# **Business Report for the 17th Year**

# Nobelpharma Co., Ltd.

[From January 1, 2019 to December 31, 2019]

# **Business Report**

(From January 1, 2019 to December 31, 2019)

# 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. <u>General</u>
  - 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. <u>Personnel</u>
  - 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. <u>Capital</u>
  - 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 dividen da
    - \*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</li>
  \*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) Don't be afraid to buy time for money
  - 3) No overtime work considered good
  - 4) Consider patient needs, scientific rationality and nature of laws/regulations when pursuing higher quality in products/data
  - 5) 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

The Company will celebrate its 17th anniversary in June 2020. The number of employees exceeds 300, and those who were present when the Company was founded have decreased. It is necessary to advance the company and to make it require stricter compliance with the corporate mission, management policy and action criteria.

The Company experienced a so-called harassment incident in the second half of 2019. The company auditors pointed out some omission in the process of request for approval on disbursement in the headquarters. Furthermore, there were some cases that appeared to fray over information disclosure and securing of transparency. By reflecting on ourselves, we seem to be losing our robustness.

Based on such reflection, Sales & Marketing hired external consultants to conduct training for corporate mission, management policy and action criteria, which has demonstrated considerable effect. In 2020, PMS Regulatory Compliance & Assurance will provide similar training. In addition, the Company released the "Message to line managers" as attached at the end of the Business Report to thoroughly prevent any harassment.

|                                       | mil    | yen        | ¥7           | % to tota | l sales |
|---------------------------------------|--------|------------|--------------|-----------|---------|
|                                       | 2018   | 2019       | Year-on-year | 2018      | 2019    |
| Sales                                 | 10,568 | 13,403     | 126.8%       | 100.0%    | 100.0%  |
| Cost of goods sold                    | 1,450  | 1,466      | 101.1%       | 13.7%     | 10.9%   |
| Gross profit                          | 9,118  | 11,937     | 130.9%       | 86.3%     | 89.1%   |
| SG&A expense                          | 7,240  | 8,921      | 123.2%       | 68.5%     | 66.6%   |
| * Personnel cost                      | 2,254  | 2,401      | 106.5%       | 21.3%     | 17.9%   |
| * R&D expenses                        | 1,917  | 2,311      | 120.6%       | 18.1%     | 17.2%   |
| Operating income                      | 1,877  | 3,015      | 160.6%       | 17.8%     | 22.5%   |
| Non-operating income/expenses         | 82     | riangle 64 |              |           |         |
| Ordinary income                       | 1,960  | 2,951      | 150.5%       | 18.6%     | 22.0%   |
| Extraordinary income/loss             | △101   | 93         |              |           |         |
| Net income before tax                 | 1,859  | 3,045      | 163.8%       | 17.6%     | 22.7%   |
| Income taxes                          | 422    | 674        | 159.7%       | 4.0%      | 5.0%    |
| Net income                            | 1,437  | 2,370      | 164.9%       | 13.6%     | 17.7%   |
| Net income per employee ('000<br>yen) | 5,841  | 7,476      |              |           |         |
| Retained earnings brought forward     |        |            |              |           |         |
| Beginning balance                     | 673    | 2,093      |              |           |         |
| Prior period adjustment               | -      |            |              |           |         |
| Dividend                              | 17     | 359        |              |           |         |
| Net income                            | 1,437  | 2,370      |              |           |         |
| Ending balance                        | 2,093  | 4,104      |              |           |         |

# 1.2. Progress and Results of Operations

\* Major items included in SG&A expenses.

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

Total sales in 2019 were 13,403 million yen, up 26.8% year-on-year. Nobelzin<sup>®</sup> and Lunabell<sup>®</sup> family (Lunabell<sup>®</sup> LD, Lunabell<sup>®</sup> ULD, Jemina<sup>®</sup> and Frewell<sup>®</sup>) posted sales of 8,053 million yen and 2,822 million yen, respectively, accounting for 62.3% and 21.8%, respectively, of total products sales.

The cost of goods sold was 1,466 million yen, up 1.1% year-on-year, accounting for 10.9% of total sales (2018: 13.7%). Sales, general and administrative expenses totaled 8,921 million yen, an increase in 23.2% year-on-year, accounting for 66.6% (2018: 68.5%), mainly including personnel expenses of 2,401 million yen, up 6.5% year-on-year, and 17.9% (2018: 21.3%) of total sales, R&D expenses of 2,311 million yen, up 20.6% year-on-year, and 17.2% (2018: 18.1%) of total sales, sales promotion expenses of 1,780 million yen and outsourcing expenses of 1,199 million yen. Sales promotion expenses mainly included 1,328 million yen of sales commission on Nobelzin<sup>®</sup> and Jemina<sup>®</sup> to MEDICEO CORPORATION, ASKA Pharmaceutical Co., Ltd. and SHIKOKU YAKUGYO Co., LTD. Outsourcing expenses mainly included 110 million yen for safety information processing support operation by CMIC, 57 million yen for call center operation by EP-PharmaLine, and 52 million yen for business management service by HisanagaCo., Ltd.

As a result, operating profit was 3,015 million yen, up 60.6% year-on-year, and it accounted for 22.5% (2018: 17.8%) of total sales.

Ordinary profit was 2,951 million yen, up 50.5% year-on-year, accounting for 22.0% (2018: 18.6%) of total sales, after recording non-operating income of 8 million yen including subsidy revenue of 6 million yen, more than offset by non-operating expenses of 73 million yen including interest expenses of 34 million yen and bond interest expenses of 14 million yen.

For extraordinary profit, insurance proceeds of 93 million yen were recorded due to a loss resulting from typhoon damage of Alabel<sup>®</sup> in Kansai International Airport in 2018.

With the income taxes of 674 million yen, net income was 2,370 million yen, up 64.9% year-on-year, accounting for 17.7% (2018: 13.6%) of total sales, and net income per employee was 7 million yen (2018: 5 million yen).

Retained earnings brought forward as of December 31, 2019 were 4,104 million yen, with the beginning balance of retained earnings brought forward of 2,093 million yen and a dividend payment of 359 million yen.

To sum up our activities in 2019, we have taken a step towards a new stage, i.e. toward a global/centennial company through: (1) Strong sales expansion of Nobelzin<sup>®</sup> and gaining steady cash flows, as a potential primary source of revenue following Lunabell<sup>®</sup>; (2) showing successful results of access to a strong sales and distribution network through strengthening capital tie-up with Medipal Holdings Corporation; (3) steady advancement of preparation for a structure of overseas expansion including China and Europe after establishment of a subsidiary in the U.S. under the strategy of selling three products of Rapalimus<sup>®</sup>, TITANBRIDGE<sup>®</sup> and Retympa<sup>®</sup> in these three overseas subsidiaries; (4) secured cash flows and an improvement of trust by academia allowed us to strengthen a system to introduce new seeds; and (5) an increase in R&D expenses by 20% year-on-year.

The details are explained below.

