Business Report for the 19th Year
(Translation)

Nobelpharma Co., Ltd.

[From January 1, 2021 to December 31, 2021]

Business Report

(From January 1, 2021 to December 31, 2021)

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.

Policies

1. General
   1) Give priority to legal and ethical compliance in the course of business--never prioritize loyalty to company over moral.
   2) Share our Mission, Policies and Code of Conduct among all stakeholders (employees, shareholders, officers)
   3) Pursue evolution of the Company, yet becoming larger is not our main goal
   4) Ensure transparency and disclosure
   5) 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
      * "Select few" = experienced experts passionately devoted to working, irrespective of gender, age, nationality, religion or preference
   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: up to 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) Set a specific deadline date at the beginning to pursue the goal without worrying about possible delays
      * Stay away from “approximately/around” and “early/late ~,” etc.
   4) If problems or mistakes occur, prevent their expansion first before preventing reoccurrence
   5) Speedy decisions by managers who have authority of million(s) yen projects*
      * 3 million for Division Manager; 1 million for Department/Branch Manager/PM/PL

4. Cost/Efficiency:
   1) Never take or lead to wasteful actions
   2) No overtime is considered optimal
   3) Consider patient needs, scientific rationality and laws/regulations when pursuing higher quality in products/data
   4) Pursue cost reduction with the principle of multiple sources, while regarding providers as partners

5. Communications/Relationship:
   1) Embrace inter-departmental advice and cooperation—hiding in silos is a symptom of “Big Company” Disease
   2) Superiors to confidently entrust tasks to subordinates, but never leave unmanaged
   3) Hear anyone out--never interrupt in the middle
   4) Start with the conclusion/result when explaining/responding
   5) Greetings may seem small, but they are important

1.2. Noteworthy Points in 2021

1.2.1. Sales exceeded 20 billion yen for the first time. NOBELZIN® Tablets and JEMINA® contributed to this, with profits exceeding the plan.

- A total of about 22.73 million yen in interim bonuses was paid at the end of 2021. Eligible employees were those who were highly evaluated in 2020.

1.2.2. Drug development has entered a new era. Globally, COVID-19 vaccines were developed at an unexpectedly rapid rate and launched and supplied in units of 1 billion vials within 1 year after the genetic information of the virus was decoded.

- In life cycle management (LCM) of existing drugs, approval was obtained for a new granule formation of NOBELZIN® and for an additional indication of RAPALIMUS® Tablets for refractory lymphatic diseases, and approval applications were submitted for additional indications of UNITALC® for secondary intractable pneumothorax as well as for additional indications of LUNABELL® and JEMINA® for adjusting the timing of initiation of regulated ovarian stimulation in assisted reproductive technology. None of these are new active ingredients.
- A PIII trial of NPC-26 (GM-CSF, sargramostim) for the treatment of COVID-19 was initiated but ended in failure.
- NPC-SE36 (malaria vaccine) was wholly unable to match the speed of COVID-19 vaccine development throughout the world. The bottlenecks were production and funding.

1.2.3. It is now time to question whether the policy of outsourcing 100% of production can be maintained.

- Owing to the influence of scandal, the contract manufacturer was not able to demonstrate the expected mobility.
- Misreading of demand for MELATOBEL® granules, which became available for long-term administration in June 2021, led to inquiries about the possibility of increasing production more than two-fold, but the contract manufacturer was unable to meet the increase, and shipments were adjusted.
- The same contract manufacturer has been preparing for production of NOBELZIN® Granules, which were included in the NHI price list in May 2021, but as of March 2022, the timing of production and sale remains unclear.
- We have proceeded with the development of the granule formulation of RAPALIMUS® as LCM, but the application will be delayed by 3 months due to failure in the development of the formulation.
- As a result, we were unable to meet medical needs and caused tremendous inconvenience to patients and medical institutions.
- Also, lost profits occurred. Total lost profits for the 3 drugs are estimated at 900 million yen in 2021 and 1 billion yen in 2022.
- Many of the products that will be under development from now on are biologics, and our ability to accommodate them is insufficient.
- We will need to reconsider the production system for overseas supply.
- Our corporate mission includes not only pharmaceuticals but also medical devices. In fact, we have obtained a license for TITANBRIDGE® and are selling it in Japan. However, when we look at overseas development, the need for a QMS system premised on the ability to respond to overseas demand stands out clearly. This has an impact on the medical devices under development, and the Supply Chain & Manufacturing, Overseas Business Development, and PMS Regulatory Compliance & Assurance divisions are working together to make preparations hurriedly.

