Business Report

(From January 1, 2018 to December 31, 2018)

1. Nobelpharma

1.1. Corporate Mission, Policy and Action Criteria

Corporate Mission

The Company's mission is to "Contribute to society by providing necessary but neglected pharmaceuticals and medical devices." Sales and profits are important management indicators that should be pursued; however, we regard these to be the result of carrying out the mission, as well as a means to accomplish the mission.

The management policy and action criteria are as cited below:

Policy

1. General
    1) Share Mission, Policy and Action Criteria among all stakeholders (employees, shareholders, officers)
        *Unable to share without routine review
    2) Pursue evolution, yet upsizing is not our goal
    3) Comply with regulations and ethical codes
    4) Ensure transparency and disclosure
    5) Launch out overseas
2. Personnel
    1) Value employees and families, respecting self-development
    2) Value "Selected Few" and create an environment for the "Selected Few" to enjoy working
        * "Selected 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 in products and data
    2) Ensure post-marketing safety
    3) Search for seeds externally
4. Capital
    1) Profits as a result/means of achieving the Mission
    2) Focus on higher return on sales/profits per employee
    3) Investment decision by observing damage of failure, not unreliable counts of success
    4) Profits distribution to shareholders (dividends)/employees/internal reserve
        *Dividends: 1/3 of profits after tax
        *Employees: Up to dividends
    5) Asset management only with principal guarantee

Action Criteria

1. Principle

    Give priority to patient benefits if inconclusive
2. Challenge
    1) YMWS: "Yatte Minakucha Wakaranai, shikashi Songiri wo tamerauna"= You never know unless you try, but do not hesitate to cut losses.
    2) ZY: "Zenrei ga nainara Yattemiru"= If no precedence, try first.
3. Speed
    1) Never forget patients are waiting

2) Set a deadline first (specific date) regardless of possible delay
   *Off Limits = “about - ,” “early/late - ,” etc.
3) If there is a failure/trouble, prevent expansion first, then recurrence
4) Fast decisions for < X mil yen by the person responsible
   *X = 3 for Div Mngr; 1 for Dept Mngr/Branch Mngr/PM/PL

4. Cost/Efficiency

1) Never carry/purchase deadwood, never take/cause wasteful actions
2) No overtime work considered good
3) Consider patient needs, scientific rationality and nature of laws/regulations when pursuing higher quality in products/data
4) Pursue cost reduction with the principle of multiple sourcing, while regarding providers as partners

5. Communication/Relationship

1) Never prioritize loyalty to company over morals
2) Rejecting inter-departmental advice and cooperation is a symptom of Big Company Disease.
3) Superiors to confidingly entrust tasks to subordinates, but to never leave them unmanaged
4) Hear anyone out and never interrupt them
5) Start with a conclusion when explaining/responding
6) Mere greetings are significant

1.2. Progress and Results of Operations

	mil yen		Year-on-year	% to total sales	
	2017	2018		2017	2018
Sales	7,236	10,568	146.0%	100.0%	100.0%
Cost of goods sold	1,247	1,450	116.3%	17.2%	13.7%
Gross profit	5,989	9,118	152.2%	82.8%	86.3%
SG&A expense	6,013	7,240	120.4%	83.1%	68.5%
* Personnel cost	1,821	2,254	123.8%	25.2%	21.3%
* R&D expenses	1,676	1,917	114.4%	23.2%	18.1%
Operating income	△23	1,877	-%	△0.3%	17.8%
Non-operating income/expenses	185	82			
Ordinary income	161	1,960	1,212.1%	2.2%	18.6%
Extraordinary income/loss	△60	△101			
Net income before tax	101	1,859	1,837.4%	1.4%	17.6%
Income taxes	48	422	878.6%	0.7%	4.0%
Net income	53	1,437	2,704.3%	0.7%	13.6%
Net income per employee (‘000 yen)	205	5,841			
Retained earnings brought forward					
Beginning balance	679	673			
Prior period adjustment	△27	-			
Dividend	31	17			
Net income	53	1,437			
Ending balance	673	2,093			

* Major items included in SG&A expenses

Total sales in 2018 were 10,568 million yen, up 46% year-on-year. Nobelzin® and Lunabell® posted sales of 4,633 million yen and 2,835 million yen, respectively, accounting for 47.1% and 28.8%, respectively, of total products sales.

The cost of goods sold was 1,450 million yen, up 16.3% year-on-year, accounting for 13.7% of total sales (2017: 17.2%). Sales, general and administrative expenses totaled 7,240 million yen, an increase in 20.4% year-on-year, accounting for 68.5% (2017: 83.1%), mainly including personnel expenses of 2,254 million yen, up 23.8% year-on-year, and 21.3% (25.2% in 2017) of total sales, R&D expenses of 1,917 million yen, up 14.4% year-on-year, and 18.1% (2017: 23.2%) of total sales, outsourcing expenses of 935 million yen and royalty expenses of 423 million yen. Outsourcing expenses mainly included 141 million yen for call center operation by EP-PharmaLine, 89 million yen for safety database construction and operation by CMIC, and 52 million yen for business management service by Hisanaga & Company. Royalty expenses were running royalties of 275 million yen and 116 million yen, respectively, to Jansen Pharma and Pfizer.