# 1.3. Domestic sales

The table below shows sales by product in 2019 on a wholesale price (NHI price) basis.

| Brand Name  | Launch               | Indication   | Sales (on a<br>price (NHI p<br>(Yen in r | Year-on-<br>year |           |
|---|----------------------|--|--|------------------|-----------|
|   |                      |  | 2018 [1]                                 | 2019 [2]         | ([2]/[1]) |
| Nobelzin®   | Apr 2008<br>Mar 2017 | Wilson's isease,<br>hypozincemia   | 5,245                                    | 9,123            | 174.0%    |
| Lunabell <sup>®</sup> LD<br>Lunabell <sup>®</sup> ULD | Jul 2008<br>Sep 2013 | Dysmenorrhea   | 9,640                                    | 4,375            | 45.4%     |
| Nobelbar®   | Dec 2008             | Neonatal seizures,<br>status epilepticus                                   | 115                                      | 100.0%           |           |
| Fostoin <sup>®</sup>                                  | Jan 2012             | Status epilepticus, prevention of postoperative seizures, etc.             | 1,133                                    | 1,036            | 91.4%     |
| Gliadel®  | Jan 2013             | malignant glioma   | 978                                      | 890              | 91.0%     |
| Alabel®   | Sep 2013             | diagnosis of malignant glioma  | 294                                      | 284              | 96.6%     |
| Indacin®  | Jan 2013             | patent ductus arteriosus of prematurity                                    | 60                                       | 50               | 83.3%     |
| Cosmegen®   | Jan 2013             | Wilms' tumor,<br>choriocarcinoma, pediatric<br>solid malignant tumor, etc. | 19                                       | 22               | 115.8%    |
| Unitalc®  | Dec 2013             | prevention of recurrent<br>malignant pleural effusion                      | 69                                       | 69               | 100.0%    |
| Respia®   | Dec 2014             | apnea of prematurity   | 229                                      | 231              | 100.8%    |
| Rapalimus®  | Dec 2014             | lymphangioleiomyomatosi s  | 249                                      | 276              | 110.8%    |
| Zanosar®  | Feb 2015             | gastroenteropancreatic<br>neuroendocrine tumor                             | 368                                      | 416              | 113.0%    |
| Rapalimus <sup>®</sup> Gel                            | Jun 2018             | Skin lesions associated with tuberous sclerosis                            | 148                                      | 385              | 260.1%    |
| Titanium bridge                                       | Jul 2018             | Adductor spasmodic<br>dysphonia  | 15                                       | 46               | 306.7%    |
| Jemina®   | Oct 2018             | Dysmenorrhea   | 125                                      | 994              | 795.2%    |
| Retympa®  | Dec 2019             | tympanic membrane<br>perforation   | 1  | -                |           |
| Total   |                      |  | 18,687                                   | 18,312           | 98.0%     |

In 2019, the Company positioned Nobelzin<sup>®</sup>, Jemina<sup>®</sup> and Rapalimus<sup>®</sup> as the products to most focus on as well as to spread and expand, and launched a new product, Retympa<sup>®</sup>, in December. We achieved sales of 18.3 billion yen compared with the target of 17.7 billion yen on a wholesale price (NHI price) basis.

Most of our products including Nobelzin<sup>®</sup> are medicines that are no substitute, and we are working on spreading and expanding them based on guidelines and evidence. With regard to our core products, we

have collaborated with the Medipal Holdings Group mainly in Web seminars and expert's movies to promote product value cognitive activities and confirmation of prescription.

In 2019, sales of Lunabell<sup>®</sup>, which had been our core product so far, were expected to decline significantly due to the launch of its generic formulation. In order to cover the expected sales decline, we actively have Web and area seminars for the promotion of our new product, Jemina<sup>®</sup>, mainly in the GP market in cooperation with ASKA Pharmaceutical and the Medipal Holdings Group.

As of December 31, 2019, 89 MRs cover the entire country, of which 24 MRs are sent by the Medipal Holdings Group. We aim at MR activities by a selected few and are also actively engaged in PR activities in channels other than MRs by improving the customer center and the website. Sales of Nobelzin<sup>®</sup> grew through sales promotion activities using the AR (authorized medical sales representatives who passed the MR certification exam) function of the Medipal Holdings Group, and we use this initiative for Jemina<sup>®</sup> and Rapalimus<sup>®</sup> Gel.

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

#### 1.4. Overseas sales

International Clinical Development Div. of Research & Development examined business expansion in the U.S. and Europe, and China Business Office of President's Office was responsible for business expansion in China. As of April 1, 2019, the Company established Overseas Business Development to consolidate and execute overseas business expansion. Rapalimus<sup>®</sup> Gel (NPC-12G) and TITANBRIDGE<sup>®</sup> (NPC-17) were granted approvals under the "Sakigake" fast-track review system in Japan. We aim at obtaining approvals and selling three products (these two products and Retympa<sup>®</sup> (NPC-18)) in the U.S., China and Europe.

In the U.S., on June 3, 2019, Nobelpharma America, LLC, a wholly-owned subsidiary of Nobelpharma Co., Ltd., was registered in Delaware, which opened an office in Bethesda, Montgomery County of Maryland in October, as the first overseas office of the Company. A president sent from the Japan headquarters is stationed and has recruited local employees and developed various office regulations, and also commenced the preparation for local release of Rapalimus<sup>®</sup> Gel.

In China, we filed an application for the approval of Rapalimus<sup>®</sup> Gel, and the filing was officially accepted in October 2019. While the filing is pending for review at this moment, we are preparing for incorporation in view of an approval in 2020. In China, we are examining the acquisition of approvals and sales of three other existing products in addition to the above three products.

In Europe, we have conducted market research in preparation for business expansion of Rapalimus<sup>®</sup> Gel and TITANBRIDGE<sup>®</sup>. EU regulations require an entity within the EU to file and gain an approval for a new drug. Thus, we are preparing for incorporation in June 2020.

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

Retympa<sup>®</sup>, a treatment for tympanic membrane perforation, was granted a marketing approval in September 2019 following approvals of Rapalimus<sup>®</sup> Gel, a treatment for skin lesions associated with tuberous sclerosis, and Jemina<sup>®</sup>, a treatment for dysmenorrhea, in 2018, and Melatobel<sup>®</sup> (melatonin, a treatment for insomnia associated with childhood neurodevelopmental disorder) filed in April 2019 is expected to be granted an approval in March 2020. In addition, the Company completed the First in Human trial (PI) for cytomegalovirus (CMV) antibody (NPC-21), the Company's first antibody drug, an IND was filed to the U.S. FDA in December 2019 and a US-Japan international joint clinical trial has started in January 2020.

We have started a full-scale examination on overseas development in 2017 under the policy of obtaining approvals of three products of Rapalimus<sup>®</sup> Gel, TITANBRIDGE<sup>®</sup> and Retympa<sup>®</sup> in three regions of North America, China and Europe. In 2018, the Company has started meetings with the FDA for development and NDA filing in the U.S. for Rapalimus<sup>®</sup> Gel that the FDA designated as an orphan drug in 2017, and filed an NDA to the FDA in February 2020. In China, we filed an application for the approval in September 2019 after the consultation with the authorities. In Europe, we have continued discussions with local authorities. We also hold Q-sub meeting with the FDA and continue activities for

the EU CE marking certification for TITANBRIDGE<sup>®</sup>. The third study was commenced for malaria vaccine (NPC-19, prevention of falciparum malaria) in Africa in 2018, and it was transferred to cohort 2 (age of 12 to 24 months) in 2019.