1.2.4. We have shifted our sales methods from the conventional visits and face-to-face meetings to a system that centers around digital transformation (DX). In addition, we expect to shift from the current push-type products to pull-type products in 2024, and our sales organization and evaluation method have been changed to accommodate this.

1.2.5. With the strengthening of overseas expansion, the system and structure of PMS Regulatory Compliance & Assurance have been improved to enable it to serve as the global head in adapting to the pharmaceutical regulatory requirements in each country.

- In addition to its regular operations related to reexamination, safety management, post-marketing surveillance, and quality, PMS Regulatory Compliance & Assurance has also been pressed to handle the fallout of scandals at contract manufacturers.

1.2.6. Work from home (WFH), which started in March 2020, has become routine.

- The average attendance rate was low at 5.4% (as of December 2021), and the average overtime hours and the rate of leave taking were favorable at 1.6 hours and 63.9%, respectively.
- The number of employees increased by 6.7% from the moving average of 329 in 2020 to 351 in 2021, and total personnel expenses increased by 4.3% from 3,427 million yen to 3,574 million yen.
- The average age is 52.6 and the average length of service is 5.0 years.
- There may now be overstaffing in the Sales & Marketing, particularly at the head office.
- The number of employees who joined the company after the transition to regular WHF has exceeded 100, and real interactions among employees have decreased. There are concerns about lack of communication and weakening of the sense of belonging to the company. As a countermeasure, we require managers to hold regular 1on1 meetings with their subordinates, and we recommend social gatherings within the group while providing assistance. However, this may not always be sufficient.

1.2.7. In line with our management policy of “launching business overseas”, we began making efforts at overseas expansion early on.

- We are making preparations to market new products ourselves overseas, beginning with sale of RAPALIMUS® Gel (NPC-12G), a drug designated for SAKIGAKE review, in the US (application in February 2020), China (application in September 2019), and Europe (application in November 2021).
- We now have 19 overseas employees in the U.S., 8 in China, and 9 in Europe (as of December 2021).
- Although review is on track in all of these regions, GMP on-site inspections by the US FDA are significantly delayed owing to travel restrictions imposed by COVID-19, resulting in significant delays in approvals.
- In order to strengthen our product lineup overseas, we are trying to advance overseas development not only of RAPALIMUS® Gel but also RETYMPA® (NPC-18) and TITANBRIDGE® (NPC-17), but we have not been able to fully accommodate this owing to a lack of personnel.
- Development of MELATOBEL® in China is making progress, but application has been delayed because of a scandal at the contract manufacturer.

1.2.8. We are trying to procure large-scale funding and are considering public listing to strengthen the production system and accelerate development and overseas expansion.

- In connection with this, we have newly established a Vaccine Business Division and Communications Depertment.
- In addition to financing from investors by listing our company, we are also trying to obtain grants from overseas public institutions and the Japanese government.

1.2.9. With a view to strengthening our biologics business and vaccine business, we have acquired an equity stake in two companies (VLP Therapeutics and Evec Inc.)

1.2.10. We have also newly established a Compliance Division to strengthen legal compliance in Japan and overseas and handle company-wide risk management.

1.3. Progress and Results of Operations

	mil yen		Year-on-year (%)	% to total sales	
	2020	2021		2020	2021
Sales	16,929	20,741	122.5	100.0	100.0
Cost of goods sold	1,676	2,076	123.9	9.9	10.0
Gross profit	15,253	18,664	122.4	90.1	90.0
SG&A expense	11,705	14,130	120.7	69.1	68.1
* Personnel expenses	2,715	2,754	101.4	16.0	13.3
* R&D expenses	3,374	4,636	137.4	19.9	22.4
Operating income	3,547	4,534	127.8	21.0	21.9
Non-operating income/expenses	-80	212	308.5	-	1.0
Ordinary income	3,466	4,747	136.9	20.5	22.9
Extraordinary income/loss	-	-9	-	-	-
Net income before tax	3,466	4,738	136.7	20.5	22.8
Income taxes	955	1,187	124.2	5.6	5.7
Net income	2,511	3,551	141.4	14.8	17.1
Net income per employee (’000 yen)	7,195	10,204			
Retained earnings brought forward					
Beginning balance	4,104	5,825			
Dividend	789	508			
Net income	2,511	3,551			
Ending balance	5,825	8,868			

* 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.

