply Chain & Manufacturing Division)
Executive Officer	Eijiro Akatsu	(Deputy Head of Administrative Affairs & Corporate Planning Division/General Manager of Corporate Finance 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 Departments 1 and 2)
Executive Director	Tsutomu Iwasa	(General Manager of West Japan Sales Department)
Executive Director	Yasuo Satake	(General Manager of HR & General Affairs 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	<u>Sachiko Ezo</u>	(Director of Medical Division)
Executive Director	<u>Yoshinobu Takahashi</u>	(Deputy Head of Sales & Marketing Division/General Manager of Marketing Communication Department/Product Marketing Department 3 and Marketing Communication Department)
Executive Director	<u>Rongzhe Jiang</u>	(General Manager, Jiangsu Nobelpharma Co., Ltd.)

### 2.3.2. Remuneration paid to directors and company auditors

Classification	Headcount	Amount paid
Directors	7	15.6 million yen
Company auditor	2	4,800,000 yen
Total	9	20.4 million 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.

< Remainder of this page intentionally left blank >

Attachment

Revised on January 19, 2023  
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. Please note that we are not necessarily saying that you have no qualification as line manager just because you cannot carry out on 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 guide 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.

END OF DOCUMENT