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, 2020. 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.

|   | Compound                           | Indication  | Licensor  | Development<br>stage    | Estimated approval | Classification |
|---|------------------------------------|---|---|-------------------------|--------------------|----------------|
| 1 | NPC-15<br>Melatonin                | Sleep disorders in<br>children with<br>neurodevelopmental<br>disorder | In-house  | NDA<br>submitted        | Mar 2020           | Ι              |
| 2 | GM-CSF<br>Sargramostim             | Pulmonary proteinosis   | Partner<br>Therapeutics Inc.                          | pre NDA                 | Sep 2021           | II             |
| 3 | NPC-09<br>Acetylneuraminic<br>acid | Distal myopathy   | In-house  | PIII(Clinical<br>trial) | Dec 2022           | III            |
| 4 | NPC-21<br>CMV antibody             | CMV infection   | Evec Inc.   | PII                     | TBD                | Ι              |
| 5 | NPC-22<br>Skopolamin               | Salivation  | Kitasato<br>University                                | PI                      | TBD                | IV             |
| 6 | NPC-x4<br>P092                     | Prion disease   | Gifu University                                       | Non-clinical            | TBD                | IV             |
| 7 | NPC-x5                             | Jaw bone regeneration   | Niigata University                                    | Non-clinical            | TBD                | III            |
| 8 | NPC-x6                             | -   | Hiroshima<br>University<br>Repertoire<br>Genesis Inc. | Non-clinical            | TBD                | III            |

| A. | New Drugs and Medical Devices |
|----|-------------------------------|
|    |                               |

| <u>р</u> . | Life Cycle Manager        |   |  |                      | 1                  |                    |
|------------|---------------------------|---|--|----------------------|--------------------|--------------------|
|            | Compound                  | Indication  | Licensor   | Development<br>stage | Estimated approval | Classifi<br>cation |
| 1          | NPC-02<br>Nobelzin®       | Child's preparation<br>(new formulation)                              | National Center for<br>Child Health and<br>Development | NDA submitted        | Dec 2020           | III                |
| 2          | NPC-05<br>Unitalc®        | Refractory pneumothorax<br>(new indication)                           | PII  | Jun 2022             | III                |                    |
| 3          | NPC-06<br>Fostoin®        | Nerve field<br>(new indication)                                       | Pfizer Inc.  | PII                  | TBD                | Ι                  |
| 4          | NPC-12<br>Rapalimus®      | Refractory lymphatic<br>disease<br>(new indication)                   | Gifu University  | PIII                 | Jun 2021           | III                |
| 5          | NPC-12<br>Rapalimus®      | Fbrodysplasia ossificans<br>progressiva<br>(new indication)           | Kyoto University                                       | PII/III              | Mar 2022           | III                |
| 6          | NPC-12<br>Rapalimus®      | Pendred syndrome<br>(new indication)                                  | Keio University  | PI/IIa               | Dec 2021           | III                |
| 7          | NPC-12<br>Rapalimus®      | Epilepsy with focal<br>cortical dysplasia type II<br>(new indication) | Showa University                                       | PII                  | TBD                | IV                 |
| 8          | NPC-12<br>Rapalimus®      | Idiopathic multicentric<br>Castleman's disease<br>(new indication)    | Nagasaki University                                    | PII                  | TBD                | IV                 |
| 9          | NPC-12G<br>Rapalimus® Gel | Neurofibromatosis type I<br>(new indication)                          | Osaka University                                       | PII/III              | Sep 2022           | III                |

# B. Life Cycle Management (LCM)

# C. Overseas Development

|   | Compound  | Indication                        | Licensor                   | Development<br>stage        | Estimated approval | Classif<br>ication |  |  |  |
|---|---|-----------------------------------|----------------------------|-----------------------------|--------------------|--------------------|--|--|--|
|   |   |                                   |                            | USA : NDA<br>submitted      | Dec 2020           |                    |  |  |  |
| 1 | 1 (Rapalimus <sup>®</sup> Gel)  | Hemangiofibroma                   | -                          | China : NDA<br>submitted    | Aug 2020           | Ι                  |  |  |  |
|   |   |                                   |                            | EU : pre NDA                | TBD                |                    |  |  |  |
| 2 | NPC-19<br>(NPC-SE36)<br>Malaria vaccine                                       | Prevention of falciparum malaria  | Osaka University<br>GHIT   | PIb                         | TBD                | Ι                  |  |  |  |
| 3 | NPC-18<br>(Retympa®)  | Tympanic perforation              | MEEI/Harvard<br>University | PII                         | TBD                | III                |  |  |  |
| 4 | NPC-17<br>Thyroid cartilage<br>fixation device<br>(TITANBRIDGE <sup>®</sup> ) | Adductor spasmodic<br>dysphonia - |                            | Preparing<br>Clinical trial | TBD                | III                |  |  |  |

As a matter requiring special attention, NPC-19 and NPC-21 were selected by Cyclic Innovation for Clinical Empowerment (CiCLE), a program launched by Japan Agency for Medical Research and Development (AMED).

# 1.6. Finding of New Themes

Project Planning & Development is responsible for core roles for the Company's open innovation. Specifically, its role is classified into (1) Finding and research for new themes (drugs and medical devices) that become future pillars of the Company's business, (2) In/out-licensing negotiations with a new development theme, (3) Support for commercialization and collaborative research of academia seeds that are considered promising, (4) Financing and support of development expenses including acquisition of public subsidy. It proceeds with its task in strong collaboration with other divisions including Research & Development and Business Development & IP Management. The following showed major achievements in 2019.

- Promotion of a joint program with academia for the purpose of finding seeds
- Conclusion of evaluation and joint commercialization for tissue-engineered medical products, etc.
- Conclusion of collaborative research agreement with academia for multiple seeds
- Finding and search of seeds of many overseas companies and VCs, and negotiation of licensing

Upon promoting in-licensing and collaborative research, we place the primary focus on whether these seeds met our mission, and conducted various and many evaluations including medical drugs (low molecular, peptide, antibody and oligonucleotide therapeutics), medical devices and tissue-engineered medical products (regenerative medicine/cellular therapeutics and gene therapy). In addition, with a view to finding and obtaining information on better seeds as well as realizing early commercialization, we have promoted a joint business with academia to find seeds and plan to start in 2020.

#### 1.7. Business Development & IP Management

Business Development & IP Management is a keystone of our business, which is responsible for business development, intellectual property rights and agreements in the Company. 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) Alliance management, (4) Research, planning of preventive measures and management of in-licensing of intellectual property, (5) Response to company-wide technical agreement, and (6) Procurement negotiations.

The following showed major achievements in 2019.

- Conclusion of an agreement for patent, data, and know-how license of malaria vaccine
- Conclusion of an agreement for patent and data license of TITANBRIDGE<sup>®</sup>
- Acquisition of license required for development and manufacturing of a treatment for CMV infection from Lonza
- Negotiation to expand a territory of b-FGF license agreement
- Various arrangements and negotiations with the existing partners and development of a route for obtaining overseas new information (U.S. and China)

The number of patent families with which the Company is involved is 41 due to an increase in collaboration with academia. The Company filed patent applications that were closely related to each theme of LCM and actively filed trademarks on the names of company and products overseas in preparation for overseas activities.

