Business Report

(From January 1, 2017 to December 31, 2017)

1. Nobelpharma

1.1. Progress and Results of Operations

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: The action criteria were slightly changed.

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

As of March 2018, the Company is marketing the 12 new ethical drugs listed below. In March 2017, Nobelzin®, our first pharmaceutical product, obtained an approval for a new indication of hypozincemia in addition to Wilson's disease.

	Brand Name	Launch	Indication	Route of Administration	Licensor	2017 Sales (NHI price basis) Yen in millions	Sales Channel	Remarks
1	Nobelzin®	Apr 2008	Wilson's disease Hypozincemia (approved in March 2017)	Oral Administration	Teva (Wilson's disease only)	2,089	Direct	
2	Lunabell® LD Lunabell® ULD	Jul 2008 Sep 2013	Dysmenorrhea	Oral Administration	Janssen	9,912	Nippon Shinyaku Fuji Pharma	Both products distributed by two companies
3	Nobelbar®	Dec 2008	Neonatal seizures, status epilepticus	Intravenous injection	In-house	112	Direct	
4	Fostoin®	Jan 2012	Status epilepticus, prevention of postoperative seizures, etc.	Intravenous injection	Pfizer	1,232	Eisai	Co-promotion
5	Gliadel®	Jan 2013	malignant glioma	Interstitial chemotherapy	Eisai	982	Marketing Approval (MA) transferred to Eisai	Co-promotion (Contracted product)
6	Alabel®	Sep 2013	diagnosis of malignant glioma	Oral Administration	SBI Pharmaceuticals (medac)	294	Direct	
7	Indacin®	Jan 2013	patent ductus arteriosus of prematurity	Intravenous injection	Lundbeck	71	Direct	MA transferred from MSD
8	Cosmegen®	Jan 2013	Wilms' tumor, choriocarcinoma, pediatric solid malignant tumor, etc.	Intravenous injection	Lundbeck	17	Direct	MA transferred from MSD
9	Unitalc®	Dec 2013	prevention of recurrent malignant pleural effusion	Intrapleural	Novatech	69	Direct	
10	Respia®	Dec 2014	apnea of prematurity	Intravenous injection/oral liquid	Nippon Boehringer	211	Direct	
11	Rapalimus®	Dec 2014	lymphangioleiomyomatosis	Oral Administration	Pfizer	211	Direct	
12	Zanosar®	Feb 2015	gastroenteropancreatic neuroendocrine tumor	Intravenous injection	Keocyt	343	Direct	
	Total					15,554		

(Note) The total sales included sales of Foscavir®, whose sales were terminated in 2017.

Sales increased significantly due to the growth of adoption and prescription of Nobelzin® for hypozincemia. Sales of Lunabell® exceeded the budget significantly as the impact of the generic drug of Lunabell® LD was minimized. Sales of Zanosar® increased strongly from the previous year though it fell short of the budget. Sales of Fostoin® and Gliadel® decreased negatively affected by competitive products.

Sales for each product were shown in the above table and the total sales were 15,554 million yen on a wholesale price (NHI price) basis and 6,675 million yen on a Company price basis. Sales of the Company from the Lunabell® family were 3,014 million yen, accounting for 45.2% of total sales. Adding royalty revenue of 561 million yen, total sales in 2017 were 7,236 million yen, up 6.6% year-on-year.

The cost of goods sold was 1,247 million yen, down 22.9% year-on-year, accounting for 17.2% of total sales (2016: 23.8%). Sales, general and administrative expenses totaled 6,013 million yen, up 11.2% year-on-year, accounting for 83.1% (2016: 79.6%), mainly including personnel expenses of 2,046 million yen, up 6.7% year-on-year, and 28.3% (2016: 28.2%), R&D expenses of 1,676 million yen, up 4.5% year-on-

year, and 23.2% (2016: 23.6%), royalty expenses of 721 million yen and outsourcing expenses of 677 million yen. Royalty expenses were running royalties of 566 million yen and 121 million yen, respectively, to Jansen Pharma and Pfizer. The outsourcing expenses mainly included 78 million yen for call center operation by EP-PharmaLine, 78 million yen for safety database construction and operation by CMIC, 41 million yen for outsourcing expense of drug use investigation by A2 Healthcare Corp., 37 million yen for business management service by Hisanaga & Company and 35 million yen for system development by Perspective Co., Ltd.

The resulting operating loss was 23 million yen (2016: operating loss of 233 million yen), accounting for 0.3% of total sales (2016: 3.4%).

Ordinary income was 161 million yen (a loss of 56 million yen in 2016), accounting for 2.2% (2016: 0.8%) of total sales, after recording non-operating income of 267 million yen including subsidy revenue of 198 million yen partly offset by non-operating expenses of 81 million yen including interest expenses of 33 million yen and bond interest expenses of 21 million yen.

An extraordinary loss of 60 million yen was posted as a loss related to the recall of Lunabell® ULD.