As a result, operating profit was 1,877 million yen, a decrease in 23 million yen year-on-year and accounted for 17.8%, down 0.3% year-on-year, of total sales.

Ordinary profit was 1,960 million yen, a jump of 1,212.1% year-on-year, accounting for 18.6% (2017: 2.2%) of total sales, after recording non-operating income of 173 million yen including subsidy revenue of 169 million yen partly offset by non-operating expenses of 90 million yen including interest expenses of 37 million yen and bond interest expenses of 14 million yen.

An extraordinary loss of 101 million yen was recorded due to a loss resulting from typhoon damage of Alabel® in Kansai International Airport. The loss for Alabel® will be recorded as extraordinary income in 2019 as the Company will receive the insurance.

With the income taxes of 422 million yen, net income was 1,437 million yen, a jump of 2,704.3% year-on-year, accounting for 13.6% of total sales (2017: 0.7%), and net income per employee was 5 million yen (2017: 0.2 million yen).

Retained earnings brought forward as of December 31, 2018 were 2,093 million yen, with the beginning balance of retained earnings brought forward of 673 million yen and a dividend payment of 17 million yen.

In March 2018, Medipal Holdings Corporation acquired 20% of outstanding shares of the Company through a private placement. We expect to build a stronger partnership and enhance a smooth personal exchange with Medipal.

Under Medical's collaborative effort for sales of Nobelzin®, the Company achieved sales of 10 billion yen for the first time along with a growth of income.

To sum up our activities in 2018, we have taken the first step in the new stage, i.e. toward a global/centennial company through: (1) newly launching three products, potential primary sources of revenue following Lunabell®, in Japan; (2) gained access to a strong sales and distribution network through strengthening capital tie-up with Medipal Holdings Corporation; (3) secured solid cash flows through Nobelzin®; (4) successfully developed more than one original product made in Japan; (5) these products enabled us to gain a foothold in the US, China and Europe; and (6) these cash flows and an improvement of trust by academia allowed us to strengthen a system to introduce new seeds.

The details are explained below.

1.3. Domestic sales

The table below shows sales by product in 2018 on a wholesale price (NHI price) basis.

Brand Name	Launch	Indication	Sales (on a wholesale price (NHI price) basis) (Yen in millions)		Year-on-year ([2]/[1])
			2017 [1]	2018 [2]	
Nobelzin®	Apr 2008 Mar 2017	Wilson's disease, hypozincemia	2,089	5,245	251.1%
Lunabell® LD Lunabell® ULD	Jul 2008 Sep 2013	Dysmenorrhea	9,912	9,640	97.3%
Nobelbar®	Dec 2008	Neonatal seizures, status epilepticus	112	115	102.2%
Fostoin®	Jan 2012	Status epilepticus, prevention of postoperative seizures, etc.	1,232	1,133	92.0%
Gliadel®	Jan 2013	malignant glioma	982	978	99.5%
Alabel®	Sep 2013	diagnosis of malignant glioma	294	294	100.1%
Indacin®	Jan 2013	patent ductus arteriosus of prematurity	71	60	84.9%
Cosmegen®	Jan 2013	Wilms' tumor, choriocarcinoma, pediatric solid malignant tumor, etc.	17	19	112.5%
Unitalc®	Dec 2013	prevention of recurrent malignant pleural effusion	69	69	99.5%
Respia®	Dec 2014	apnea of prematurity	211	229	108.3%
Rapalimus®	Dec 2014	lymphangioleiomyomatosi s	211	249	118.1%
Zanosar®	Feb 2015	gastroenteropancreatic neuroendocrine tumor	343	368	107.2%
Rapalimus® Gel	Jun 2018	Skin lesions associated with tuberous sclerosis	-	148	-
Titanium bridge	Jul 2018	Adductor spasmodic dysphonia	-	15	-
Jemina®	Oct 2018	Dysmenorrhea	-	125	-
Total			15,554	18,687	120.1%

In 2018, the Company positioned Nobelzin® as the product to most focus on as well as to spread and expand, and it also launched three new products, of which, two products were designated under the "Sakigake" fast-track review system (Rapalimus® Gel in June and TITANBRIDGE® in July) and a treatment for dysmenorrhea (Jemina® in October). We achieved sales of 18.7 billion yen compared with the target of 18.1 billion yen on a wholesale price (NHI price) basis.

Most of our products including Nobelzin® are medicines that are no substitute, and we are working on spreading and expanding them based on guidelines and evidence.

Sales of Lunabell®, which have been our core product so far, are expected to decline significantly in the future as a generic drug of Lunabell® ULD was launched in December 2018. We launched a new product, Jemina®, which is replacing Lunabell®, and in addition, launched an authorized generic (AG) of Lunabell® ULD under cooperation with ASKA Pharmaceutical. Co., Ltd. in order to offset a decrease in revenue.

As of March 1, 2019, 86 MRs cover the entire country, of which 23 MRs are sent by the Medipal Holdings Group. We aim at MR activities by Selected Few and are also actively engaged in PR activities in other channels than MRs by enhancing the customer center and Web site. Sales of Nobelzin® grew followed by sales promotion activities using the AR (authorized medical sales representatives who passed MR certification exam) function of the Medipal Holdings Group, and we use this initiative for Jemina® and Rapalimus® Gel.