Business Development & IP Management added one contracted staff member in law-related tasks for technical service contracts, strived to understand all matters and consolidated contact points with lawyers.

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

#### 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 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 group relations.

The Division added two staff members to further enhance development and regulatory affairs, and strengthened development and regulatory affairs as well as administrative procedures (the Japanese Ministry of Health, Labour and Welfare (MHLW) and Pharmaceutical and Medical Devices Agency (PMDA)). In addition, since 2018, we undertook systematization of operations (digitization of application/approval information management and NDA filing), which had been insufficient so far, and realized digitization of NDA filing in 2019.

Regulatory Affairs continued to confirm and discuss with relevant departments (Product Management and Quality Assurance) about change control to prevent the "difference between certificates of approval for manufacture and sale and the actual status of manufacturing," and responded to the authority adequately as needed so as to maintain a stable supply.

The In-house Product Material Committee reviewed 408 sales promotion materials of drugs, almost double from the previous year. The Committee revised and advised as necessary to ensure that adequate sales promotion materials are provided. In accordance with the guidelines on providing sales information of ethical drugs released by the Japanese Ministry of Health, Labour and Welfare ("MHLW"), we established a new supervising office for providing sales information and accordingly, the Product Material Committee was transferred to "Review Office" within this supervising office.

For NHI price related work by Public Relations, Retympa<sup>®</sup> 250µg Set for Otology has been listed on the NHI price list. An injection/IV charge related to this drug (application of tympanic perforation closure technique) was also set so as to realize its smooth insurance coverage. In addition, Regulatory Affairs addressed more than ten projects for the calculation of the estimated NHI price and feasibility study of planning and developed products. Public Relations added a staff member to provide a higher accurate evaluation that is capable of promptly responding to an increase in developments originated by academia and changes in the circumstance of the NHI price.

As for activities in the industry, in April 2019, Samurai Biotech Association, for which the Company works as a board member and coordinator office, was transformed into a general incorporated association. In addition, Samurai Biotech Association successfully participated in the industry hearing conducted by the special committee for NHI drug prices of the Central Social Insurance Medical Council.

In terms of patient group relations, the Company has communications with 24 patient groups and lent its meeting rooms 18 times a year and in addition, 38 employees actively participated as volunteers so as to maintain a good relationship with them. Further, we held four in-house seminars in which leading members of patient groups were lecturers to promote better understanding of employees about intractable diseases.

#### 1.9. 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 continued to work on increasing inventories of products and materials. In 2019, the second OEM supplier for Nobelzin<sup>®</sup> tablet started production. In January 2020, the Company filed an application for the approval of Nobelzin<sup>®</sup> granule, child's preparation of Nobelzin<sup>®</sup>. We plan to launch this product in 2021 and continue to discuss with our OEM suppliers to build a structure of stable supply. As the current supplier's lot size is too big to adequately adjust inventories of Indacin<sup>®</sup>, we are preparing for transferring production to another supplier.

In addition, we established two logistics centers in both West and East Japan to prepare for disaster.

We have put into place a production system for new Melatobel<sup>®</sup> granule, and prepare for the first shipment with estimated manufacturing and marketing approval to be granted in March 2020.

In 2019, capital investment related to production included HPLC devices (9.1 million yen, excluding tax) for shipping inspection of Zanosar<sup>®</sup>. The devices are currently operated by an analyzing company we outsource shipping inspection to.

#### 1.10. Pharmacovigilance & Quality Assurance

PMS Regulatory Compliance & Assurance works on business improvement in a cost-conscious way in compliance with related laws and regulations, by posting its mission as the three pillars of passing re-examinations, causing no drug-induced diseases and quality assurance and stable supply of products.

In terms of re-examinations, we completed PMDA's series of compliance inspections of reexamination for Nobelzin<sup>®</sup>, a treatment for Wilson's disease, Nobelbar<sup>®</sup>, a treatment for neonatal seizures, and Fostoin<sup>®</sup> by February 2020. As the Company has established systems under GPSP and GVP and reviewed operation flows so far, the number of inquiries for the compliance inspection was drastically improved to zero for Nobelbar<sup>®</sup>, a treatment for neonatal seizures, and and 10 for Nobelzin<sup>®</sup>, a treatment for Wilson's disease, compared with 77 for Lunabell<sup>®</sup> LD.

In terms of safety-related matters, we completed post-marketing surveillance of Jemina<sup>®</sup> and are currently conducting post-marketing surveillance of Retympa<sup>®</sup>. In 2019, the number of domestic and overseas adverse event reports was 5,057 and 3,650, respectively, almost the same level in 2018 (5,438 and 3,612, respectively). Approximately 40% of domestic adverse event cases related to Nobelzin<sup>®</sup>, a treatment for hypozincemia, and a half of overseas cases related to Rapalimus<sup>®</sup>.

In terms of post-marketing surveillance-related matters, a general use survey of Jemina<sup>®</sup> was started in June 2019 in collaboration/cooperation with ASKA Pharmaceutical, and we are preparing for a general use survey of Retympa<sup>®</sup> to begin in June 2020 in collaboration/cooperation with the Medipal Holdings Group. In December, 2019, the interim report of the survey was submitted to PMDA to dismantle a condition for approval of Zanosar<sup>®</sup> (all-case surveillance).

In terms of quality-related matters, we filed GMP compliance inspection on approvals in FY2019 (21 applications for 13 products), obtained notifications of result for all products and completed GMP compliance inspection. For release decision of products and APIs, we decided on more than 100 lots that were mainly APIs and formulation of Nobelzin® to ensure a stable supply of products.

#### 1.11. Funding and Major Lenders

In 2019, the Company borrowed 1,200 million yen and repaid and redeemed 1,411 million yen to financial institutions.

The resulting balance of loans payable and bonds as of December 31, 2019 was 5,203 million yen. As the Company has cash and deposits of 4,990 million yen, the actual amount of borrowing is 212 million yen (2018: 627 million yen).

As of December 31, 2019, the status of borrowing is as follows:

| Loans payable     |                               |   |  |  |  |  |
|-------------------|-------------------------------|---|--|--|--|--|
| Mizuho Bank, Lto  | 1.                            | 1,700 million yen                         |  |  |  |  |
| Sumitomo Mitsui   | Banking Corporation           | 400 million yen                           |  |  |  |  |
| MUFG Bank, Ltd    | •                             | 625 million yen                           |  |  |  |  |
| The Shoko Chuki   | n Bank, Ltd.                  | 204 million yen                           |  |  |  |  |
| The Tokyo Shink   | in Bank                       | 150 million yen                           |  |  |  |  |
| Japan Finance Co  | rporation                     | 43 million yen                            |  |  |  |  |
| Total             | -                             | 3,122 million yen                         |  |  |  |  |
| Japan Agency for  | Medical Research and Developm | nent 380 million yen                      |  |  |  |  |
| Corporate bond    |                               |   |  |  |  |  |
| 2nd straight bond | Osaka Soda Co., Ltd.          | 500 million yen (Maturity: Dec 2024)      |  |  |  |  |
| 4th straight bond | Mizuho Bank, Ltd.             | 500 million yen (Maturity: Dec 2021)      |  |  |  |  |
| 5th straight bond | The Shoko Chukin Bank, Ltd.   | Ltd. 100 million yen (Maturity: Mar 2020) |  |  |  |  |

300 million yen (Maturity: Mar 2022)

300 million yen (Maturity: May 2026)

1,700 million yen

| 1.12. | Financial Results, Assets and 2016 Forecast |
|-------|---|

6th straight bond

7th straight bond

Total

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

Resona Bank, Ltd.

