Creating long-term value

Research

Driving forward drug discovery to consistently identify new FIC and LIC compounds

Progress in Fiscal 2015

In the past fiscal year, we continued to create new drug development candidates focusing on two of our core therapeutic areas – infectious diseases and pain and CNS disorders. At the same time, we advanced research to maximize the value of new drug development candidates that have the potential to become FIC or LIC drugs. We also actively participated in joint research projects with external partners in order to boost research productivity and improve the accuracy of drug performance forecasting.

In the area of infectious diseases, we discovered two drug candidates for the treatment of multidrug-resistant Gram-negative bacterial infections in collaboration with GSK. We will progress the development of S-649266 as a new drug development candidate and GSK will separately progress the development of a backup drug candidate. Both compounds, which have different profiles, have the potential to contribute to the treatment of serious infectious diseases in the area of Gram-negative bacterial infections, which have become a major public health challenge worldwide. In the area of pain and CNS disorders, we worked to strengthen our pipeline, identifying a drug development candidate for the treatment of central neuropathic pain and a new BACE\(^1\) inhibitor candidate for the treatment of Alzheimer’s disease, discovered in collaboration with US company Janssen Pharmaceuticals.

As part of our efforts to improve research productivity, we established a joint research project to discover new opioid analgesics with Pionnier, a carve-out venture\(^2\) created by the Osaka Chamber of Commerce and Industry and other partners, and we started working with Nissan Chemical Industries, a company with strong capabilities in compound design and organic synthesis, to identify new antifungal agents. We also began collaborating with PeptiDream, aiming to build on our already strong position in small-molecule drug development.

These initiatives are just some of the steps we took in fiscal 2015 to advance proprietary research and generate synergies with partners that fit well with our strengths, aiming to build a pipeline of drugs for the medium and long term and reinforce our manufacturing capabilities.

\(^1\) Beta-secretase: A type of protein-cleaving enzyme secretase.

\(^2\) A type of venture company formed by spinning off a promising business to generate further growth. The original company typically maintains links with the carved out business.

Objectives for Fiscal 2016

We aim to discover two or more drug development candidates in target therapeutic areas in SGS2020, as well as strengthen drug discovery capabilities through new collaborations with academia and industry in Japan and overseas, helping us advance research that generates a steady stream of potential FICs and LICs.

Drug discovery capabilities that lead to groundbreaking new drugs

The development of dolutegravir was led by the finding that an HIV integrase inhibitor binds to active sites. This unique discovery triggered the start of internal competition to synthesize a new superior family of compounds, with the commitment of our research team ultimately leading to the creation of dolutegravir. This also prompted us to initiate research into compounds that inhibit the cap endonuclease of the influenza virus based on evidence of the same binding behavior. Our research team, confident that they could use the same approach for influenza drug development as they had in HIV drug development, took their know-how from dolutegravir in a new direction, resulting in the discovery of anti-influenza drug candidate S-033188. This illustrates how passing on and cultivating expertise is a key part of our approach to small-molecule drug discovery at Shionogi.
Fighting the global threat of infections

Multidrug-resistant bacteria, tuberculosis and malaria are a growing threat to human health worldwide. Outbreaks of emerging infections such as the Ebola, Zika and Dengue viruses are also a serious public health issue that threatens human life. The issue of multidrug-resistance needs to be tackled urgently on a global scale and has been flagged as a serious problem by the World Health Organization (WHO) and the leaders of the G7 nations.

Meanwhile, many global pharmaceutical companies have withdrawn from drug discovery in the field of infectious diseases, as treatment periods tend to be short, limiting opportunities for profits. Against this backdrop, the Shionogi Group is leveraging its long track record in the field to actively develop new treatments for infectious diseases. Specifically, two compounds have progressed to late stage global development. One is S-649266, a promising candidate for the treatment of multidrug-resistant Gram-negative bacterial infections such as multidrug-resistant Pseudomonas aeruginosa and multidrug-resistant Acinetobacter baumannii for which there are currently no treatment options. The other is S-033188, a highly effective treatment against the influenza virus, a pandemic risk. Shionogi is actively involved in the search for treatments for multidrug-resistant tuberculosis and pathogens that cause neglected tropical diseases (NTDs) through industry-academic collaborations and other partnerships.

We will continue to focus on drug discovery in this field in order to rapidly develop new treatments, aiming to help as many people as possible conquer these life-threatening diseases.