Total sales in 2021 were 20,741 million yen, up 22.5% year-on-year. NOBELZIN® and dysmenorrhea (LEP) family (LUNABELL® LD, LUNABELL® ULD, JEMINA® and Frewell®) posted sales of 12,633 million yen and 4,587 million yen, respectively, accounting for 62.2% and 22.6%, respectively, of total product sales.

The cost of goods sold was 2,076 million yen, up 23.9% year-on-year, accounting for 10.0% of total sales (2020: 9.9%). Selling, general and administrative expenses totaled 14,130 million yen, an increase of 20.7% year-on-year, accounting for 68.1% (2020: 69.1%), mainly including personnel expenses of 2,754 million yen, up 1.4% year-on-year, and 13.3% (2020: 16.0%) of total sales, R&D expenses of 4,636 million yen, up 37.4% year-on-year, and 22.4% (2020: 19.9%) of total sales, sales promotion expenses of 3,363 million yen and outsourcing expenses of 1,433 million yen. Sales promotion expenses mainly included 2,793 million yen of sales commission on NOBELZIN®, JEMINA® and MELATOBEL® to MEDICEO CORPORATION, ASKA Pharmaceutical Co., Ltd. and SHIKOKU YAKUGYO Co., LTD. Outsourcing expenses mainly included 274 million yen for business management services and indirect department operations outsourcing to Hisanaga & Co. Ltd., 137 million yen for safety information processing support operation by CMIC, 75 million yen for royalties on Medichat by Medipal Holdings Corporation, and 67 million yen for call center operation by EP-PharmaLine.

As a result, operating income was 4,534 million yen, up 27.8% year-on-year, and it accounted for 21.9% (2020: 21.0%) of total sales.

Ordinary income was 4,747 million yen, up 36.9% year-on-year, accounting for 22.9% (2020: 20.5%) of total sales, after recording non-operating income of 272 million yen including subsidy income of 259 million yen, with non-operating expenses of 60 million yen including interest expenses of 34 million yen and bond interest expenses of 11 million yen.

With income taxes of 1,187 million yen, net income was 3,551 million yen, up 41.4% year-on-year, accounting for 17.1% (2020: 14.8%) of total sales, and net income per employee was 10 million yen (2020: 7 million yen).

Retained earnings brought forward as of December 31, 2021 were 8,868 million yen, with the beginning balance of retained earnings brought forward of 5,825 million yen and a dividend payment of 508 million yen.

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1.4. Domestic sales

The table below shows sales by product in 2021 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 (%)
				2020	2021	
Obstetrics and Gynecology Family	LUNABELL® LD LUNABELL® ULD	Jul 2008 Sep 2013	Dysmenorrhea	3,104	2,983	96.1
	JEMINA®	Oct 2018	Dysmenorrhea	2,326	3,258	140.0
	FREWELL® LD FREWELL® ULD	Dec 2018	Dysmenorrhea	3,525	4,190	118.9
Subtotal				8,955	10,431	116.5
Pediatric Family	NOBELBAR®	Dec 2008	Neonatal seizures, status epilepticus	107	110	102.8
	INDACIN®	Jan 2013	Patent ductus arteriosus of prematurity	49	44	91.1
	COSMEGEN®	Jan 2013	Wilms' tumor, choriocarcinoma, pediatric solid malignant tumor, etc.	24	21	86.9
	Respia®	Dec 2014	Apnea of prematurity	224	226	101.0
	Melatobel®	Jun 2021	Sleep-onset difficulty associated with neurodevelopmental disorder in children	224	1,163	517.5
Subtotal				628	1,564	249.0
NOBELZIN® Family	NOBELZIN®	Apr 2008 Mar 2017	Wilson's disease, hypozincemia	11,895	14,750	124.0
Subtotal				11,895	14,750	124.0
Neurosurgery Family	Fostoin®	Jan 2012	Status epilepticus, prevention of postoperative seizures, etc.	945	933	98.7
	GLIADEL®	Jan 2013	Malignant glioma	849	781	92.0
	Alabel®	Sep 2013	Diagnosis of malignant glioma	297	313	105.4
Subtotal				2,091	2,027	96.9
Respiratory Family	Unitalc®	Dec 2013	Prevention of recurrent malignant pleural effusion	71	74	104.2
	RAPALIMUS®	Dec 2014	Lymphangioleiomyomatosis	314	372	118.4
Subtotal				385	446	115.8
Otolaryngology Family	TITANBRIDGE®	Jul 2018	Adductor spasmodic dysphonia	38	25	64.4
	RETYMPA®	Dec 2019	Tympanic perforation	63	89	140.5
Subtotal				101	114	112.9
Other Drug Families	ZANOSAR®	Feb 2015	Gastroenteropancreatic neuroendocrine tumor	356	329	92.4
	RAPALIMUS® Gel	Jun 2018	Skin lesions associated with tuberous sclerosis	376	360	95.9
Subtotal				732	689	94.1
Total				24,787	30,021	121.1