With the income taxes of 20 million yen and income taxes-deferred of 27 million yen, net income was 53 million yen, down 43.5% year-on-year, accounting for 0.7% of total sales (2016: 1.4%), and net income per employee was 205,000 yen (2016: 399,000 yen).

Retained earnings brought forward as of December 31, 2017 were 673 million yen, with the beginning balance of retained earnings brought forward of 651 million yen, a decrease in 27 million yen from 679 million yen as of December 31, 2016 due to adjustment of the beginning balance to reflect expenses incurred in the previous year, and a dividend payment of 31 million yen.

To sum up our activities in 2017, increases in sales and income due to changes in product mix with lower cost rate, partially offset by application expenses of new products included in research and development expenses and initial sales expenses, contributed to improvement of ordinary income by an increase in 217 million yen from the previous year, without slowing down research and development.

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Item	mil yen		Year-on-year	% to total sales	
	2016	2017		2016	2017
Sales	6,791	7,236	106.6%	100.0%	100.0%
Product sales	6,004	6,675	111.2%	88.4%	92.2%
Other	787	561	71.3%	11.6%	7.8%
Cost of goods sold	1,617	1,247	77.1%	23.8%	17.2%
Gross profit	5,174	5,989	115.8%	76.2%	82.8%
SG&A expense	5,407	6,013	111.2%	79.6%	83.1%
* Personnel cost	1,917	2,046	106.7%	28.2%	28.3%
* R&D expenses	1,603	1,676	104.5%	23.6%	23.2%
* Commission fee	714	677	94.8%	10.5%	9.4%
* Loyalty expenses	701	721	103.0%	10.3%	10.0%
Operating income	△233	△23	-	△3.4%	△0.3%
Non-operating income	242	267	110.4%	3.6%	3.7%
Non-operating expenses	65	81	125.2%	1.0%	1.1%
Ordinary income	△56	161	-	△0.8%	2.2%
Extraordinary income	243	-	-	3.6%	-
Extraordinary loss	49	60	122.7%	0.7%	0.8%
Net income before tax	137	101	73.5%	2.0%	1.4%
Income taxes	43	48	109.9%	0.6%	0.7%
Net income	93	53	56.5%	1.4%	0.7%
Ordinary income per employee (‘000 yen)	△239	624	-	-	-
Net income per employee (‘000 yen)	399	205	51.3%	-	-
Retained earnings brought forward					
Beginning balance	637	679	-	-	-
Prior period adjustment	-	△27	-	-	-
Retirement of treasury stock	-	-	-	-	-
Dividend	52	31	-	-	-
Net income	93	53	-	-	-
Ending balance	679	673	-	-	-

* Major items included in SG&A expenses

1.2. Sales

Sales on a wholesale price (NHI price) basis in 2017 are summarized as follows.

Brand Name	Wholesale sales (NHI price basis, mil yen)		Year-on-year ([2]/[1])
	2016 [1]	2017 [2]	
Nobelzin®	230	2,089	908%
Lunabell® (LD), ULD	10,122	9,912	98%
Nobelbar®	124	112	90%
Fostoin®	1,390	1,232	89%
Foscavir®	421	10	2%
Gliadel®	1,077	982	91%
Alabel®	287	294	102%
Indacin®	75	71	95%
Cosmegen®	18	17	94%
Unitalc®	67	69	104%
Respia®	193	211	109%
Rapalimus®	182	211	115%
Zanosar®	276	343	124%
Total	14,463	15,554	108%

In 2017, we positioned Nobelzin®, which obtained an approval for a new indication of hypozincemia, as the product to most focus on and aimed at sales targets on a wholesale price (NHI price) basis of 15.1 billion yen including 9 billion yen of Lunabell®, 2.4 billion yen of Nobelzin® and 3.7 billion yen of other. As a result, we achieved sales of 15.5 billion yen including 9.9 billion yen of Lunabell®, 2.1 billion yen of Nobelzin® and 3.5 billion yen of other.

For Nobelzin®, the most focused on product in 2017, the Company's MRs promoted sales to hospitals with 200 beds or more, with contracting co-promotion to the Medipal Holdings Group, our general agent of direct sales products, and ASKA Pharmaceutical Co., Ltd. for gynecology and obstetrics, to those with 199 beds or less, and accordingly, sales significantly increased to 2.1 billion yen though it fell short of the plan of 2.4 billion yen. 880 hospitals with 200 beds or more and 10,400 medical institutions with 199 beds or less adopted Nobelzin®, and we expect further expansion of the number of medical institutions adopting the drug and prescription.

Lunabell®, our core product, is marketed on complete consignment basis by Nippon Shinyaku and Fuji Pharma. As a generic competitor of Lunabell® LD was launched in December 2015, sales of Lunabell® significantly dropped in 2016. In 2017, however, the total Lunabell® family increased by 900 million yen compared with the budget (sales of 9.9 billion yen, 110% of the budget and down 2% year-on-year).