Shionogi’s infectious disease target research areas

<table>
<thead>
<tr>
<th>Research areas</th>
<th>Unmet medical needs and disease background</th>
<th>Research strategy</th>
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| Severe Infections | • Bacterial infections  
• Fungal infections | Requirement for  
• Drugs for antibiotic-resistant bacteria  
• Improvement in compliance (early hospital discharge, high barrier to the development of resistance)  
• Safe and efficacious antifungal drug | • Develop drugs for antibiotic-resistant bacteria by β-lactam chemistry  
• Develop drugs for fatal systemic fungal infections |
| Viral Infections | • HIV  
• Respiratory virus | Increased risk of HIV infection with lifestyle changes  
• Requirement for  
  - Improvement in QOL* of HIV patients (long-term use, long administration interval, high barrier to the development of resistance)  
  - Efficacious drugs for respiratory virus infection | • Expand HIV pipeline by FIC/LIC drug discovery  
• Develop anti-respiratory virus drugs by original compound design |
| Emerging Infections | •Emerging/re-emerging infectious disease | Outbreak of emerging/re-emerging infectious diseases  
• Requirement for efficacious drugs | • Drug discovery through external collaborations |

* QOL: Quality of Life
Progress in Fiscal 2015
Almost all our development projects advanced as planned in fiscal 2015. In global drug development, we submitted NDAs in Japan and the US for Naldemedine, a treatment for opioid-induced constipation (OIC). Global Phase III trials progressed smoothly for thrombocytopenia treatment Mulpleta and for S-649266, a treatment for multidrug-resistant Gram-negative bacterial infections. We also entered into a global license and collaboration agreement with Roche to develop and commercialize anti-influenza drug S-033188, which has been designated for priority review by the Ministry of Health, Labour and Welfare in Japan. A Phase II trial in Japan for S-033188 confirmed sufficient evidence of efficacy and safety to progress to the next stage of clinical trials.

Cymbalta, one of our strategic products in Japan, was approved for the additional indications of pain associated with fibromyalgia and chronic lower back pain, and we submitted an NDA for the additional indication of pain associated with osteoarthritis. Mulpleta was granted approval in Japan and we submitted an NDA for S-877503 for the treatment of attention-deficit hyperactivity disorder (ADHD).

Objectives for Fiscal 2016
In fiscal 2016, we will push ahead with the global development of S-649266 and S-033188, aiming to continue making a significant contribution to society as one of the leading pharmaceutical companies in infectious disease treatments worldwide. In pain and CNS disorders, one of our core therapeutic areas, we plan to submit an NDA in Japan for S-877489, another ADHD treatment but with a different mechanism of action than S-877503. We will also apply for non-cancer pain indications for OxyContin and for abuse-deterrent OxyContin formulations.

To continue implementing high-quality, expeditious clinical trials, we will strengthen global operations and adopt standardized processes. We will also generate further efficiency gains and improve cost management to ensure patients worldwide have access to the best possible medicines.

NDAs submitted for Naldemedine in Japan and the US
Naldemedine, an original Shionogi compound, moved into human clinical trials in 2009. Since then, the drug has been tested in a total of 22 clinical trials in 18 countries worldwide, involving over 3,000 healthy subjects and patients with OIC. The COMPOSE program, launched in 2013 in Japan, the US and Europe, is the first-ever global program of Phase III clinical trials for an original Shionogi compound run solely by the Shionogi Group. Following the trials, we submitted NDAs in Japan and the US in March 2016. We have positioned Naldemedine as a first-in-class (FIC) and last-in-class (LIC) drug in Japan and as an LIC drug in the US, aiming to help patients suffering from OIC gain access to the best possible treatment. In 2017, we expect Naldemedine to improve QOL for patients with OIC, giving them an effective and safe treatment while having no adverse impact on the analgesic mechanism of opioids.
Progress in Fiscal 2015
The CMC Research Division plays a vital role in realizing Shionogi’s vision for creating and producing even better medicines.

The progress we made in fiscal 2015 underscored the global competitiveness of our technologies. We submitted NDAs for Naldemedine in Japan and the US in line with our planned timeframe and our technologies supported significant advances in the development of anti-influenza drug candidate S-033188, which is designated a fast-track review candidate under Japan’s priority review system. S-033188 was developed at unprecedented speed and we were able to significantly reduce the cost of synthesizing active pharmaceutical ingredients.

We also prepared new investigational drugs in a timely manner for S-649266 Phase III clinical trials in accordance with rules for multiple jurisdictions. In addition, we made solid progress in NTE development*, which brings together all our drug formulation technologies, helping us take an important first step on the road to building a hybrid business model encompassing both new drug discovery and NTE development.

*New therapeutic entity development: Development of new dosage forms, new administration routes and new indications with known compounds.