In fiscal 2021, we focused on our 3 main products (NOBELZIN®, JEMINA® and MELATOBEL®). However, a supply problem with MELATOBEL® occurred in June, limiting our ability to propose prescribing to physicians after lifting of the restriction on long-term prescriptions (June). Also, due to the influence of COVID-19, 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. Even under this environment, sales amounted to 30 billion yen in FY 2021, up 21.1% year-on-year, compared with the sales target of 29.2 billion yen (on a wholesale price (NHI price) basis).

1.5. Research and Development (Japan and overseas)

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

Overseas Development as of March 1, 2022. 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	Sep 2023	II
2	NPC-09 Aceneuramic acid	Progressive muscle weakness in GNE myopathy	In-house	PIII	Sep 2023	II
3	NPC-25	hypozincemia	In-house	PIII	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	Sep 2026	IV
6	NPC-27 Vaccinia virus vaccine	Coronavirus disease 2019 (COVID-19)	Tokyo Metropolitan Institute of Medical Science	Non-clinical	TBD	III
7	NPC-28 Cultured periosteal cells	Jawbone regeneration	Niigata University Kohjin Bio Co., Ltd.	Non-clinical	TBD	III
8	P092	Prion disease	Gifu University	Non-clinical	TBD	IV
9	Next-generation T-cell therapy	TBD	Hiroshima University Repertoire Genesis Inc.	Non-clinical	TBD	III
10	GAIA-102	Neuroblastoma	Gaia BioMedicine Inc. Kyushu University	Non-clinical	TBD	III
11	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-05 Unitalc®	Intractable pneumothorax (new indication)	National Hospital Organization Nagoya Medical Center	Application	Mar 2022	III
2	IKH-01/NPC-01 LUNABELL® LD/ULD	Adjusting the timing of initiation of regulated ovarian stimulation in assisted reproductive technology (new indication)	Janssen	Application	Mar 2022	II

3	NPC-16 JEMINA®	Adjusting the timing of initiation of regulated ovarian stimulation in assisted reproductive technology (new indication)	In-house	Application	Mar 2022	II
4	NPC-12 RAPALIMUS®	Intractable vascular tumor/vascular malformation (new indication)	Gifu University	PIII	Jan 2024	II
5	NPC-06 Fostoin®	Pain associated with herpes zoster (new indication)	Pfizer Inc.	PII/III	Dec 2024	I
6	NPC-12 RAPALIMUS®	Fibrodysplasia ossificans progressiva (new indication)	Kyoto University	PII/III	Plan to cancel	III
7	NPC-12 RAPALIMUS®	Pendred syndrome (new indication)	Keio University	PII	TBD	III
8	NPC-12 RAPALIMUS®	Epilepsy with focal cortical dysplasia type II (new indication)	Showa University	PII	TBD	IV
9	NPC-12 RAPALIMUS®	Idiopathic multicentric Castleman's disease (new indication)	Nagasaki University	PII	TBD	IV
10	NPC-12 RAPALIMUS®	Primary immunodeficiency syndrome (new indication)	Tokyo Medical and Dental University	PII	TBD	IV
11	NPC-26 Sargramostim	Pulmonary non-tuberculous mycobacteriosis (new indication)	Niigata University, Tokyo Medical and Dental University	PII	TBD	I