Sales of another core product of Fostoin® achieved the budget but fell short of the previous year's result (sales of 1.2 billion yen, 102% of the budget and down 11% year-on-year). Sales of Zanosar®, which launched in February 2015, grew significantly from the previous year though falling short of the budget by appealing its position in guidelines (sales of 300 million yen, 96% of the budget and up 24% year-on-year).

As of March 1, 2018, 83 MRs cover the entire country, of which 29 MRs are sent by the Medipal Holdings Group. We aim at MR activities with high quality by a Selected Few and are also actively engaged in handling of inquiries through other channels than MRs by enhancing the customer center and Web site. The sales method using the AR function of the Medipal Holdings Group successfully increased sales of Nobelzin®, which is a new method that has never been applied in the pharmaceutical industry.

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

1.3. Manufacturing and Capital Expenditure

The Company has no manufacturing facilities of its own, and outsources manufacturing of both APIs and products to domestic and overseas manufacturers. Accordingly, we undertake initiatives by setting a stable supply of products as one of the big targets. We are working on building a stable supply system for products outsourcing to overseas manufacturers, and aim at building a stable supply system by adding domestic manufacturers to ensure multiple suppliers.

For Fostoin® intravenous injection supply from domestic API and formulation manufacturers was started, and we started the primary packaging for Rapalimus® tablet in Japan to prevent defects arising from the primary packaging by overseas manufacturers, which is running steadily.

Meanwhile, the reduction of cost of goods manufactured is also an important issue in manufacturing. The aforementioned shift of manufacturing of Fostoin® intravenous injection and Rapalimus® tablet to Japan resulted in a decrease in cost per year of 90 million yen and 6 million yen, respectively. In 2017, we completed mechanization of the visual inspection for Respia® intravenous injection/oral liquid and accordingly, we expect the annual cost reduction effect of 20 million yen in 2018.

In view of the expansion of demand for Nobelzin® arising from a new indication, we are significantly increasing our capacity of supply. In 2016 and 2017, we produced 13 million tablets for 25 mg tablet and 50 mg tablet, respectively. This can be satisfied with the majority of demand expected in 2018, not only meeting with 2017 demand. In addition, our API manufacturer established a new production line of zinc acetate for the Company and our formulation manufacturer increased production capacity. By these measures, we can increase production volume and reduce cost further in 2018.

In 2017, our capital investment was for the following one equipment.

> Cross rotary mixer: (Manufacturing equipment for Nobelzin® granule scheduled to be launched in 2019, investment amount of 15 million yen, to be placed in Choseido Pharmaceutical Co.,Ltd., an OEM supplier)

1.4. Research and Development

In the past the Company mainly developed drugs that had already been approved in Europe and the US but were not approved in Japan (“unapproved drugs”), and smoothly obtained approvals. Recently, the long-lasting social issue of unapproved drugs has been largely solved and the Company is shifting its target seeds to more difficult drugs that originated in Japan.

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, 2018. Many are drugs based on new concepts that originated in Japan. Of these, we have voluntarily developed new drugs of melatonin (NPC-15, a treatment for sleep disorders in children with neurodevelopmental disabilities) and Jemina® combination drug (NPC-16, a treatment for dysmenorrhea, Ultra-LEP combination drug) without public support funds.

In 2017, a new medical device, TITANBRIDGE® (NPC-17 for adductor spasmodic dysphonia) and newly indicated Nobelzin® (NPC-02, a treatment for Hypozincemia), our LCM product, were approved. Rapalimus® Gel (NPC-12G, a treatment for skin lesions associated with tuberous sclerosis) was approved in March 2018, and Jemina® combination tablet is expected to be approved in June 2018. Following these products, we are currently preparing for filing NDA for NPC-18, a treatment for tympanic perforation.

The Company has been proceeding with the full-scale examination on overseas development since 2017 based on a strategy of obtaining approvals for three products of TITANBRIDGE®, Rapalimus® Gel, and NPC-18 in three regions including North America, Europe and China. Rapalimus® Gel was designated as an orphan drug by the US FDA in 2017. We are preparing for a challenge test in Germany for malaria vaccine (NPC-19, prevention of falciparum malaria) in parallel with the third study in Africa to be commenced in 2018.

As for the financing method for development funds including Overseas Development, we are considering obtaining pubic funds in addition to operating income and intend to introduce risk money according to the degree of risk of the theme.