Objectives for Fiscal 2016
As the pace of global drug development accelerates, we have been given a greater role in delivering high-quality, easy-to-use medicines that satisfy the needs of patients and medical professionals worldwide. In line with this wider role, the CMC Development Laboratories was renamed the CMC R&D Division, effective from the start of fiscal 2016. In the year ahead, we will push forward with the strategic development of new drugs and NTE development, focusing on the establishment of commercial production processes for abuse-deterrent OxyContin formulations, approval for Naldemedine and the steady development of S-033188. We will use our high value-added “enhanced product development” approach to address today’s healthcare needs, aiming to deliver superior drugs that improve QOL for patients in need of new treatments.

Note: CMC (Chemistry, Manufacturing and Control): Drug substance manufacturing process studies, pharmaceutical development studies, and quality control studies.

Enhanced Product Development
We achieved a number of positive outcomes in fiscal 2015. We improved the absorbability of Mulipleta’s active pharmaceutical ingredient, which dissolved slowly in the gastrointestinal tract. Building on our existing research in absorption enhancement technology, we developed a formulation that adds a solubilizing agent to the active pharmaceutical ingredient, improving absorption and helping to improve patient health. With Crestor orally disintegrating (OD) tablets, we created the world’s first trilayer OD tablet that fully disintegrates in the mouth. The active pharmaceutical agent is contained in a middle layer, while the top and bottom layers contain sweetening agents that also protect the drug from light. We also successfully developed Naldemedine, which demonstrates high levels of stability and homogeneity for an ultra-low dose drug, and pushed ahead with the development of S-649266 using our strengths in freeze-drying technologies. Going forward, we will continue to leverage technologies that enhance the performance, stability and absorbability of active pharmaceutical ingredients to develop superior medicines.
Creating long-term value

Progress in Fiscal 2015
We launched a number of new drugs in fiscal 2015, including Actair and Mulpleta. We also secured marketing approval for Crestor orally disintegrating (OD) tablets, one of our strategic lifecycle management (LCM) products. The new Crestor OD tablets were launched in June 2016. The Manufacturing Division made a significant contribution to the launch of these new products in the past fiscal year, in line with the goal of “producing the best possible medicines” in the Company Policy of Shionogi.

We also pushed ahead with our Mother Factory Concept*1 aimed at ensuring stable supplies of high-quality products. Under this concept, the production of long-listed drugs has been outsourced to external contract manufacturing organizations (CMOs).

*1 Mother Factory Concept: A manufacturing strategy that allows us to respond flexibly to fluctuations in sales volumes throughout the product lifecycle. This involves actively using CMOs worldwide to manufacture Shionogi products when capacity is exceeded at proprietary plants.

Objectives for Fiscal 2016
A number of new products are planned for NDA or launch in fiscal 2016 and beyond. We have to be ready to start commercial production at our Kanegasaki Plant and Settsu Plant and also at Shionogi Pharma Chemicals Co., Ltd, a Shionogi consolidated subsidiary.

Our anti-influenza drug candidate S-033188 has been designated as a fast-track review candidate under Japan’s priority review system and S-649266, a candidate for the treatment of multidrug-resistant Gram-negative bacterial infections, has been designated as a qualified infectious disease product (QIDP)*2 by the US Food and Drug Administration (FDA). This highlights the significant potential of both drug candidates. We are also preparing to support the launch of Naldemedine, an OIC treatment for which we have simultaneously submitted NDAs in both Japan and the US. We are putting in place a production system that will be compliant with regulations in each market.

In Japan, Shionogi is targeting the early launch of two attention-deficit hyperactivity disorder (ADHD) drug candidates, S-877503 and S-877489.

Using this almost unprecedented number of upcoming drug launches, we aim to demonstrate Shionogi’s strengths in manufacturing technologies over the next few years and is therefore a crucial period for the Manufacturing Division.

We are committed to delivering new Shionogi drugs to patients as rapidly as possible. Everyone in the Manufacturing Division will work as one to achieve this goal with our upcoming drug launches, while also cooperating closely with related divisions.

*2 New drugs developed to treat drug-resistant infectious diseases that are granted this status are eligible to receive five years of marketing exclusivity in addition to certain exclusivity already provided under US law.
Strengths and features of shionogi’s manufacturing sites

01 Kanegasaki Plant

Integrated production of β-Lactam antibiotics

The Kanegasaki Plant has an integrated production system for cephem- and carbapenem-based antibiotics, covering active pharmaceutical ingredients (API), formulation manufacturing and packaging. This allows us to deliver high-quality products to patients worldwide.