Resona Bank, Ltd.

In the next year, the Company expects an increase in sales but a decrease in profits as R&D and overseas investment will grow significantly, though profits are supposed to grow as sales will increase.

| Mil yen except for*         | 2016<br>(Actual results)<br>14th year | 2017<br>(Actual results)<br>15th year | 2018<br>(Actual results)<br>16th year | 2019<br>(Actual results)<br>17th year | 2020<br>(Forecasts)<br>18th year |
|-----------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|----------------------------------|
| Sales                       | 6,791                                 | 7,236                                 | 10,568                                | 13,403                                | 17,228                           |
| Ordinary income             | riangle 56                            | 161                                   | 1,960                                 | 2,951                                 | 2,298                            |
| Net income                  | 93                                    | 53                                    | 1,437                                 | 2,370                                 | 1,503                            |
| *Net income per share(Note) | 8,000yen                              | 4,000yen                              | 111,000yen                            | 175,000yen                            | 111,000yen                       |
| Total assets                | 7,671                                 | 8,975                                 | 12,204                                | 14,138                                | 16,716                           |
| Net assets                  | 691                                   | 685                                   | 3,319                                 | 5,330                                 | 6,246                            |
| *Equity ratio               | 9.0%                                  | 7.6%                                  | 27.2%                                 | 37.7%                                 | 37.4%                            |
| *Net asset per share(Note)  | 59,000yen                             | 58,000yen                             | 245,000yen                            | 394,000yen                            | 461,000yen                       |

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

#### 1.13. Employees

As of March 1, 2020, the number of employees is 317 (including a total of 111 including 40 seconded employees, 26 temp staff members, 44 contract employees and one counsellor but excluding directors and employees seconded to external organizations) with an average age of 51.5. The number of employees increased by 48 compared with 269 as of March 1, 2019. The average number of years of continuous services (seconded employees and temp staff members are not included in the counting) is 4.5 years.

Total personnel expenses of the overall company in 2019, including expenses for seconded employees and temp staff members, were 3,019 million yen, an increased in 8.6% compared with 2,779 million yen in 2018. This was mainly due to an increase in the number of employees to strengthen sales of new products such as Nobelzin<sup>®</sup> and to prepare for overseas business. A new MR team dedicated to the gynecological field was established for the launch of Jemina<sup>®</sup>.

Although the Company does not recruit new graduates simultaneously, we recruit postdoctorals and those with equivalent status regularly. Since 2012, we have recruited over ten, who work mainly in Research & Development and Project Planning & Development. Currently, we have no prospective employee this April but have accepted one foreign student for an internship. We have also actively transferred temp staff members to direct employment and in 2019, 13 staff members became our full-time employees. As we promoted mid-career recruitment of young and middle-aged people, the average age was six years younger than the peak time (57.7 years old as of March 2012) with improvement of the balance of age composition.

Due to such initiatives as review of work process, IT promotion including telework, health management and support for balancing child care and work as well as a continuous approach to transform the working style, monthly average overtime in the entire company was 9.2 hours, falling below ten hours for four consecutive years. The rate of annual paid leave taken by employees was 75.3%, maintaining the high level. However, as overtime increased slightly and the rate of annual paid leave taken decreased slightly, we will encourage employees to apply the home teleworking and flex-time system and make it a goal for all employees to obtain extended leave provided by the Company's regulations.

#### 1.14. Issues

Issues that each division should address are as follows:

- (1) To get a new MR evaluation system across to all MRs (Sales & Marketing), and to further enhance basic education (mission & action criteria) (PMS Regulatory Compliance & Assurance)
- (2) To plan to make a profit from overseas business in the year 2023, to obtain manufacturing and marketing approval by itself and to sell the products through its own distribution channel. Overseas Sales should withdraw from an area where it cannot expect to make a profit in a single year as of November 2022. (Overseas Business Development)
- (3) To reinforce education for managers and non-management employees, and to provide education on the Company's mission, management policy and action criteria thoroughly (Administrative Affairs & Corporate Planning).
- (4) To actively introduce new development themes from academia and business companies (Project Planning & Development, and Business Development & IP Management)
- (5) To change the current system to a global one to ensure that each division addresses requests from overseas subsidiaries in line with the expansion of overseas business (Overseas Business Development, Research & Development, PMS Regulatory Compliance & Assurance, Regulatory Affairs, Supply Chain & Manufacturing, and Administrative Affairs & Corporate Planning)

The mission of domestic sales is to further reinforce domestic sales in 2020. To this end, AMs (area managers) will be appointed in branches in order to develop them as a branch manager's right-hand man who can generate an area strategy by themselves for support so as to strengthen sales capabilities. In addition, we plan to provide position-based training, management training and MR evaluation training to improve the quality of MR activities.

For Nobelzin<sup>®</sup>, the mission is to get creative with the way that we go about our business to continue the momentum so far. Recognition of Jemina<sup>®</sup> launched in 2018 has increased after the dismantling of prescription limitations. In 2020, it is necessary to grow in the GP market promptly for a further increase in the market share. To this end, we consider that we have to work with our co-promotion partners of ASKA Pharmaceutical and the Medipal Holdings Group, particularly for Jemina<sup>®</sup>. Retympa<sup>®</sup> launched in December 2019 is a novel product as a treatment for tympanic membrane perforation and is highly valued by specialty doctors. We will make a great effort to penetrate the product promptly into the market through activities without MRs (IT, Web site and remote MRs). We filed an NDA for NPC-15 (Melatobel<sup>®</sup>) in April 2019 and expect to obtain an approval in March 2020. We will work toward delivering the product to patients as soon as possible.

The mission of overseas sales is that three overseas bases in the U.S., China and Europe will realize the expectation of making a profit in a single year as of November 2022. Basically, overseas bases strive to obtain manufacturing and marketing approval by themselves and to sell the products through their own distribution channel. Meanwhile, under the Company's action criteria of "Don't hold back from buying time with money," we will make an effort to take measures to deliver the world's first drugs to patients waiting for such drugs as soon as possible with the idea of alliance with other companies. In addition, in order to launch three overseas bases simultaneously, we have to change functions of each division in the Japan headquarters to the global one. We have to proceed with the preparation in the shortest amount of time while the schedule of development and approval is uncertain, and we plan to run local subsidiaries by a compact organization as much as possible in close collaboration with in-house departments as well as external companies and consultants that support us.

In the U.S., we are recruiting local employees and plan to prepare for the launch of Rapalimus<sup>®</sup> Gel by the end of December 2020. As NDA filing was conducted by the Japan headquarters, a local subsidiary will act as a sales company. In addition, we are examining the moving up of the timing of NDA filing for Retympa<sup>®</sup>.