For the logistics of the direct-sales products, the Medipal Holdings Group has exclusively taken over the distribution.

1.4. Research and Development (Japan and overseas)

Rapalimus® Gel, a treatment for skin lesions associated with tuberous sclerosis, and Jemina®, a treatment for dysmenorrhea, were approved in 2018 and by following them, we filed NDA for NPC-18, a treatment for tympanic perforation. In addition, the Company achieved expected purpose for the First in Human trial (PI) for cytomegalovirus (CMV) antibody (NPC-21), the Company's first antibody drug, and PIII trial for NPC-15, melatonin.

The Company has been proceeding with the full-scale examination on overseas development since 2017 based on a plan of obtaining approvals for three products of TITANBRIDGE®, Rapalimus® Gel, and NPC-18 in three regions including North America, Europe and China. In 2018, the Company has started meetings with FDA for development and NDA filing in the U.S. for Rapalimus® Gel that FDA designated as an orphan drug in 2017, and hold Q-sub meeting with FDA for TITANBRIDGE®. The third study was commenced for malaria vaccine (NPC-19, prevention of falciparum malaria) in Africa in 2018.

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, 2019. 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 : Short term approval expected with a theme from academia such as a university. 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-18 bFGF, etc.	Tympanic perforation	TRI (Note) Kaken Pharmaceutical	Filed	Sep 2019	III
2	NPC-15 Melatonin	Sleep disorders in children with neurodevelopmental disorder	In-house	Clinical trial in preparation	Mar 2020	I
3	GM-CSF Molgramostim	Pulmonary proteinosis	Savara Inc.	PIII (Global clinical trial)	Jun 2021	II
4	NPC-09 Acetylneuraminic acid	Distal myopathy	In-house	PII/III	TBD	III
5	NPC-21 CMV antibody	CMV infection	Evec Inc.	PI	TBD	I
6	NPC-22 Skopolamin	Salivation	Kitasato University	Non-clinical	TBD	IV
7	NPC-x4 P092	Prion disease	Gifu University	Non-clinical	TBD	IV

Note: TRI (Translational Research Center for Medical Innovation)

B. Life Cycle Management (LCM)

	Compound	Indication	Licensor	Development stage	Estimated approval	Classification
1	NPC-02 Nobelzin®	Child's preparation (new formulation)	National Center for Child Health and Development	PIII	Dec 2020	III
2	NPC-05 Unitalc®	Refractory pneumothorax (new indication)	National Hospital Organization Nagoya Medical Center	PII	Sep 2021	III
3	NPC-06 Fostoin®	Nerve field (new indication)	Pfizer Inc.	PII	TBD	I
4	NPC-12 Rapalimus®	Refractory lymphatic disease (new indication)	Gifu University	PIII	Dec 2020	III
5	NPC-12 Rapalimus®	Fbrodysplasia ossificans progressiva (new indication)	Kyoto University	PII/III	Dec 2020	III
6	NPC-12 Rapalimus®	Pendred syndrome (new indication)	Keio University	PI/IIa	TBD	IV
7	NPC-12 Rapalimus®	Epilepsy with focal cortical dysplasia type II (new indication)	Showa University	PII	TBD	IV
8	NPC-12G Rapalimus® Gel	Neurofibromatosis type I (new indication)	Osaka University	PII/III	Dec 2021	IV

C. Overseas Development

	Compound	Indication	Licensor	Development stage	Estimated approval	Classification
1	NPC-19 (NPC-SE36) Malaria vaccine	Prevention of falciparum malaria	Osaka University GHIT	PIb	TBD	I
2	NPC-18 bFGF, etc.	Tympanic perforation	MEEI/Harvard University	PII	TBD	III
3	NPC-17 Thyroid cartilage fixation device (TITANBRIDGE®)	Adductor spasmodic dysphonia	-	Clinical trial in preparation	TBD	III
4	NPC-12G Rapalimus® Gel	Hemangiofibroma	-	Clinical trial in preparation	TBD	I

Rapalimus® Gel (NPC-12G) and TITANBRIDGE® (NPC-17) launched in 2018 deserve special mention, as they are drugs designated under the "Sakigake" fast-track review system, one of the important measures of the Japanese Ministry of Health, Labour and Welfare ("MHLW"), and they were also designated as an orphan drug and medical device, respectively.

1.5. Finding of New Themes

Business Development & Strategy is responsible for core roles for the Company's open innovation. Specifically, its role is classified into (1) Planning and research for new themes (drugs and medical devices), (2) In/out-licensing negotiations with a new development theme, (3) Acquisition of public subsidy and financing of development expenses, (4) Support for commercialization of academia seeds, (5) Alliance management, (6) Intellectual property management and technology-related contracts, and (7) Procurement negotiations.

The following showed major achievements in 2018.