The operating environment surrounding β-Lactam antibiotic production in Japan has changed in recent years, with a growing number of companies deciding to withdraw from domestic production of API due to tighter regulations and the rising cost of production. These drug companies now import API from China, South Korea and India and then complete the manufacturing process in Japan. However, we remain committed to our integrated manufacturing approach at the Kanegasaki Plant, including the production of API. Overseas production has cost benefits, but we are concerned about the risk of API quality issues and potential obstacles to stable supplies. Our integrated production system allows us to rapidly resolve any issues that may arise in production by working closely and quickly with teams inside the Company, minimizing the risk of supply shortages. Also, our “Shionogi quality” approach is not limited to the quality of finished products. It also includes environmental protection, such as reducing energy consumption and CO2 emissions in our manufacturing activities, and ensuring safe and healthy working environments for personnel at all our plants.

The Kanegasaki Plant has started preparing for commercial production of S-649266, a drug candidate currently under global development for the treatment of multidrug-resistant Gram-negative bacterial infections. This drug will also be manufactured by the plant’s integrated production system. Everybody at the Kanegasaki Plant is committed to rapidly starting production of S-649266 so that people suffering from multidrug-resistant infections worldwide will be able to access the drug as soon as possible.

By maximizing our strengths as a Company – strong research capabilities in infectious diseases and integrated production technologies covering API, formulation manufacturing and packaging – we will fight the global threat of emerging infectious diseases and multidrug-resistant infections.

02 Settsu Plant

A flexible production system that can handle small batch manufacturing and multiple products

The Settsu Plant manufactures pharmaceutical products (except antibiotics) in tablet, capsule and injectable forms in accordance with PIC/S*1 and GMP*2. Using flexible production facilities and technologies that can handle small batch manufacturing and multiple product lines, the Settsu Plant constantly seeks to improve productivity and deliver strategic products such as Cymbalta and Irbetan to patients.

The Settsu Plant played a key role in the launch of several new drugs recently: Actair in November 2015, Muplepta in December 2015 and Crestor OD tablets in June 2016.

Going forward, the plant will continue to use its experience and expertise in drug manufacturing, including safety and the environment, to play its part in maintaining “Shionogi quality.” Specifically, the Settsu Plant will work to ensure the rapid launch of upcoming global drugs, such as anti-influenza drug candidate S-033188, OIC drug Naldemedine and ADHD drug candidates S-877503 and S-877489.

By establishing highly efficient manufacturing processes and supplying the best possible medicines, we will help to protect the health and wellbeing of patients worldwide.

*1 The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme
*2 GMP (Good Manufacturing Practice)
Creating long-term value

Global SCM

Ensuring the stable supply of products in the global market and contributing to profits

Progress in Fiscal 2015
The mission of the Global SCM Division is to contribute to customer satisfaction and help the "Shionogi family" generate profits by continuously optimizing the global supply chain around the stable supply of products.

In fiscal 2015, we strategically reviewed contracts and purchasing conditions with our domestic and overseas suppliers and overhauled logistics operations. This generated cost savings that helped Shionogi achieve profitability at the operating income level excluding royalty income. By optimizing inventories further, we reduced inventory assets and contributed to stronger cash flow. The Global SCM Division also helped to drive sales growth by reinforcing the manufacturing system for the active pharmaceutical ingredient in anti-HIV agent Tivicay, ensuring stable supplies. Ahead of the planned launch of Naldemedine, a new treatment for opioid-induced constipation, we put in place a global sales and supply chain structure.

Objectives for Fiscal 2016
One of our goals is to reinforce global supply chain management functions to support the smooth launch and stable supply of Shionogi’s growing portfolio of proprietary drugs. We have therefore positioned fiscal 2016 as a crucial year to push ahead with our mission and build a supply chain system that ensures Shionogi achieves its SGS2020 targets. We will work to link procurement, manufacturing and distribution functions more closely to create a fully optimized supply structure that also takes into account the requirements of business continuity plans (BCPs).

In Japan, Crestor OD tablets have been launched and Cymbalta has been approved for additional indications. Overseas, Naldemedine is on track for launch after other recent global drug launches such as antibiotic doripenem and Osphena. Our mission at the Global SCM Division is to ensure patients worldwide continue to have access to these and other drugs. Partnering with other Shionogi business divisions will be crucial to achieving this mission.

Powerful SCM Capabilities—Supporting Shionogi’s Bottom Line
Starting in fiscal 2014, we consolidated SCM functions within the Global SCM Division. This created a joint management system that integrates the Group’s supply chain from upstream through to downstream areas. Effective fiscal 2016, the division was reorganized into two departments, the Supply Business Strategy Department and the Supply Operation Department, to strengthen our business strategy and supply operation functions.