In China, we will establish a local subsidiary in June 2020 and start operations to obtain manufacturing and marketing approval for Rapalimus<sup>®</sup> Gel. The application for the approval of the product was filed by the Japan headquarters. We may require a large amount of costs to obtain business permits in China, and it should be necessary to elaborate somewhat though we will not change our policy of selling the products through our own distribution channel. We will accelerate obtaining approvals of three overseas products of Rapalimus<sup>®</sup> Gel, TITANBRIDGE<sup>®</sup> and Retympa<sup>®</sup> in China, and examine obtaining approvals for three other products that are released in Japan.

In Europe, we will establish a local subsidiary in June 2020 and start operations to obtain manufacturing and marketing approval for Rapalimus<sup>®</sup> Gel. The application for the approval will be filed by a local subsidiary and basic functions as a pharmaceutical company, including quality assurance, safety control and medical affairs, will be completed within the local subsidiary under the support of the Japan headquarters. We are also preparing for the EU CE marking certification for TITANBRIDGE<sup>®</sup> as an approach to the EU. The application for the approval of Retympa<sup>®</sup> is examined to be moved up.

Research & Development will push ahead of the development schedule, with the aim of obtaining an approval of NPC-02 granule, a treatment for Wilson's disease and hypozincemia, in December 2020. The

development schedule is set out below. Also, we will promote a clinical trial of NPC-06, a treatment for neurological disorder, and early launch of LCM for Retympa<sup>®</sup> and Melatobel<sup>®</sup>.

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

| Compound       | 2019 | ) |                            |        |            |         |        | 20      | )20    |       |                    |               | -     |               |             | 2021   |               |        |                             |                             |              |      |           |       |    |                | 202         |
|----------------|------|---|----------------------------|--------|------------|---------|--------|---------|--------|-------|--------------------|---------------|-------|---------------|-------------|--------|---------------|--------|-----------------------------|-----------------------------|--------------|------|-----------|-------|----|----------------|-------------|
| Compound       | 11 1 | 2 | 1                          | 2      | 3          | 4       | 5      | 6       | 7      | ٤     | 3 9                | 10            | 11    | 12            | 1           | 2      | 3             | 4      | 5                           | 6                           | 7            | 8    | 9         | 10    | 11 | 12             | 1           |
| NPC-15         |      | İ |                            |        | (3)<br>App | rovec   | ł      |         |        |       |                    |               |       |               |             |        |               |        |                             |                             |              |      |           |       |    |                |             |
| NPC-02 granule |      |   | (1) <mark></mark><br>Filed |        |            |         |        |         | 1      |       |                    | -             |       |               | 2)<br>prove | d      |               |        |                             |                             |              |      |           |       |    |                |             |
| GM-CSF         |      |   |                            |        |            |         |        |         |        |       |                    |               |       | (12)<br>Filed | 1           |        |               |        |                             | _                           |              |      | (9)<br>Ap | prov  | ed |                |             |
| NPC-12 LM/CVA  |      | I | P-I                        | II (L  | M, ir      | ς<br>   |        | r-initi | · ·    |       | F                  | )<br>iled     |       |               |             |        |               |        |                             | (6)<br>Ap                   | prove        | d    |           | (10)  |    |                |             |
| NPC-12 FOP     |      |   |                            |        |            | }       | ,      |         | 1      |       | or-init<br>nitiate | tiated)<br>d) |       | $\Rightarrow$ | •           |        |               |        |                             |                             | 7) ⊏<br>iled |      |           | Filec | 1  |                |             |
| NPC-12 Pendred |      | 1 |                            |        |            | P-I     | /lla ( | inves   | ligat  | or-ir | nitiate            | d)            |       |               |             |        |               |        | (5) <mark>L</mark><br>Filed | _                           |              |      |           |       |    | )<br>(1:<br>Ap | 2)<br>prove |
| NPC-05         |      |   | P-II                       | (inve  | estig      | ator-   | initia | ted)    |        |       |                    |               |       |               |             |        |               |        |                             | (6) <mark>_</mark><br>Filed |              |      |           | 1     |    |                |             |
| NPC-12G        |      | 1 |                            | P-II   | /111 (     | nves    | tigat  | or-ini  | tjateo | d)    |                    |               |       |               | I           |        | $\Rightarrow$ |        |                             |                             |              |      |           |       |    | (12)<br>Filed  |             |
|                |      |   |                            |        |            |         |        |         |        | Lor   | ng-ter             | mad           | ninis | tration       | trial (o    | linic  | al tria       | l by o | comp                        | any)                        |              |      |           |       |    |                |             |
| NPC-09         |      |   |                            |        |            |         |        |         |        |       |                    |               |       |               | P-III       | (clini | cal t         | ial by | / com                       | pany                        | )            |      |           |       |    |                |             |
| NPC-06         |      | Ì | P                          | -11 (N | lerv       | e field | ± 1)   |         | 1      |       |                    |               |       |               |             |        |               |        |                             |                             |              |      |           |       |    |                |             |
|                |      | 1 | P                          | -11 (N | lerv       | e field | d 2)   |         | Ļ      |       |                    | 7             |       |               |             |        |               |        |                             |                             | P-III        | (Ner | rve fi    | ¢ld1) | )  |                |             |
| NPC-21         |      |   |                            |        |            | F       | P-II U | IS-Ja   | ģan I  | Inter | rnatio             | nal C         | inica | l Trial       |             |        |               |        |                             |                             | ,            |      |           |       |    |                |             |
| NPC-22         |      |   |                            |        |            | P-      | 1      |         | 1      |       |                    | -             |       |               |             |        |               |        |                             |                             |              | P-I  | 1/111     | {     | _  |                | I<br>I      |

# A. Status of Domestic Development

#### B. Status of Overseas Development

| Commound             | Year          | 2019   |               | 20              | 020          |              | 2021       |       |               |           |               |  |  |  |  |  |  |  |
|----------------------|---------------|--------|---------------|-----------------|--------------|--------------|------------|-------|---------------|-----------|---------------|--|--|--|--|--|--|--|
| Compound             | Month         | 11 12  | 1 2 3         | 4 5 6           | 7 8 9        | 10 11 12     | 1 2 3      | 4 5 6 | 789           | 10 11 12  | 12            |  |  |  |  |  |  |  |
| ND0 400              | U.S.          |        | (2)<br>NDA    |                 |              | (12)<br>Appr | oved       |       |               |           |               |  |  |  |  |  |  |  |
| NPC-12G              | China         |        |               | (8)<br>Ap       |              | \$d          |            |       |               |           |               |  |  |  |  |  |  |  |
|                      | Europe        |        |               |                 | (9)<br>Filed |              |            |       |               |           | Î             |  |  |  |  |  |  |  |
|                      | U.S.          |        | R             | sponse to Q-    | submission   |              |            |       | Clinical stud | y         | $\rightarrow$ |  |  |  |  |  |  |  |
| NPC-17               | China         |        |               |                 |              |              |            | P-III |               | ⇒         |               |  |  |  |  |  |  |  |
|                      | Europe        |        |               |                 |              | Review for   | CE marking |       |               |           |               |  |  |  |  |  |  |  |
|                      | U.S.          |        | P             | II (investigato | r-initiated) |              |            |       | P-III         |           | $\rightarrow$ |  |  |  |  |  |  |  |
| NPC-18               | China         |        |               |                 |              |              | P-III      | ]     | $\rightarrow$ |           |               |  |  |  |  |  |  |  |
|                      | Europe        |        |               |                 |              |              |            |       | P-III         |           | Î             |  |  |  |  |  |  |  |
| NPC-SE36<br>(NPC-19) | Over-<br>seas | P-lb ( | Burkina Faso) |                 |              |              |            |       |               | CHMI test | Î             |  |  |  |  |  |  |  |

The task to find seeds for new research is to strengthen and accelerate the preparation for a new development theme continuously. Upon finding seeds, we will focus on the point that these seeds meet the Company's mission (providing necessary but neglected pharmaceuticals and medical devices) and actively introduce and commercialize them from academia and bio ventures from scientific and objective viewpoints. 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.