- Conclusion of a partnership agreement with public institution
- Conclusion of an in-licensing agreement with Evec Inc. for a treatment for CMV infection
- Conclusion of an agreement with LTT Bio-Pharma Co., Ltd. for new indication of the existing products
- Conclusion of memorandum with ASKA Pharmaceutical. Co., Ltd. for OEM agreement and supply of Lunabell® AG
- Support for acquiring subsidy for collaborative research with academia
- Conclusion of collaborative research agreement and provision of research data agreement with multiple academia
- Selection of TITANBRIDGE® by Development of Medical Devices through Collaboration between Medicine and Industry (Standardization and Development/Overseas Development) of Japan Agency for Medical Research and Development (AMED)

In 2018, the Company increased the number of staff engaged in intellectual property rights. The number of patent families with which the Company is involved is 36 (2017: 33) due to an increase in collaboration with academia. We reviewed more than 130 cases resulting from an increase in law-related tasks for technical service contracts. We also worked on employee education and enlightenment activities and hold 11 intellectual property right workshops including four basic classes and seven classes handling popular topics.

The Company engaged in more than 50 purchase negotiations and contributed to achievement of reasonable costs.

1.6. Manufacturing and Capital Expenditure

Most of our products are medicines that are no substitute. The Company has no manufacturing facilities of its own, and outsources manufacturing of both APIs and products to domestic and overseas manufacturers. Under such circumstances, we believe that the stabilization of the drug supply becomes strong by (1) having many inventories of not only products but also important materials, and (2) by ensuring multiple OEM suppliers. In 2019, we secured the second OEM supplier for Nobelzin®. Accordingly, we can cover the majority of expected demand for Nobelzin® in 2019 while we manufactured Nobelzin® tablet of 36 million in 2018. In contrast, we cannot avoid loss on disposal due to a wrong demand forecast as we have many inventories. In 2018, we recognized loss on disposal of inventories of 16 million yen for Rapalimus® Gel but it was within our expectations. We established two logistics centers in both West and East Japan to prepare for disaster and ensure BCP.

The Company has put into place a production system for three new products (Rapalimus® Gel, TITANBRIDGE® and Jemina®) and shipped for the first time. All three products are supplied steadily.

Meanwhile, the reduction of cost of goods manufactured is also an important issue in manufacturing. In 2019, cost of sales increased 16.3% year-on-year while product sales grew 46.0% year-on-year due to reduction of import price of Alabel® and outsourcing expenses of Nobelzin®.

For this period, there was no capital investment related to production.

1.7. Pharmacovigilance & Quality Assurance

Pharmacovigilance & Quality Assurance works on business improvement in a cost-conscious way in compliance with related laws and regulations, by posting its mission of (1) quality assurance and stable supply of products, (2) causing no drug-induced diseases, and (3) passing re-examinations.

We completed compliance inspection of re-examination for Lunabell® ULD in February 2018, and re-examination was completed in March 2019. We filed re-examination of Nobelzin®, a treatment for Wilson's disease, in April 2018 and are working on responding to inquiries. We filed re-examination of Nobelbar®, a treatment for neonatal seizures, in January 2019 and are preparing for compliance inspection.

In terms of safety-related matters, we completed post-marketing surveillance of Rapalimus® Gel and are currently conducting post-marketing surveillance of Jemina®. In 2018, the number of domestic and overseas adverse event reports was 5,438 and 3,612, respectively, 1.5 times and 3.0 times, respectively, compared with 3,583 and 1,198, respectively, in 2017.

In terms of post-marketing surveillance-related matters, a specific use survey of Nobelzin®, a treatment for hypozincemia, reached the target number of registered cases in September 2018 as we strengthened the collaboration/cooperation system with the Medipal Holdings Group. For use investigation of TITANBRIDGE®, we started a new scheme investigation in collaboration with Translational Research Center for Medical Innovation in July 2018.

In terms of quality-related matters, we conducted a GMP audit for 12 manufacturing bases in our OEM suppliers.

1.8. Regulatory Affairs and Negotiations

Regulatory Affairs is responsible for administrative procedures related to the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (PMD Act), negotiations of NHI price and material price, and research and proposals on NHI price system reform, and works to prevent the Company from deviating from medical related laws and regulations. It is also responsible for patient relations.

The Company added a staff in Regulatory Affairs to provide development and regulatory affairs with more strategic feature and to strengthen development and regulatory affairs and administrative procedures (to the Japanese Ministry of Health, Labour and Welfare (MHLW) and Pharmaceutical and Medical Devices Agency (PMDA)). In addition, we undertook systematization of operations (digitization of application/approval information management and NDA filing), which have been insufficient so far, and aim at starting operation by the end of March 2019.

Regulatory Affairs continued to confirm and discuss with relevant departments (Product Management and Quality Assurance) about the “difference between certificates of approval for manufacture and sale and the actual status of manufacturing,” the pending issue in the entire pharmaceutical industry in 2016, and responded to the authority adequately as needed. Accordingly, there was no material problem.

In-house Product Material Committee reviewed 220 sales promotion materials of drugs. The Committee revised and advised as necessary to ensure that adequate sales promotion materials are provided.

Further, Regulatory Affairs undertook a new business of a feasibility study of planning and developed products so that it added a staff in 2019 in order to prepare a system to provide highly precise evaluations promptly corresponding to an increase in new products developed by academia and changes in NHI price conditions.

In terms of industry group activities, Samurai Biotech Association aims at becoming a general incorporated association to raise its status and the Company, as its coordinator company, proceeds with the preparations.