Development items are classified into the following six classifications based on the market size:

I : Potential primary sources of revenue following Lunabell® (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.
V : LCM of the existing commercialized products. Lower development cost and increased marginal profit expected.
VI : Theme under research (No applicable item in the table below)

A. New Drugs and Medical Devices

	Compound	Indication	Licensor	Development stage	Estimated approval	Classification
1	NPC-17 Thyroid cartilage fixation device (TITANBRIDGE®)	Adductor spasmodic dysphonia	Foundation of Biomedical Research and Innovation (Kobe) Kumamoto University Wakayoshi Seisakusho	Approved	Dec 2017 (Approved)	III
2	NPC-16 Ultra-LEP combination drug (Jemina® combination tablet)	Dysmenorrhea	In-house	Under review	Jun 2018	I
3	NPC-18 bFGF, etc.	Tympanic perforation	Foundation of Biomedical Research and Innovation (Kobe) Kaken Pharmaceutical	Clinical trial in preparation	Dec 2018	III
4	NPC-15 Melatonin	Sleep disorders in children with neurodevelopmental disabilities	In-house	PIII	Mar 2020	I
5	GM-CSF Molgramostim	Pulmonary proteinosis	Savara Inc.	PIII (Global clinical trial)	Sep 2020	II
6	NPC-09 Acetylneuraminic acid	Distal myopathy	In-house	PII/III	TBD	III
7	NPC-x3 Pyruvic acid	Mitochondrial disorders	Kurume University	PII	TBD	IV
8	NPC-20 (SR-16234) SERM	Endometriosis	SRI	PI in preparation	TBD	I
9	NPC-21 CMV antibody	CMV infection	Undisclosed	PI in preparation	TBD	I
10	NPC-22 Skopolamin	Salivation	Kitasato University	Non-clinical	TBD	IV
11	NPC-x4 P092	Prion disease	Gifu University	Non-clinical	TBD	IV

B. Life Cycle Management (LCM)

	Compound	Indication	Licensor	Development stage	Estimated approval	Classification
1	NPC-02 Nobelzin®	Hypozincemia (new indication)	-	Approved	Mar 2017 (Approved)	I
2	NPC-12G Rapalimus® Gel	Skin lesions associated with tuberous sclerosis (new indication, new formulation)	Osaka University	Approved	Mar 2018 (Approved)	III
3	NPC-02 Nobelzin®	Child's preparation (new formulation)	National Center for Child Health and Development	PIII	Jun 2020	III
4	NPC-05 Unitalc®	Refractory pneumothorax (new indication)	National Hospital Organization Nagoya Medical Center	PII	Sep 2020	III
5	NPC-06 Fostoin®	Nerve field	Pfizer Inc.	PII in preparation	TBD	V
6	NPC-12 Rapalimus®	Refractory lymphatic disease (new indication)	Gifu University	PIII	Sep 2020	III
7	NPC-12 Rapalimus®	Fbrodysplasia ossificans progressiva (new indication)	Kyoto University	PII	Sep 2020	III
8	NPC-12 Rapalimus®	Pendred syndrome (new indication)	Keio University	PII	TBD	IV
9	NPC-12 Rapalimus®	Epilepsy with focal cortical dysplasia type II (new indication)	Showa University	PII in preparation	TBD	IV
10	NPC-12 Rapalimus®	Prevention of GVHD after hematopoietic stem cell transplantation (new indication)	Hiroshima University	PII in preparation	TBD	IV
11	NPC-12G Rapalimus® Gel	Neurofibromatosis type I (new indication)	Osaka University	PII/III in preparation	TBD	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.	Myringa regeneration	MEEI	PII	TBD	III
3	NPC-17 Thyroid cartilage fixation device (TITANBRIDGE®)	Adductor spasmodic dysphonia	-	Clinical trial in preparation	TBD	III
4	NPC-12 G Rapalimus® Gel	Hemangiofibroma	-	Clinical trial in preparation	TBD	III

TITANBRIDGE® (NPC-17) and Rapalimus® Gel (NPC-12G) deserve special mention, as they were 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 demonstrated positive outcomes in their clinical studies. So, the Company filed the NDA after completion of "Comprehensive evaluation under the Sakigake system" in 2017. NPC-17 was approved in December 2017 with less than six months from the NDA filing in June 2017 and likewise, NPC-12G was approved in March 2018 with less than six months from the NDA filing in October 2017. These two products were also designated as an orphan drug and medical device, respectively.

In addition, 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. We are committed to promoting development in both Japan and abroad in collaboration with AMED.

1.5. Business Development & Strategy

Business Development & Strategy is responsible for core roles for the Company's open innovation as well as for planning and contacts for business negotiations in Japan and abroad. Specifically, its role is classified into (1) Planning and research for new themes and feasibility study, (2) In/out-licensing negotiations with a potential business partner for a new development theme, (3) Acquisition of public subsidy and financing of development expenses for commercialization, (4) Alliance management with the existing partners, (5) Intellectual property management and technology-related contracts, and (6) Procurement negotiations. The following is a summary of each initiative in 2017.

(1) The Company is cultivating a considerable number of new seeds including some projects from domestic universities and public research institutions as well as foreign companies, actively researching and evaluating them, and considering suitability with the Company's mission and for potential commercialization. As a part of such activities, we entered into 1) joint research agreements with two universities under the basic agreement for access to seeds entered into with Foundation for Biomedical Research and Innovations in 2016, 2) a partner agreement with a public research institution, and 3) agreements with two universities for an investor-initiated trial for a new indication of the existing products.