C. Overseas Development

	Compound	Indication	Licensor	Development stage	Estimated approval	Classification
1	NPC-12G (RAPALIMUS® Gel)	Angiofibroma	-	USA: Filed China: Filed Europe: Filed	Jul 2022 Jun 2022 Apr 2023	I
2	NPC-17 Thyroid cartilage fixation device (TITANBRIDGE®)	Adductor spasmodic dysphonia	-	US: Clinical trial in preparation Europe: CE marking in process	TBD Dec 2022	III
3	NPC-18 (RETYMPA®)	Tympanic perforation	MEEI/ Harvard/ NY University	PII	TBD	III
4	NPC-19 (NPC-SE36) Malaria vaccine	Prevention of falciparum malaria	Osaka University GHIT	PIb	TBD	I
5	NPC-15 (MELATOBEL®)	Sleep-onset difficulty associated with neurodevelopmental disorder in children	-	China: Preparation for filing	Sep 2023	I
6	NPC-02 (NOBELZIN®)	Wilson's disease	-	China: Preparation for filing	Dec 2023	II

1.6. Funding and Major Lenders

In 2021, the Company borrowed 2,500 million yen, and repaid and redeemed 995 million yen to financial institutions.

As a result, as of the end of December 2021, the balance of loans payable and bonds was 7,587 million yen, and the balance of cash and deposits was 7,048 million yen.

As of December 31, 2021, the status of borrowing is as follows:

Loans payable

Mizuho Bank, Ltd.	2,400 million yen
Sumitomo Mitsui Banking Corporation	550 million yen
MUFG Bank, Ltd.	1,300 million yen
The Bank of Yokohama, Ltd.	100 million yen
The Shoko Chukin Bank, Ltd.	508 million yen
The Tokyo Shinkin Bank	250 million yen
Japan Finance Corporation	78 million yen
Total	5,186 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)
6th straight bond	Resona Bank, Ltd.	300 million yen (Maturity: Mar 2022)
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		1,850 million yen

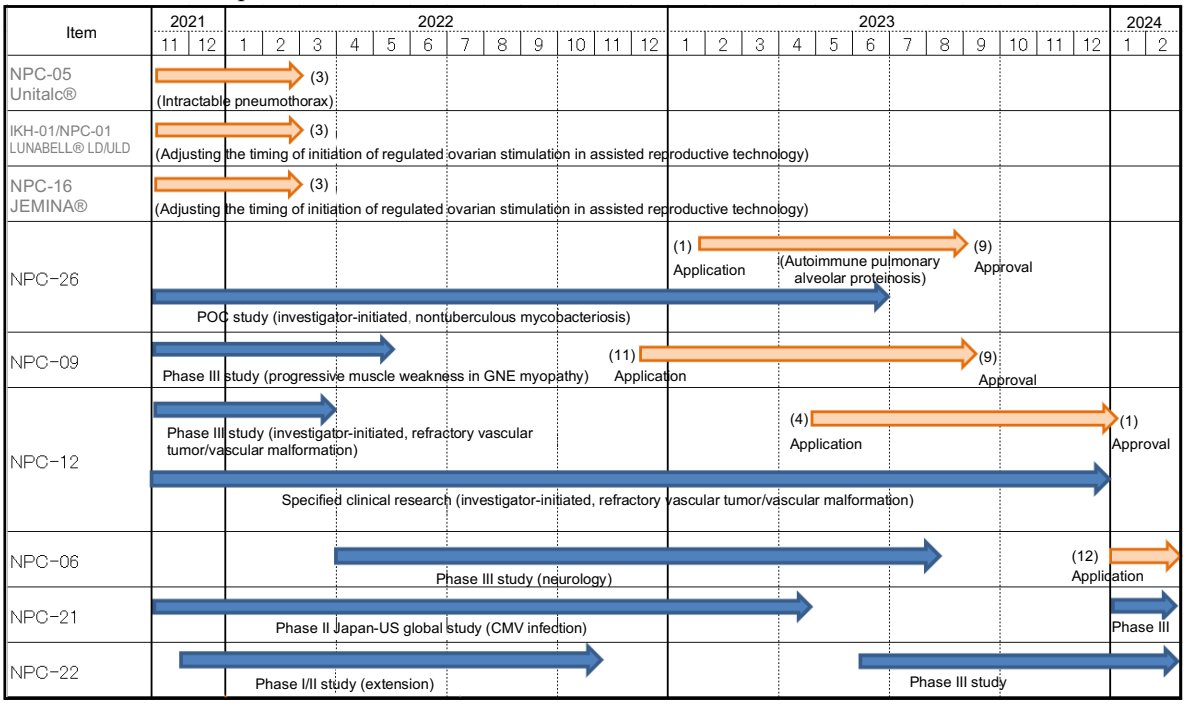
1.7. Financial Results, Assets, 2022 Forecast, and Development Schedule