In terms of patient relations, the Company has communications with 22 patient groups and lent its meeting rooms 26 times a year and in addition, 39 employees actively participated as volunteers. Accordingly, the Company received a high evaluation from patient groups with keeping a good relationship. Further, we hold three in-house seminars in which leading members of patient groups are lecturers to bring the fresh voices of patients to our employees.

1.9. Funding and Major Lenders

In 2018, the Company borrowed 1,380 million yen and repaid 1,678 million yen to financial institutions.

The resulting balance of loans payable and bonds as of December 31, 2018 was 5,414 million yen. As the Company has cash and deposits of 4,787 million yen, the actual amount of borrowing is 627 million yen (2017: 1,430 million yen).

As of December 31, 2018, the status of borrowing is as follows:

Long-term loans payable

Mizuho Bank, Ltd.	1,210 million yen
Sumitomo Mitsui Banking Corporation	930 million yen
MUFG Bank, Ltd.	337 million yen
The Shoko Chukin Bank, Ltd.	271 million yen
The Tokyo Shinkin Bank	166 million yen
Japan Finance Corporation	98 million yen
Resona Bank	20 million yen
Total	3,034 million yen

Japan Agency for Medical Research and Development380 million yen

Balance of bonds

2nd straight bond -> Osaka Soda Co., Ltd.	500 million yen (Redemption: Dec 2024)
3rd straight bond -> Medipal Holdings Corporation	600 million yen (Redemption: May 2019)
4th straight bond -> Mizuho Bank, Ltd.	500 million yen (Redemption: Dec 2021)
5th straight bond -> The Shoko Chukin Bank, Ltd.	100 million yen (Redemption: Mar 2020)
6th straight bond -> Resona Bank, Ltd.	300 million yen (Redemption: Mar 2022)
Total	2,000 million yen

1.10. Financial Results, Assets and 2016 Forecast

The Company's financial results, assets and 2018 forecasts are as follows:

mil yen except for *	2015 (Actual results) 13th year	2016 (Actual results) 14th year	2017 (Actual results) 15th year	2018 (Actual results) 16th year	2019 (Forecasts) 17th year
Sales	7,435	6,791	7,236	10,568	12,642
Ordinary income	△270	△56	161	1,960	1,369
Net income	157	93	53	1,437	953
*Net income per share (Note)	5,000 yen	8,000 yen	4,000 yen	111,000 yen	70,000 yen
Total assets	9,671	7,671	8,975	12,204	12,330
Net assets	984	691	685	3,319	4,437
* Equity ratio	10.2%	9.0%	7.6%	27.2%	35.9%
*Net asset per share (Note)	84,000 yen	59,000 yen	58,000 yen	245,000 yen	911,000 yen

(Note) As the Company split its shares in 2017, the number of shares in 2015 and 2016 is converted into the number after the stock split.

1.11. Employees

As of March 1, 2019, the number of employees is 269 (including a total of 103 including 35 seconded employees, 22 temp staff, and 46 contract employees but excluding directors and employees seconded to external organizations) with an average age of 51.9. The number of employees increased by 10 compared with 259 as of March 1, 2018.

Total personnel costs including expenses for seconded employees were 2,254 million yen, up 23.8% year-on-year. The major reason of increase was an increase in the number of staff due to reinforcement of manpower in sales departments associated with an increase in demand for Nobelzin® and launching of new products as well as preparations for overseas business. Although the Company does not recruit new graduates simultaneously, we recruit postdoctorals and those with equivalent status regularly. We recruited two in 2016 and one 2017, and additionally one will join us this April. We have recruited more than ten in total since 2012 and plan to continue to recruit a few every year. We promote temp staff and contracted employees to full-time positions in principle.

We continue to take such initiatives as review of work process, IT promotion and transformation of working style to reduce overtime. In 2018, monthly average overtime in the entire company was 8.7 hours, falling below ten hours for three consecutive years. The rate of annual paid leave taken by employees in 2018 was 81.3%, up 5% year-on-year, maintaining the high level.

In terms of the personnel system, we prioritize health management (Note) initiative and "Support for balance of work and childcare" based on the Act on Advancement of Measures to Support Raising Next-Generation Children and are working on various new themes.

We have paid cash incentives to employees based on the company regulations and in 2019, a total of approximately 166 million will be paid as incentives. It is equivalent to about a half of the dividend payment scheduled in 2019 and the average incentive per employee including seconded employees is approximately 680,000 yen.

(Note) "Health management" is a management method taking into account employees' health from the viewpoint of a company's sustainable growth.

1.12. Issues

In 2019, company-wide issues are six as follows:

(1) Preparation for new development theme and relevant nurturing and recruitment of development staff (Business Development & Strategy, Research & Development)
(2) Acquire approvals and build sales systems in the U.S., China And Europe (Research & Development, President Office)
(3) Secure cash flows to accelerate the above initiatives, completion of reinforcement of domestic sales and nurturing/recruitment of frontline sales personnel and marketing (Marketing & Sales)
(4) Further expansion of Nobelzin®, early growth of Jemina® and Rapalimus® Gel that lag behind, and smooth launch of NPC-18, a new drug to be approved that is a treatment for tympanic perforation (Marketing & Sales)
(5) Filing NDA for NPC-15 (melatonin) in April 2019 and preparation for domestic development of GM-CSF
(6) Acquire profitable NHI price for approved drugs

The mission of domestic sales (Sales & Marketing) is to complete the reinforcement of domestic sales in 2019 and achieve the sales plan of 18.6 billion yen on a wholesale price (NHI price) basis. For Nobelzin®, the mission is to try various measures to continue the momentum so far. We are far from satisfied with initial sales of Jemina® and Rapalimus® Gel launched in 2018 and it is necessary to grow them earlier. To this end, we consider that we have to work with our co-promotion partners of ASKA Pharmaceutical. Co., Ltd. and the Medipal Holdings Group particularly for Jemina®. Although we do not expect large sales for TITANBRIDGE®, as NPC-18, a treatment for tympanic perforation, which is scheduled to be launched in 2019, is a medicine in the same otological field, we will take measures for the otological field and look into the future.