(2) Conclusion of an in-licensing agreement with a domestic venture company for a treatment for CMV infection in January 2018

(3) Negotiations for intellectual property issues for application and selection of our two proposals of malaria vaccine and CMV infection in CiCLE sponsored by AMED

(4) Completion of compensation issues of the existing agreement and termination of collaboration under the existing agreement

(5) The number of patent families with which the Company is involved is 33 (2016: 23) mainly due to an increase in collaboration with academia. We also hired a new lawyer to strengthen a backup system of technology-related contracts, reviewing more than 110 cases in a half year.

(6) The Company engaged in more than 30 purchase negotiations to reduce costs, which may impact on 2018 and onward.

1.6. Pharmacovigilance & Quality Assurance

Pharmacovigilance & Quality Assurance is largely responsible for three areas: (1) quality assurance for manufacturing, (2) safety control for the vigilance of side effects and adverse events and (3) Post-marketing Surveillance (PMS) for pharmacovigilance. The objectives of (1) is quality assurance and stable supply of products, and (2) and (3) are to avoid causing drug-induced diseases and to pass re-examinations, and it is important to achieve these objectives efficiently within pertinent laws and regulations.

We filed re-examination of Lunabell® ULD and completed compliance inspection in February 2018. Currently, the authorities are reviewing its re-examination application documents. For Nobelbar®, the Company received a notice of re-examination result in December 2017, and it passed re-examination through the result of not meeting any of the events of denial (Category 1).

In terms of safety-related matters, we adequately carried out post-marketing surveillance of Nobelzin® associated with a new indication of hypozincemia and worked on collecting safety information. Also, we revised package inserts of five products.

In terms of post-marketing surveillance-related matters, we commenced a specific use survey of Nobelzin®, a treatment for hypozincemia, using the collaboration/cooperation system with the Medipal Holdings Group. For use investigation of TITANBRIDGE®, we are proceeding with planning and implementation under a new scheme in collaboration with Foundation for Biomedical Research and Innovations.

In terms of quality-related matters, in line with the NDA filing of TITANBRIDGE®, we completed compliance inspection of QMS (Quality Management System) in October 2017.

In 2017, the number of domestic and overseas adverse event reports was 3,583 and 1,198, respectively. In 2016, it was 5,100 and 1,865, respectively.

The table below shows the comparison of personnel cost and general and administrative expenses in Pharmacovigilance & Quality Assurance in 2016 and 2017.

	2016 (‘000 yen)	2017 (‘000 yen)
Personnel cost	314,981	325,694
General and administrative expenses	449,336	318,250
Total	764,317	643,944

In 2017, we improved resources and work process including enhancement of data quality while we responded to re-examination of two products, established QMS system of medical device and started a use survey of two products. As a result, we reduced entire expenses by 15% compared with 2016.

1.7. Regulatory Affairs

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 works on obtaining a fair price of the Company’s products and maximizing business value through NHI price negotiations along with research and proposal activities.

In terms of development, Regulatory Affairs, jointly with Research & Development, discusses all our products with PMDA.

After the Japanese Ministry of Health, Labour and Welfare (MHLW) requested all pharmaceutical companies in Japan to review certificates of approval, Regulatory Affairs held regular meetings with Product Management and Quality Assurance to obtain and check information/data on drug manufacturing by domestic and overseas OEM suppliers and to detect early any difference between certificates of approval and the actual status of manufacturing, and ensure prompt responses to the authorities.

In-house Product Material Committee reviewed 139 sales promotion materials of drugs while the industry set self-standards and required preparing and providing reasonable sales promotion materials. The Committee revised and advised as necessary to ensure that adequate sales promotion materials are provided to medical institutions.

In terms of patient relations, the Company has communications with 20 patient groups and lent its meeting rooms 27 times a year and in addition, 35 employees actively participated as volunteers. Accordingly, the Company received a high evaluation from patient groups with keeping a good relationship.

For NHI/material price-related matters, an increase in staff enabled improvement of precision of the estimated NHI price of development candidates and also contributed to improving the probability of business feasibility. In addition, we explained Cosmegen®, an unprofitable item, to the authorities and realized price revision of 20% in NHI price revision in April 2018.

The Company proceeds with research and proposal activities on healthcare policy in Japan including NHI price reform through activities as a board member of Samurai Biotech Association. Samurai Biotech

Association submitted a request to the Minister of MHLW, gave opinions before the Special Committee on Drug Prices in Central Social Insurance Medical Council and participated in the hearing by the Care Working Group in Regulatory Reform Promotion Council, and produced the results.

Regulatory Affairs increased staff in both regulatory affairs and NHI price operations to strengthen and enhance development regulatory affairs and NHI price negotiations.