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

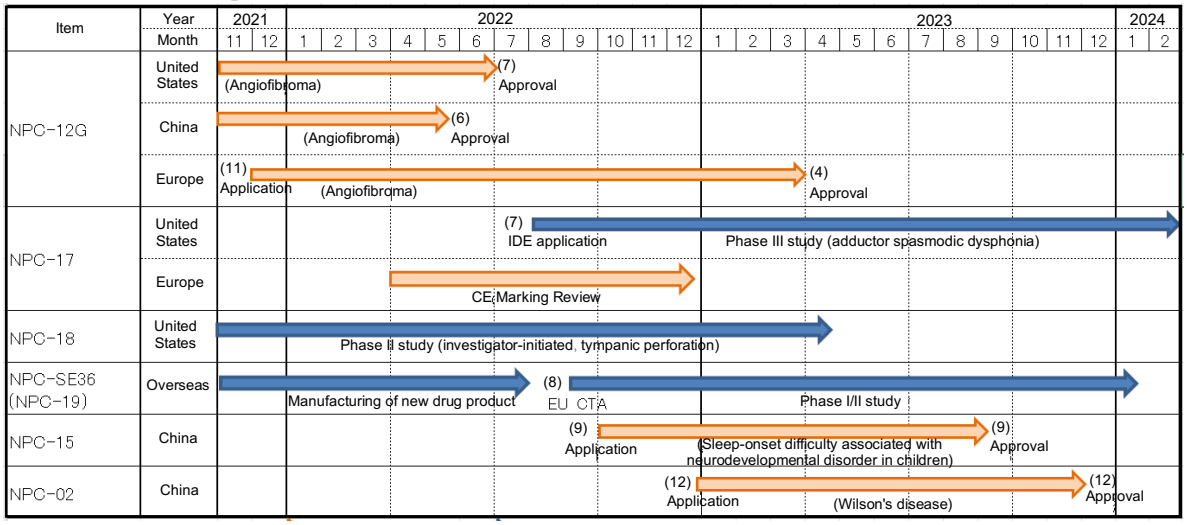
In the coming fiscal year, we plan to increase sales, with the driving force provided by newly marketed products as well as our existing major products, but because we expect to continue to make substantial R&D investments and overseas investments, as we did last year, we anticipate increased revenue but decreased profits.

Mil yen except for *	2018 (Actual results) 16th year	2019 (Actual results) 17th year	2020 (Actual results) 18th year	2021 (Actual results) 19th year	2022 (Forecasts) 20th year
Sales	10,568	13,403	16,929	20,741	24,843
Ordinary income	1,960	2,951	3,466	4,747	3,672
Net income	1,437	2,370	2,511	3,551	2,401
* Net income per share	111,000 yen	175,000 yen	185,000 yen	262,000 yen	177,000 yen
Total assets	12,204	14,138	18,574	23,008	24,371
Net assets	3,319	5,330	7,052	10,094	11,470
* Equity ratio	27.2%	37.7%	38.0%	43.9%	47.1%
* Net assets per share	245,000 yen	394,000 yen	521,000 yen	746,000 yen	848,000 yen

A. Domestic Development Schedule



B. Overseas Development Schedule



1.8. Status of Compliance

We are advancing the construction of a compliance system for our company.

First, the Code of Conduct in our corporate philosophy was revised to show everyone inside and outside the Company that legal and regulatory compliance is our top priority as the starting point for our Code of Conduct. In addition, we established compliance rules, formulated a basic philosophical approach to compliance efforts at our company, and prepared a “Compliance Manual” for employees, which has been distributed to all employees and discussed in explanatory meetings to make certain that everyone in the Company is aware of the compliance system.

We have established the role of executive officer in charge of compliance, to be filled by the general manager of the Compliance Division. The Compliance Division was established in July and consists of

two departments, the Compliance Promotion Department and the Clinical Quality Assurance Department. Sales Information Activity Supervision Group has been established within the Compliance Promotion Department (promoted to department in February 2022) and a GCP QA Group and PV&CS QA Group within the Clinical Quality Assurance Department. We have appointed persons in charge of compliance in each division and each branch office of Sales & Marketing, and they play a central role in compliance based on the characteristics of each division. A meeting of persons in charge of compliance is held every three months to communicate our compliance policy, disseminate information on the training plan, and promote cooperation among persons in charge of compliance. In addition, to deliberate important matters related to compliance, a Compliance Committee has been established with the president and executive officers as members of its Management Committee.