Other missions include re-building of our sales approach taking into account the impact of the working style reform of doctors and guidelines on providing sales information as a recent trend.

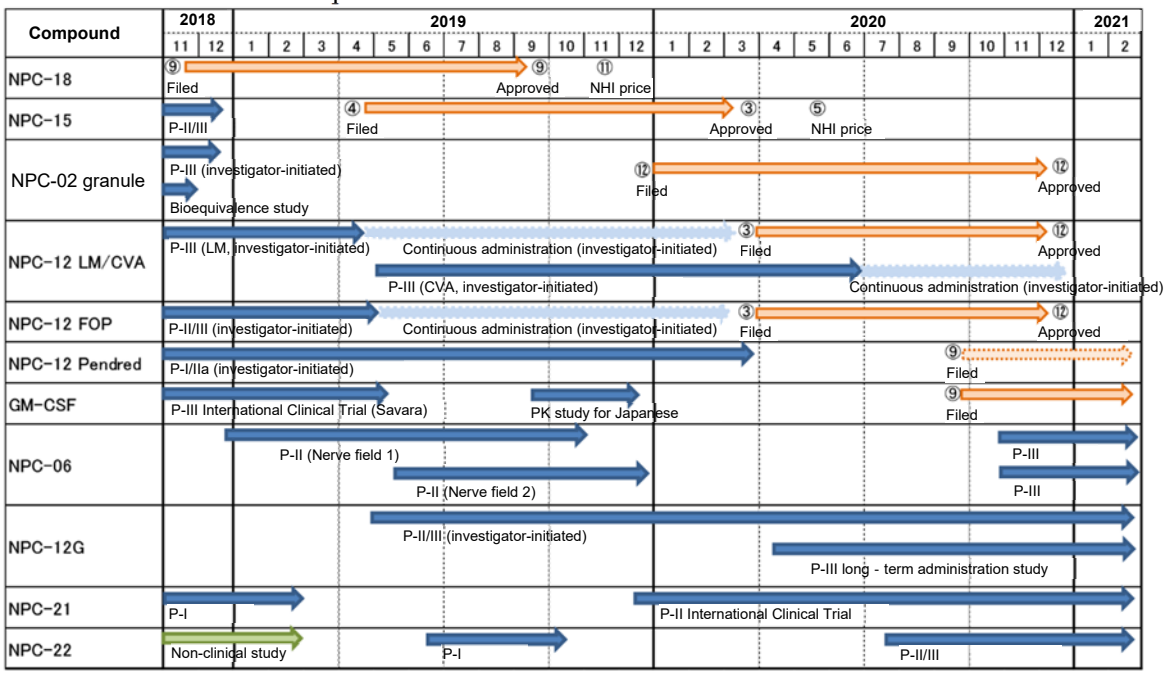
The task to find new themes (Business Development & Strategy) is to strengthen and accelerate the preparation for a new development theme. We will actively introduce and commercialize seeds that meet the Company's mission (providing necessary but neglected pharmaceuticals and medical devices) from academia and bio ventures. We will further promote support for commercialization of academia seeds to ensure a smooth shift to a development phase from a basic study through our involvement with the initial stage.

We continue to make an effort to acquire public subsidy and financing of development expenses for commercialization.

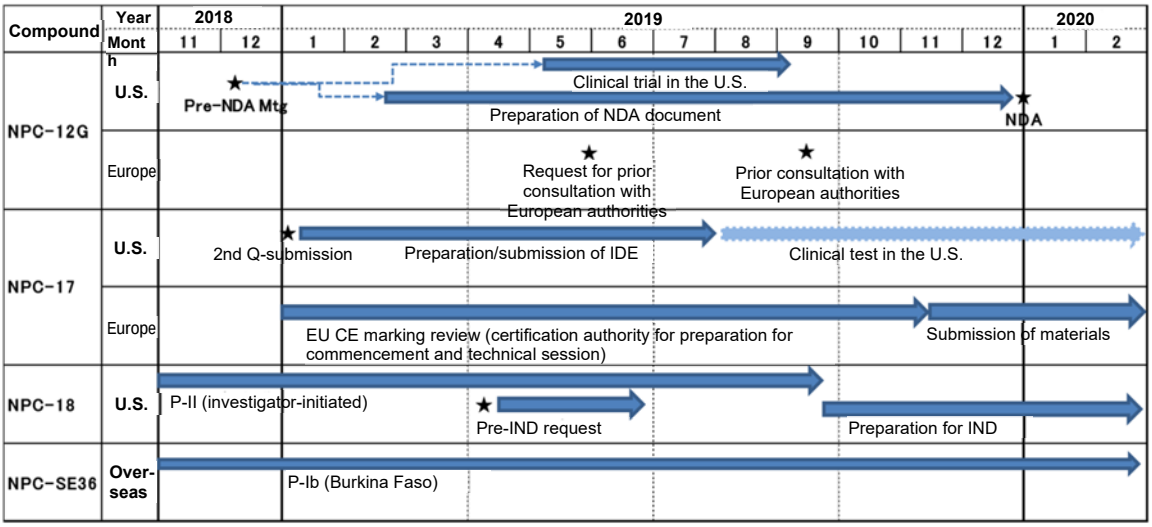
Research & Development will push ahead the development schedule, with the aim of obtaining an approval of NPC-18, a treatment for tympanic perforation, in September 2019 and submitting the NDA for NPC-15, melatonin in April 2019. The development schedule is set out below.