1.8. Funding and Major Lenders

In 2017, the Company borrowed 2,100 million yen and repaid 906 million yen to financial institutions.

The resulting balance of loans payable and bonds as of December 31, 2017 was 5,712 million yen. As the Company has cash and deposits of 4,282 million yen, the actual amount of borrowing is 1,430 million yen (2016: 861 million yen).

As of December 31, 2017, the status of borrowing is as follows:

Short-term loans payable	
Sumitomo Mitsui Banking Corporation, Kandaekimae Branch	500 million yen
Long-term loans payable	
Mizuho Bank, Ltd., Yokoyamacho Branch	1,080 million yen
Sumitomo Mitsui Banking Corporation, Kandaekimae Branch	590 million yen
The Shoko Chukin Bank, Ltd., Kanda Branch	392 million yen
The Bank of Tokyo-Mitsubishi UFJ, Ltd., Odenmacho Branch	297 million yen
Japan Finance Corporation	121 million yen
The Tokyo Shinkin Bank, Nihonbashi Branch	72 million yen
Resona Bank, Akihabara Branch	60 million yen
Total	2,612 million yen
Balance of bonds	
Straight bond	
2nd straight bond -> Osaka Soda Co., Ltd.	500 million yen
3rd straight bond -> Medipal Holdings Corporation	1,200 million yen
4th straight bond -> Mizuho Bank, Ltd.	500 million yen
5th straight bond -> The Shoko Chukin Bank, Ltd.	100 million yen
6th straight bond -> Resona Bank, Ltd.	300 million yen
Total	2,600 million yen

1.9. Financial Results, Assets and 2016 Forecast

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

mil yen except for *	2014 12th year	2015 13th year	2016 14th year	2017 (Actual results) 15th year	2018 (Forecasts) 16th year
Sales	6,628	7,435	6,791	7,236	10,160
Ordinary income	577	△270	△56	161	607
Net income	240	157	93	53	402
* Net income per share	182,000 yen	54,000 yen	80,000 yen	4,000 yen	29,000 yen
Total assets	9,291	9,671	7,671	8,975	9,105
Net assets	1,238	984	691	685	2,415
* Equity ratio	13.2%	10.2%	9.0%	7.6%	26.5%
* Net asset per share	941,000 yen	844,000 yen	593,000 yen	58,000 yen	178,000 yen

(Note) In FY2017, one common share of the Company was divided into ten (10) shares of common share.

1.10. Employees

As of March 1, 2018, the number of employees is 259 (including a total of 100 including 34 seconded employees, 19 temp staff, and 47 contract employees but excluding directors) with an average age of 52.0. The number of employees increased by 24 compared with 235 (including seconded employees) as of March 1, 2017.

Total personnel costs including expenses for seconded employees and temp staff were 2,110 million yen, up 8.0% year-on-year, of which, expenses for temp staff were 63 million yen. The major reason of increase was recruitment of 15 contract MRs, mainly young staff, with an aim of reinforcing and increasing staff in sales departments in preparation for new indication of Nobelzin® and a series of launching of new products in the future. The number of staff in other departments slightly increased other than an increase in staff associated with preparation 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 additionally one will join us this April. We have recruited nine postdoctorals in total since 2012 and plan to continue to recruit a few every year.

The average age of the Company has been younger through these recruiting activities, which is intended to compensate for bias toward seniors and to maintain and revitalize the organization.

Although certain departments kept monthly average overtime of more than 20 hours, overtime was improved in the entire company due to a review of work process and split of work and promotion of various systems in view of work-life balance. In FY2017, monthly average overtime was approximately 9 hours, which was the same as the previous year. In line with dissemination of various systems related to transformation of working style, the rate of annual paid leave taken by employees in 2017 was 76.1%, maintaining a high level as in the previous year.

In January 2017, we renewed the personnel system drastically for the first time since the establishment, including a review of the compensation package, introduction of the retirement lump-sum grants system and transparent personnel evaluation system. We strive to disseminate these initiatives over the year and also work on such themes as transformation of working style and healthy management. Specifically, we have launched various systems including promotion of taking paid leave, teleworking, consecutive leave system and encouraging use of a help program to quit smoking.

1.11. Issues

In 2018, there are five company-wide issues as follows:

(1) Strengthening sales of Nobelzin® and securing profit
(2) Obtaining approvals of development items as planned and obtaining profitable drug prices
(3) Full-scale development for overseas marketing authorization and preparation of overseas sales

(4) Active access to seeds from academia
(5) Optimization of cost of related operations such as post-marketing surveillance and effective use of external resources

The Sales & Marketing mission is to ensure achievement of this year's sales target of 17.7 billion yen (8.3 billion of Lunabell®, 6 billion yen of Nobelzin® and 3.4 billion yen of other direct sales and co-promotion products) on an NHI price (wholesale price) basis. The most important mission is to achieve sales of Nobelzin® that meet or exceed its sales target of 6 billion yen. As measures to strengthen sales of Nobelzin®, we established the Nobelzin® Mobilization Project Division in the previous year to actively recommend zinc substitution therapy (Nobelzin®) to all hospital departments. We will make further efforts to spread Nobelzin®. In particular, in the first half of 2018, Sales & Marketing will invest 70% of its operating resources (manpower, goods and capital) in "hypozincemia" of Nobelzin®. Regarding the practitioner market to which the Company does not have access, the Medipal Holdings Group to which we outsource full operations from promotion to PMS is working on it as a top priority. The Company also outsourced similar business to ASKA Pharmaceutical Co., Ltd. for certain facilities of obstetrics and gynecology.