We have established a whistle-blowing system to ensure that all whistle-blowing cases are channeled to the Compliance Promotion Department. An in-house whistle-blowing contact has now been established at Cybozu, Inc., joining the existing external whistle-blowing contact (Labor Data Bank). We have also provided training on the internal reporting system to all employees to promote familiarity with the system. 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.

Our goal is to prevent legal and regulatory violations from occurring, and in the unlikely event that one does occur, prevent it from expanding in scope. To this end, the department conducts the following activities: (a) monitoring and audits, (b) information collection through the in-house whistle-blowing system, (c) investigation of whistle-blowing cases and planning of corrective action, (d) training on laws and regulations, etc., and (e) interpretation of laws and regulations, and consultation on whether situations constitute violations of laws or regulations.

We are also making efforts to manage risk company wide. First, we will identify business risks that may have a significant impact on business continuity. Then, we will determine the causes of the identified business risks and develop and implement countermeasures. Lastly, we will establish a procedure for handling business risks and develop a Business Continuity Plan (BCP).

In order to further accommodate the concept of risk-based quality assurance that has been required by ICH E6 (R2) in recent years, the Clinical Quality Assurance Department is considering and promoting more efficient and effective auditing methods. The system for PV audits will be improved to comply with global PV regulations, and related education and training of staff will be enhanced to ensure implementation and promotion of PV audits based on the global auditing plan. Use of external PV auditors will also be considered, as necessary. In addition, we will establish auditing functions and procedures to ensure the quality of computer systems (CS) related to GCP and PV functions.

1.9. Status of Administrative Departments

Management Planning: We will proceed to establish a management system suitable for expansion of business operations and overseas bases. In addition, we will promote paperless operations and enhance document control.

Accounting and Finance: We will further promote the establishment and strengthening of internal control in line with the expansion of the scale of business and overseas expansion. In addition, we will upgrade our methods of assessing and managing revenue and financial conditions at overseas bases.

Human Resources and General Affairs: We will strive to improve the rate of paid leave taking by promoting special incentive leaves and suggesting dates for taking paid leave. We are experimenting with various ways of preventing WFH from resulting in insufficient communication and an attenuated sense of belonging to the company. We will continue to hire specialized human resources for R&D, the production departments, and the bio business that will be our main focus, regardless of where they live, and we will continue to recruit postdocs. In employee education, in addition to utilizing e-learning, we will continue to conduct our internal business school. In addition, we will promote the in-house recruitment system, secondment to government, and use of temporary workers.

DX Promotion: While supporting business expansion from the IT side, we will promote business reform through the application of digital technology. 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: The Public Relations Department was established in July 2021 to promote the "provision of necessary but neglected drugs and medical devices" by conducting activities to acquaint healthcare professionals (physicians, pharmacists, nurses, etc., and relevant government offices and agencies) with our company. The Department disseminates information on our company philosophy and performance in satisfying unmet medical needs.

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 (2023)	Target
Sales	50 billion yen
Ordinary income	10 billion yen

2. Current Status of the Company

2.1. Shares (as of December 31, 2021)

(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 30, 2022, 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	(Part-time company auditor of Arara Inc.)
Director (part-time):	Takahisa Iizuka	(Deputy General Manager, Business Development Division, Medipal Holdings Corporation)
Director (part-time):	Koichi Noda	(General Manager, Financial Management Office, Inabata & Co., Ltd.)
Director (part-time):	Toshio Miyata	(Mih Clinic, President, MD, Ph.D, Professor, Waseda University)
Director (part-time):	Georg Hollander	(Professor, Department of Developmental Medicine, University of Oxford)
Audit & Supervisory Board Member (part-time):	Yoshitaka Kishi	(Former full-time company auditor, Dia Rix Co., Ltd.)
Audit & Supervisory Board Member (part-time):	Tomoyasu Toyoda	(Company auditor, Medipal Holdings Corporation)

(2) Executive Officers

As of April 1, 2022, the status of executive officers and directors is as follows:

Vice President & Chief Operating Officer	Shigeki Shimasaki	(Head of Research & Development / PMS Regulatory Compliance & Assurance)
Chief Operating Officer	Arata Tabata	(Head of Bio Business / External Relations)
Chief Operating Officer	Tetsuo Hayase	(Head of Supply Chain & Manufacturing)
Chief Operating Officer	Hitoshi Yokoyama	(Head of Sales & Marketing)
Executive Officer	Kenji Shimizu	(Deputy Head of Research and Development, General Manager of Clinical Research 2)
Executive Officer	Yoshiki Yagi	(Head of Project Planning & Development, Deputy Head of Bio Business)
Executive Officer	Toshiaki Okamura	(Head of Regulatory Affairs, General Manager of External Relations)
Executive Officer	Kozo Hayase	(Head of Administrative Affairs & Corporate Planning, Deputy Head of Bio Business, General Manager of Intellectual Property)
Executive Officer	Yoshihide Yamamoto	(Head of President Office)
Executive Officer	Hitoshi Hasegawa	(Head of PMS Regulatory Compliance & Assurance / General Marketing Compliance Officer)
Executive Officer	Masanori Osakabe	(Deputy Head of Research & Development, General Manager of Overseas Development)
Executive Officer	Yoshiki Kida	(President & CEO, Nobelpharma America, LLC)
Executive Officer	Makoto Shiragami	(Head of Compliance Division, General Manager of Compliance Promotion)
Executive Officer	Yukio Urasaki	(Head of Business Development)
Executive Director	Masato Iwamoto	(General Manager of Supply Chain Management, Supply Chain & Manufacturing)
Executive Director	Atsunori Iwao	(General Manager of Quality Assurance, Quality Assurance Officer)
Executive Director	Takako Aburada	(General Manager of CMC Development, Supply Chain & Manufacturing)

Executive Director	Shigeru Doseki	(Deputy Head of Sales & Marketing, General Manager of Product Marketing Department 5 / Product Marketing Departments 4 and 5)
Executive Director	Katsuhiro Kimura	(General Manager of Metropolitan Area, Sales & Marketing)
Executive Director	Masatomi Nemoto	(General Manager of Pharmacovigilance / Safety Management Officer)
Executive Director	Yasuo Suga	(Deputy Head of Sales & Marketing / Product Marketing Departments 1–3)
Executive Director	Tsutomu Iwasa	(General Manager of Western Japan, Sales & Marketing)
Executive Director	Makoto Matsuda	(Deputy Head of Sales & Marketing / Special Assignments)
Executive Director	Yasuo Satake	(General Manager of HR & General Affairs)
Executive Director	Takahiro Yamasaki	(President & CEO, Plusultra pharma GmbH)
Executive Director	Weidong Chen	(General Manager, Jiangsu Nobelpharma Co., Ltd.)
Executive Director	Yumi Imai	(General Manager of PMS Regulatory Compliance & Assurance)
Executive Director	Nobuyuki Sato	(General Manager of Digital Transformation, Administrative Affairs & Corporate Planning)
Executive Director	Eijiro Akatsu	(Head of Administrative Affairs & Corporate Planning, General Manager of Corporate Finance)
Executive Director	Toru Yokoyama	(General Manager of Chubu & Eastern Japan, Sales & Marketing)

(Note: Since the scope of operations includes not only vaccines but also antibody drugs, etc., the name of the division will be changed from Vaccine Business to Bio Business on April 1 to reflect the actual situation.)

(3) Resigning Director (as of March 31, 2022)
Motomichi Kono (Senior Fellow, Project Planning & Development)

2.3.2. Remuneration paid to directors and company auditors

Classification	Headcount	Amount paid
Directors	7	12,100,000 yen
Company auditor	2	4,800,000 yen
Total	9	16,900,000 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: 15 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.

2.4.4Policy 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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Attachment

September 1, 2019 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, as the company is evolving into a new stage, I thought it would be a good idea to offer some kind of 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. In any case, we are not necessarily saying that you have no qualification as line manager just because you cannot carry out on these guidelines. My intention 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, personal friends, and your family.

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.
If you are interested, visit the link below to find about Nakane Tori (Japanese only).
https://www.sanogaku.jp/course/012/

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. 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.

10. 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.

11. 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.

12. 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.

13. 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 relates to No. 11. 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.

14. 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.

15. 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. If you already own shares that are related to your work and want to sell them, it would be safer to consult with the Administration Division before you do so. Unlisted shares can be complicated, so it would be wiser not to deal with them in the first place. 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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