In view of overseas expansion, based on the aforementioned big strategy of launching three products of TITANBRIDGE®, Rapalimus® Gel, and NPC-18 in three regions including North America, Europe and China, the Company will start pre-IND/ pre-NDA/ Q-sub meetings with the US FDA, Scientific Advice meeting with the EU EMA and meeting with China's CFDA/CDE. We also push ahead the preparation for a consortium with related associations for NPC-SE36 (NPC-19, malaria vaccine) and the establishment of a production system associated with a change in manufacturing place.

A. Status of Domestic Development



B. Status of Overseas Development



As for production, Supply Chain & Manufacturing continues to work on a stable supply of the existing products. We are working on launching NPC-18, a treatment for tympanic perforation, as scheduled, which is expected to be launched in 2019, and other tasks for stable supply.

As a part of LCM of the existing products, we established new Formulation Technology Department to strengthen and work on the development of a new drug form.

As a new development theme in the future, we anticipate that bio-pharmaceuticals are increasing, so we will push ahead the establishment of a system capable of development of bio-pharmaceuticals.

Concerning the safety assurance of pharmaceutical products, Pharmacovigilance & Quality Assurance aims at improving quality and making operations more productive in compliance with related laws and regulations.

For filing of re-examination, we push ahead the introduction of a project management system to adequately manage and promote projects.

In terms of the drug use-results survey, we consider the introduction of Electronic Data Capture (EDC) system also to all-case surveillance with the view of improving quality of survey data and streamlining collection of survey slips and follow up.

For safety management, looking ahead into the future overseas business expansion, we are working on introducing the ARIS-g system, a global version of the adverse drug event report database (ARIS-j) that we introduced in 2015. As a part of paperless initiatives, we are proceeding with projects to evaluate workflows and store materials on an electronic medium.

As an effective use of outside resources, we will deepen collaboration and cooperation with the Medipal Holdings Group to secure safety of pharmaceutical products and promote and manage post-marketing surveillance.

As tasks of regulatory affairs and negotiations, Regulatory Affairs actively supports both Research & Development and Pharmacovigilance & Quality Assurance, continues to help efficient and speedy responses to the authority, and shifts to development regulatory affair operations with the aim of promoting a more strategic response of regulatory affairs. Regulatory Affairs plans to review evaluation procedures to ensure an accurate feasibility study, a new business under charge, and introduce a new database and increase by one staff. It also utilizes the know-how for negotiations of NHI/material price to involve a development strategy and support active responses to the authority from the development phase, and it aims to obtain adequate prices for new drugs and medical devices in the future. It also follows NHI price reform and health insurance reform to feed back to in-house strategies from a technical perspective. In addition, through activities of Samurai Biotech Association of which the Company is a board member, lobbying and advising the authorities will be continued.

The tasks of corporate planning and accounting (Administrative Affairs & Corporate Planning) are to increase the accuracy of budgetary variance analysis and the forecasts to implement the annual budget for certain and to put into place a system to ensure flexible management.

For financial affairs, the Company intends to mainly use cash flows arising from future operating activities. In 2019, however, we may borrow from financial institutions to maintain sufficient cash in hand to ensure a flexible response to unscheduled development fund needs as we are repaying borrowings steadily and financing conditions are positive. Also, we eye the possibility of realization of intangible assets that are not directly involved with new drug sales, our core business. We will carry out these activities in anticipation of introducing new development seeds actively from 2019 to 2021.

The Company's two proposals for prevention of falciparum malaria (NPC-19) and CMV infection (NPC-21) were selected by Cyclic Innovation for Clinical Empowerment (CiCLE), a new program launched by Japan Agency for Medical Research and Development (AMED) in FY2017. This is a loan-type system. It has an advantage of risk hedge for a company that will not be required to repay 90% of its borrowing if it should fail, but it also has a disadvantage of limiting free use of the fund as the company is required to pledge the gross amount of loan to be extended. Currently, the Company has pledged cash deposits of 2,050 million yen to AMED.

We are working on putting into place a management system for the establishment of the first overseas base to be scheduled in 2019.

As for the issue of human resources and general affairs (Administrative Affairs & Corporate Planning), we will proceed with correction of age composition and balance of employees that we have been working on so far. In addition, we think about recruitment of foreigners positively.