Business Development & IP Management will actively promote license activities for introducing new themes that can be commercialized by 2024 through a tie-up with Project Planning & Development. As we added staff members engaging in agreements, we will proceed with reflecting negotiation result of an agreement in the proposed agreement promptly so as to enter into the agreement in the short term, which is the target in 2020. In overseas expansion, we have to devote more staff members to FTO searches and support of agreements. In terms of LCM, we will actively work to secure rights promptly with the view to responding to near-future LCM which has been discussed with Research & Development. There were some cases in which Sales & Marketing disclosed information related to a patent before an application of innovation. We will educate our people about intellectual property again for recurrence prevention. In purchase negotiations, we strive to realize ongoing cost reduction by paying due attention even to details.

As tasks of regulatory affairs and negotiations, Regulatory Affairs actively supports operations of both Research & Development and PMS Regulatory Compliance & Assurance, continues to help efficient and speedy responses to the authority, and fulfills regulatory affair operations with the aim of promoting a more strategic response of regulatory affairs. We also plan to add two staff members in preparation for an increase in workload associated with control of domestic changes and support of overseas regulatory affairs.

Public Relations utilized the know-how for negotiations of NHI/material price to be involved in 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 the 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, for which the Company acts as a board member and coordinator office, lobbying and advising the authorities will be continued. An increase in staff members is planned to fulfill these operations, increase the calculation of estimated NHI price and feasibility study, and foster a negotiator.

As for production, Supply Chain & Manufacturing continues to work on a stable supply of the existing products. As product inventories of Zanosar<sup>®</sup> are maintained at those for around six months, which are lower than other products, we take care to obtain information on the manufacturing status of the next lots from a French supplier at all times in order to prevent disrupting its supply.

We are working on launching Melatobel<sup>®</sup> granule as scheduled, which is expected to be launched in 2020, and other tasks for stable supply. In addition, we will prepare for releasing Melatobel<sup>®</sup> tablet to the market as soon as possible. The preparation of manufacturing and sales of Nobelzin<sup>®</sup> granule, a new formulation to be launched in 2021, is underway.

As the launch of Rapalimus<sup>®</sup> Gel in the U.S. and China comes within reaching distance in line with the advancement of its overseas development, we added staff members to prepare for establishing a supply system of the products for overseas sales.

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

For filing of re-examination, we have prepared for the introduction of a project management system in April 2020 to adequately manage and promote projects. In addition, control power functions to address filing of re-examination and compliance were established in the Safety Measure Promotion Dept., which adequately manages and supervises preparation status.

For safety management, looking ahead into the overseas business expansion, we introduced the ARISg system in June 2019, a global version of the adverse drug event report database (ARIS-j) that we introduced in 2015. In August 2019, we also introduced "Operation Designer," an electronic medium evaluation flow system, and realized visualization and streamlining of operations including paperless initiatives.

In terms of the drug use-results survey, we have introduced the Electronic Data Capture (EDC) system to the survey of Jemina<sup>®</sup> started in June 2019 in addition to Nobelzin<sup>®</sup>, a treatment for hypozincemia, and also plan to use EDC in the survey of Retympa<sup>®</sup> that is currently being planned and Melatobel<sup>®</sup> in the future.

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 on Nobelzin<sup>®</sup>, Rapalimus<sup>®</sup> Gel, Jemina<sup>®</sup>, Retympa<sup>®</sup> and Melatobel<sup>®</sup>.

PMS Regulatory Compliance & Assurance also plans to exchange personnel with Sales & Marketing and attends in branch manager meetings and branch meetings with an aim to secure the safety of drugs within the company on a smooth and adequate basis.

The tasks of corporate planning and accounting are to establish overseas subsidiaries as scheduled and to build a back office related to accounting, tax, funding, H&R and management by making full use of outsourcing and cloud systems for support of overseas expansion with the view to establishing and operating a highly apparent management system of overseas subsidiaries. It is increasingly difficult to understand business figures due to business expansion and overseas development; therefore, we will enhance a budget control system to ensure quick and accurate understanding of these figures. In conjunction with it, we will examine an effective method to promote paperless and IT initiatives.

Cash management is planned mainly in cash flows arising from operating activities. However, we will borrow long-term funds from financial institutions to maintain sufficient cash in hand to ensure a flexible response to unscheduled fund needs since we are repaying borrowings steadily and financing conditions are currently positive.

As for the issue of human resources and general affairs, we will proceed with securing human resources to establish overseas bases in the U.S., China and Europe and to promote overseas expansion, and also recruiting human resources to reinforce domestic sales capabilities, including recruitment of foreigners in Japan.

In terms of working style reform, we actively encourage employees to apply telework, off-peak commuting and the like to ensure their safety and realize effective working as a part of initiatives for COVID-19 and natural disasters such as typhoon, flood and earthquake. We have rolled out company-wide training on harassment and work to foster employees by using e-learning to disseminate the Company's philosophy and president's message ("Request for line managers").

We are also working on introducing a new target management/evaluation system. This year, we will utilize this system to streamline processes of employee's target setting and its evaluation as well as to improve communication between supervisors and subordinates.

In February 2020, the office of Sales & Marketing, which was located separately from the headquarters building, moved to the headquarters building to address earthquake resistance and ensure smooth communication between departments.

As a measure for the spread of the infectious novel coronavirus, all employees have started to work at home in March 2020. We will take this opportunity to push ahead with home teleworking and the flexible working hours system with the aim of cutting costs by reducing office buildings by March 2021.

We set the targets for the mid-long term future vision of sales and profit as an immovable high goal named North Star. In 2019, the numerical targets in 2023 as North Star in the 2019-23 mid-term business plan were sales of 50 billion yen and ordinary profit of 10 billion yen. In the 2020-24 mid-term business plan developed in 2020, this North Star target in 2023 is highly likely to be achieved as we plan that the overseas business will make a profit in a single year in 2023.

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

#### 1.15. Other Important Matters

#### 1.15.1. Relocation of the headquarters

Nobelpharma Co., Ltd. relocated the headquarters to the following address effective April 1, 2019. Subsequently, Sales & Marketing moved to the fifth floor of the same building from Yaesu in February 2020.

New address: 1-17-24 Shinkawa, Chuo-ku, Tokyo 104-0033 New Tel: +81-3-6670-3800, Fax: +81-3-6670-3801

#### 1.15.2. Establishment of the U.S. subsidiary

In the U.S., on June 3, 2019, Nobelpharma America, LLC, a wholly-owned subsidiary of Nobelpharma Co., Ltd. and a sales company, was registered in Delaware, which opened an office in Bethesda, Montgomery County of Maryland in October, as the first overseas office of the Company. Its capital is 3 million dollars and a president sent from the Japan headquarters is stationed.