In addition, we will proceed with the smooth launch of TITANBRIDGE® approved in December 2016, Rapalimus® Gel approved in March 2017 and Jemina® combination tablet scheduled to be approved in June.

We will strengthen collaboration with the Medipal Holdings Group and promote personnel exchange.

The tasks of Business Development & Strategy to find new themes continue to include target validation presenting the relation with disease and clinical predictability, and collaboration with the aim of active introduction and commercialization of academia seeds closely taking into account safety and competition of intellectual property rights.

We continue to make an effort to acquire public subsidy and financing of development expenses for commercialization. Also, we consider external project finance in parallel.

We will proceed with negotiations for cost reduction in negotiations of alliance management in the existing business and procurement, and make an effort to acquire additional increase in revenue in negotiations of revision of the existing agreements.

Research & Development will push ahead the development schedule, with the aim of obtaining an approval of Jemina® combination tablet (NPC-16) and myringa regeneration (NPC-18) early and submitting the NDA for melatonin (NPC-15) in April 2019.

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 at the same time, the Company will file the NDA for TITANBRIDGE® in Europe and the US in 2018, and start pre-IND meetings with the US FDA and Scientific Advice meeting with the EU EMA for malaria vaccine, Rapalimus® Gel and NPC-18.

Concerning the safety assurance of pharmaceutical products, we actively examine the introduction of the EDC (Electronic Data Capture) system to improve the quality of survey data and streamlining collection of survey slips and follow up. We have already used EDC for a specific use survey of Nobelzin®, a treatment for hypozincemia, which is currently being conducted, and plan to introduce EDC for a use survey of TITANBRIDGE®, which is under planning.

For safety management, we are working on effective use of the database of the IT system (ARIS-J) that we introduced in 2015 in cooperation with IT section. In addition, we will proceed with correction of overengineered workflows and standards within the scope of compliance and from a scientific perspective. While realizing the two points of avoiding causing drug-induced diseases and passing re-examinations, we will slim down our organization and structure within the scope of compliance to reduce cost.

As an effective use of outside resources, we will deepen collaboration and cooperation with the Medipal Holdings Group and Foundation for Biomedical Research and Innovations to promote and manage post-marketing surveillance-related operations under the unprecedented new scheme.

As for production, Supply Chain & Manufacturing are working on various tasks for launching three products to be launched, Rapalimus® Gel, TITANBRIDGE® and Jemina® combination tablet, as scheduled, and ensuring stable supply.

Regulatory Affairs is now required to actively support both Research & Development and Pharmacovigilance & Quality Assurance, and to help efficient and speedy response to the authority. It also utilizes the know-how for NHI/material price negotiations 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 addition, it will scrutinize unprofitable items and apply "recalculation for unprofitable items" for certain items that it deems necessary. It also follows drastically changing NHI price reform and health insurance reform to involve in-house strategies from a technical perspective. In addition, through activities of Samurai Biotech Association of which the Company is a board member, research, lobbying and advising the authorities will be continued.

The tasks of corporate planning and accounting (Administrative Affairs & Corporate Planning) are at first, to increase the accuracy of budgetary variance analysis and the forecasts to implement the annual budget for certain and to put into place a flexible management system capable of addressing additional measures expansively in case of the slowdown of business performance. Secondly for financial affairs, we will examine financing of around 1 billion according to conditions to maintain sufficient cash in hand to ensure flexible response to unscheduled development fund needs while we have pledged cash deposits of 2,050 million yen to our two proposals adopted by CiCLE in addition to scheduled payment of the existing borrowing. Considering risky development themes and full-scale overseas development, the Company will consider flexible financing and the introduction of risk money.

As for the issue of human resources and general affairs (President's Office), we will proceed with correction of age composition and balance of employees, which has been leaning towards seniors, and accordingly, it is very important to perpetuate and activate the organization. As the average age of the Company's employees was 52 years old, keeping an aging composition, we continue to recruit postdoctorals and further promote personnel exchange with the Medipal Holdings Group. By these initiatives, we will secure and foster successors of important works/positions including the president in addition to improvement of employee composition and balance.