In terms of working style reform and support for the development of the next generation for which the Japanese government has taken an active initiative, we plan to introduce and expand flexible teleworking and leave for a refreshment/sabbatical leave system that have a more productive leave system than that in other companies in the same industry and to enhance a system supporting the balance of work and childcare. We will also actively undertake health management, aiming at non-smoking recommendations and encouraging all employees to get medical checkups.

In April 2019, the head office will be relocated for the main purpose of earthquake resistance and in addition, we will create an employee-friendly working place.

We will establish various systems including an expatriate employee system in preparation for the full-scale overseas expansion.

We set the targets for the mid-long term future vision of sales and profit as an immovable high goal named North Star. The 2019-23 mid-term business plan is formulated with (1) new development and (2) overseas expansion as the two main pillars. The numerical targets in 2023 as North Star are sales of 50 billion yen and ordinary income of 10 billion yen.

New North Star (2023)	Target
Sales	50 billion yen
Ordinary income	10 billion yen

1.13. Other Important Matters

No matters requiring special attention

2. Current Status of the Company

2.1. Shares (as of December 31, 2018)

(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 & Company (ordinary share)		10,000 shares	(73.9%)
	Medipal Holdings Corporation (ordinary share)		2,705 shares	(20.0%)
	Inabata & Co., Ltd. (ordinary share)		820 shares	(6.1%)

One share of the special-class share issued in June 2017 was repurchased as treasury stock and cancelled in January 2018.

2.2. Share Warrant

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

Not applicable

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

Not applicable

2.2.3. Share warrant in issue

Not applicable

2.3. Corporate Executives

2.3.1. Management Reshuffle

(1) Directors and Company Auditors

As of March 28, 2019, the status of full-time and part-time directors is as follows: CEO and President:

CEO and President:	Jin Shiomura	
Directors (part-time):	Isamu Sojyo	(former Executive Managing Director of Japan Intellectual Property Association)
Directors (part-time):	Nobukuni Taneya	(Part-time company auditor of Arara Inc.)
Directors (part-time):	Takahisa Iizuka	Development Division, Medipal Holdings Corporation)
Directors (part-time):	Nobukazu Kuboi	(General Manager, Financial Management Office and General Manager, Accounting Dept., Inabata & Co., Ltd.)
Directors (part-time):	Toshio Miyata	(Director of Mih Clinic Yoyogi)
Company Auditor (part-time):	Yoshitaka Kishi	(Former full-time company auditor, Dia Rix Co., Ltd.)
Company Auditor (part-time):	Tomoyasu Toyoda	(Company auditor, Medipal Holdings Corporation)

(2) Executive Officers and Directors

As of March 28, 2019, the status of executive officers and directors is as follows:

Vice President & Chief Operating Officer:	Shigeki Shimasaki	(Head of Research & Development)
Chief Operating Officer:	Arata Tabata	(Head of Business Development & IP Management)
Senior Executive Officer:	Tetsuo Hayase	(Head of Supply Chain & Manufacturing)
Executive Officer:	Kenji Shimizu	(Deputy Head of Research & Development)
Executive Officer:	Akira Ikeda	(Deputy Head of Administrative Affairs & Corporate Planning)
Executive Officer:	Masato Iwamoto	(General Manager of Supply Chain Management, Supply Chain & Manufacturing)
Executive Officer:	Hitoshi Hasegawa	(Head of PMS Regulatory Compliance & Assurance, Safety Management Officer)
Executive Officer:	Yoshiki Yagi	(Head of Project Planning & Development)
Executive Officer:	Toshiaki Okamura	(Head of Regulatory Affairs)
Executive Officer:	Kozo Hayase	(Head of Administrative Affairs & Corporate Planning)
Executive Officer:	Yoshihide Yamamoto	(Head of President's Office)
Executive Officer:	Seiu Iida	(General Marketing Compliance Offices)
Acting Executive Officer:	Hitoshi Yokoyama	(Head of Sales & Marketing, seconded from Medipal Holdings Corporation)
Executive Director:	Masanori Osakabe	(Deputy Head of Research & Development)
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	(Branch Manager of Tokyo Branch, Marketing & Sales)
Executive Director:	Katsuhiro Kimura	(Deputy Head of Marketing & Sales)
Acting Executive Director:	Shotaro Goda	(Head of Overseas Business Development, seconded from Mitsubishi Chemical Corporation)

(Note) Effective March 1, 2019, the Company abolished and separated Business Development & Strategy into new Business Development & IP Management and Project Planning & Development in order to clarify responsible operations and promote streamlining. Effective March 28, 2019, Overseas Business Development was established as a department responsible for overseas operations.

(3) Executive officers resigned (as of March 28, 2019)

Tsutomu Sugaya (scheduled to assume the office of Counsellor)

2.3.2. Remuneration paid to directors and company auditors

Classification	Head-count	Amount paid
Directors	6	9,973,000 yen
Company auditor	2	4,400,000 yen
Total	8	14,373,000 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: 13 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 to 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 our 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.

2.5. Other matters

Nobelpharma Co., Ltd. has relocated the headquarters to the following address effective April 1, 2019.
New address: 1-17-24 Shinkawa, Chuo-ku, Tokyo 104-0033
New Tel: +81-3-6670-3800, Fax: +81-3-6670-3801

End of document