#### 1.15.3. Stable supply

Despite the COVID-19 pandemic, Nobelpharma is responsible for stable supply to patients as a pharmaceutical company.

We have investigated whether there is any problem with stable supply for each supplier of additive and materials, APIs and OEM suppliers and for each affiliate in Japan and overseas. There is no problem for stable supply at this time, and we maintain inventories of the products over six months as our policy.

We will continue to secure stable supply of medical drugs.

# 2. Current Status of the Company

## 2.1. Shares (as of December 31, 2019)

| (1)   | Number of shares authorized  |                        | 50,000 shares |         |
|---|------------------------------|------------------------|---------------|---------|
| (2)   | Number of shares issued      | Ordinary share         | 13,525 shares |         |
|   |                              | Number of shareholders | 3             |         |
| (3)   | Status of Major Shareholders |                        |               |         |
| Hisanaga & Co., Ltd. (ordinary 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%)        |         |

#### 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 26, 2020, the status of full-time and part-time directors is as follows:

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

# (2) Executive Officers and Directors

| As of March 26, 2020, the | status of executive office | cers and directors is as follows: |       |
|---------------------------|----------------------------|-----------------------------------|-------|
| Vice Dussident & Chief    | Shigali Shimagali          | (II and of Dessent & Development  | ant / |

| Vice President & Chief | Shigeki Shimasaki | (Head of Research & Development / PMS |
|------------------------|-------------------|---------------------------------------|
| Operating Officer      |                   | Regulatory Compliance & Assurance)    |

| Arata Tabata<br>Tetsuo Hayase<br>Hitoshi Yokoyama<br>Kenji Shimizu | <ul><li>(Head of Business Development &amp; IP<br/>Management)</li><li>(Head of Supply Chain &amp; Manufacturing)</li><li>(Head of Sales &amp; Marketing)</li></ul>  |
|--|--|
| Hitoshi Yokoyama   |  |
| -  | (Head of Sales & Marketing)  |
| Vanii Shimizu  |  |
| Kenji Sililizu   | (Deputy Head of Research & Development)  |
| Masato Iwamoto   | (General Manager of Supply Chain<br>Management, Supply Chain &<br>Manufacturing)   |
| Yoshiki Yagi   | (Head of Project Planning & Development)   |
| Toshiaki Okamura   | (Head of Regulatory Affairs)   |
| Kozo Hayase  | (Head of Administrative Affairs & Corporate Planning)  |
| Yoshihide<br>Yamamoto  | (Head of President Office and Overseas<br>Business Development)  |
| Hitoshi Hasegawa   | (Head of PMS Regulatory Compliance &<br>Assurance / General Marketing Compliance<br>Officer)   |
| Masanori Osakabe   | (Deputy Head of Research & Development)  |
| Atsunori Iwao  | (General Manager of Quality Assurance,<br>Quality Assurance Officer)   |
| Takako Aburada   | (General Manager of CMC Development,<br>Supply Chain & Manufacturing)  |
| Shigeru Doseki   | (Region Manager of Tokyo Region)   |
| Katsuhiro Kimura   | (Region Manager of Saitama-Kanshinetsu<br>Region)  |
| Yoshiki Kida   | (President & CEO, Nobelpharma America, LLC)  |
| Masahiko Tanaka  | (General Manager of Clinical Research 3)   |
| Masatomi Nemoto  | (General Manager of Pharmacovigilance /<br>Safety Management Officer)  |
| Yasuo Suga   | (Deputy Head of Sales & Marketing)   |
| Tsutomu Iwasa  | (Region Manager of Kansai Region)  |
| Makoto Matsuda   | (Region Manager of Hokkaido/Tohoku<br>Region)  |
| Yasuo Satake   | (General Manager of HR & General Affairs)  |
| Takahiro Yamasaki  | (Managing Director-Elect of Nobelpharma subsidiary to be established in Europe)  |
| Weidong Chen   | (Director of Overseas Business<br>Development)   |
|  | Masato Iwamoto<br>Yoshiki Yagi<br>Toshiaki Okamura<br>Kozo Hayase<br>Yoshihide<br>Yamamoto<br>Hitoshi Hasegawa<br>Masanori Osakabe<br>Atsunori Iwao<br>Takako Aburada<br>Shigeru Doseki<br>Katsuhiro Kimura<br>Yoshiki Kida<br>Masahiko Tanaka<br>Masatomi Nemoto<br>Yasuo Suga<br>Tsutomu Iwasa<br>Makoto Matsuda |

(Note) The Company plans to establish local subsidiaries in Germany as a base in Europe and in China, respectively, by the second quarter of 2020.

# (3) Executive officers resigned (as of March 26, 2020)

| Akira Ikeda | (Senior Fellow, HR & General Affair Div., Administrative Affairs & Corporate |
|-------------|--|
|             | Planning)  |
| Seiu Iida   | (Head of GCP Audit Office)   |

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

| Classification  | Head-count | Amount paid    |
|-----------------|------------|----------------|
| Directors       | 6          | 9,600,000 yen  |
| Company auditor | 2          | 4,800,000 yen  |
| Total           | 8          | 14,400,000 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 year

(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 auditorWhen 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

No matters requiring special attention

16-Jul-19 From the President

#### Message to line managers

- 1.Go over the company mission, management policy, and code of conduct on a regular basis and develop a deeper understanding.
- 2. Be aware that your behavior is always being observed. Mixing public and private must be avoided by all means.
- 3. It is hard work (such as apologizing to customers) that a boss should take the lead. Subordinates respect courageous bosses.
- Be mindful of perception of favoritism.
  For example, going out for lunch or to drink with a specific subordinate (or a group).
- 5. Do not invite a subordinate of the opposite sex for a one-on-one lunch/drink. Because subordinates tend to hesitate to decline, it may be perceived as harassment.
- 6. Do not procrastinate to mend your wrong (Analects of Confucius).
- 7. Do not speak ill of people nor boast your achievements (Tori Nakane).
- 8. Speak out words of greetings when you get to the office or leave. Furthermore, if the boss is quick with jokes, the workplace becomes brighter.
- Purthermore, if the boss is quick with jokes, the workplace becomes brinder Puns are just fine.
- 9. Meet with your subordinates on a regular basis, repeatedly, one-on-one, and sober. The purpose of the meeting is to listen to your subordinates.
- 10. When scolding, one-on-one, and when praising, in front of everyone.
- 11. There is nothing good to be received by a heavy-handed order.
- Be gentle and go to all length to explain when making straight talks.
- Don't deny a subordinate's suggestion on the spot. Listen to it and, if necessary, leave a day or so before telling otherwise.
- 13. Instructions that are not in line with a subordinate's intention may also be necessary. Explain the background and purpose carefully at that time and make an effort to win the understanding.

However, after offering careful explanations three times, you may prevail with your instructions.

14. It is highly probable that a subordinate who has been carefully instructed five times and has not made improvements are not suited to the work.

It's also a way of showing love to encourage switching jobs after making him understand.

15. Simply stay away from trading shares of related parties, whether listed or not.