In order to disseminate the new personnel system introduced in January 2017 to all employees, we believe it is important to carry out necessary reviews and revisions of implementation methods flexibly to establish it as the system truly contributing to employees. We are also strongly promoting teleworking and support to quit smoking.

Overall, in 2017, income was unsatisfactory due to an increase in research and development expenses though both sales and income increased backed by the new indication of Nobelzin®. In 2018, we aim at increasing both sales and income by actively promoting investment in research and development in Japan and abroad in anticipation of an increase in sales due to full-scale sales of Nobelzin® and contribution of new drugs including TITANBRIDGE®, Rapalimus® Gel and Jemina® combination tablet.

The following shows the numerical targets for the mid-long term future vision of sales and profit as an immovable high goal named North Star. We believe that these targets are in range.

North Star	2020
Sales	20 billion yen
Ordinary income	5 billion yen
Net income	3 billion yen

1.12. Other Important Matters

No matters requiring special attention

2. Current Status of the Company

2.1. Shares (as of December 31, 2017)

(1)	Number of shares authorized		50,000 shares	
(2)	Number of shares issued	Ordinary share	11,650 shares	
		Special-class share	1 share	
(3)	Number of shareholders		4	
(4)	Status of Major Shareholders			
	Hisanaga & Company (ordinary share)		10,000 shares	(85.8%)
	Medipal Holdings Corporation (ordinary share)		830 shares	(7.1%)
	Inabata & Co., Ltd. (ordinary share)		820 shares	(7.0%)

In April 2017, one common share of the Company was divided into ten (10) shares of common share to ensure a more flexible capital policy. 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) Scheduled directors (scheduled on March 26, 2018)

Jin Shiomura	(CEO and President)
Isamu Sojyo	(former Executive Managing Director of Japan Intellectual Property Association, former General Manager of Intellectual Property Department at Mitsubishi Chemical Corporation)
Nobukuni Taneya	(Part-time director, Arara Inc.)
Takahisa Iizuka	(Deputy General Manager, Business Development Division, Medipal Holdings Corporation)
Nobukazu Kuboi	(General Manager, Financial Management Office and General Manager, Accounting Dept., Inabata & Co., Ltd.)
Toshio Miyata	(Director of Mih Clinic Yoyogi)

(2) Director to resign (scheduled on March 26, 2018)

Eiji Suzuki (Corporate advisor)

(3) Directors and Company Auditors

As of March 26, 2018, the status of full-time and part-time directors is as follows:

CEO and President:	Jin Shiomura	
Directors (part-time):	Isamu Sojyo	(former Executive Managing Director of Japan Intellectual Property Association, former General Manager of Intellectual Property Department at Mitsubishi Chemical Corporation)
Directors (part-time):	Nobukuni Taneya	(Part-time company auditor of Arara Inc.)
Directors (part-time):	Takahisa Iizuka	(Deputy General Manager, Business 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.)

(4) Executive Officers

As of March 26, 2018, the status of executive officers and directors is as follows:

Vice President & Chief Operating Officer:	Shigeki Shimasaki	(Head of Research & Development)
Chief Operating Officer:	Tsutomu Sugaya	(Head of President's Office)
Senior Executive Officer:	Tetsuo Hayase	(Head of Supply Chain & Manufacturing)
Senior Executive Officer:	Soichi Ikegaya	(General Marketing Compliance Officer, Head of Pharmacovigilance & Quality Assurance)
Senior Executive Officer:	Arata Tabata	(Head of Business Development & Strategy)
Executive Officer:	Kenji Shimizu	(General Manager of R&D Department 2)
Executive Officer:	Akira Ikeda	(Head of Human Resources and General Affairs, President's Office)
Executive Officer:	Masato Iwamoto	(General Manager of Supply Chain Management, Supply Chain & Manufacturing)
Executive Officer:	Hitoshi Hasegawa	(Head of Pharmacovigilance & Quality Assurance)
Executive Officer:	Yoshinobu Takahashi	(Head of Marketing & Sales)
Executive Director:	Yoshihide Yamamoto	(Deputy Head of Marketing & Sales)
Executive Director:	Masanori Osakabe	(Deputy Head of Research & Development)
Executive Director:	Yoshiki Yagi	(Deputy Head of Business Development & Strategy)

Executive Director:	Akira Yumoto	(Branch Manager of Tokyo Branch, Marketing & Sales)
Executive Director:	Toshiaki Okamura	(Head of Regulatory Affairs)
Executive Director:	Kozo Hayase	(Head of Administrative Affairs & Corporate Planning)
Executive Director:	Atsunori Iwao	(Quality Assurance Officer, Head of Pharmacovigilance and Quality Assurance)
Executive Director:	Takako Aburada	(General Manager of CMC Development, Supply Chain & Manufacturing)

2.3.2. Remuneration paid to directors and company auditors

Classification	Head-count	Amount paid
Directors	6	12,027,000 yen
Company auditor	1	2,738,000 yen
Total	7	14,765,000 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 1) 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.

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