The Global SCM Division will work in tandem with the Manufacturing Division to launch new cost control initiatives, including from a medium- and long-term perspective, in order to deliver further cost savings. Through collaboration with other divisions, we aim to develop and promote manufacturing strategies tailored to various product lifecycles and markets to ensure efficient allocation of resources, helping Shionogi to achieve its business plan targets and generate profits.
Promoting the Shionogi Product Policy and “Quality Culture” worldwide

In July 2015, the Corporate Quality Management Division revised the Shionogi Product Policy and formulated a new Shionogi Group Quality Policy. We did this for two main reasons. First, with Shionogi expanding its business worldwide, we needed a quality policy that complies with global standards. Second, we wanted to overhaul our stance on quality across all activities, from the quality of products themselves to the processes that support them, such as back-office operations, manufacturing and services.

Based on these quality policies, the Corporate Quality Management Division launched new quality assurance initiatives in all areas of manufacturing under the slogan “Quality Culture.” In addition to quality assurance in manufacturing processes and document management, we stepped up quality training programs at Shionogi manufacturing sites and contract manufacturing organizations based on our belief that training and education are vitally important to raise awareness of quality control from the bottom up. We are also working closely with overseas subsidiaries (Shionogi Inc., Shionogi Limited) to maintain and enhance quality on a global level, not only in GMP/GDP, but also in other areas of GxP*. Such as GCP.

*GxP is a general abbreviation for Good Practice Standards – namely, GLP (Good Laboratory Practice), GMP (Good Manufacturing Practice), GDP (Good Distribution Practice), GCP (Good Clinical Practice), GVP (Good Vigilance Practice) and GPSP (Good Post-marketing Study Practice).

New drug applications and safety monitoring

We were involved in a large number of new drug applications (NDAs), approvals and product launches in fiscal 2015. Our simultaneous NDAs for Naldemedine in Japan and the US was a first for Shionogi. We established a Naldemedine global cross-functional team covering Japan, the US and Europe to develop the regulatory strategy and safety data assessment process for the NDAs. Once consensus was reached by the team, we compiled the NDA files, supporting documents and a risk management plan (RMP) and submitted them to the authorities. Shionogi also launched Actair and Cymbalta was approved for the additional indication of chronic lower back pain. Before these drugs were rolled out, we set up a network with medical institutions and pharmacies to carry out prediction and prevention-based safety monitoring activities after launch. These new post-marketing safety monitoring approaches in Japan are helping to maximize the value of Shionogi products. Also, working with the Human Health Care Division, we plan to proactively provide information to encourage wider use of drug safety information. One example is our plan to build a pharmacoepidemiology research base and use it to develop new methods for using drug information and treatment information with partner organizations.

To achieve our SGS2020 targets, we need to reinforce our domestic business and actively grow our business overseas. As Shionogi’s operations become more global, quality risks will increase. The fundamental role of the Corporate Quality Management Division will be to predict, mitigate and eliminate those risks. We will continue to work closely with frontline personnel to ensure the quality of all processes related to Shionogi products.
Creating long-term value

Progress in Fiscal 2015

We focused on three strategic products in fiscal 2015: Crestor, Cymbalta and the Irbetan family of drugs. Crestor, which achieved blockbuster status in fiscal 2014, registered further growth, contributing to the treatment of even more patients over the past year. Sales of Cymbalta continued to grow, supported by prescriptions for major depressive disorders. We hope more patients will benefit from prescriptions of Cymbalta following its approval for the additional indication of chronic low back pain in March 2016. We also added two new drugs to our lineup in fiscal 2015: Actair sublingual tablets, an allergen immunotherapy for house-dust mite allergen launched in November 2015, and Mulpeta tablets, a Shionogi-developed thrombocytopenia treatment released in December 2015.

We overhauled our operating structure in fiscal 2015 to enable future growth. As part of moves to address changes in our business environment in Japan, the first country in the world to face challenges arising from a rapidly aging society, we are adjusting the strategic focus of the Human Health Care Division. We also established a Medical Relations Unit to respond to expected growth in local healthcare provision. The unit will work with medical representatives to develop healthcare and medical treatment proposals tailored to local needs.

Objectives for Fiscal 2016

We will target resources on Cymbalta and Crestor in fiscal 2016. Cymbalta has a novel mechanism of action as a pain relief agent. We therefore plan to initially focus on providing information about the drug’s safety to ensure patients are confident about using Cymbalta. We launched Crestor orally disintegrating (OD) tablets in June 2016 and we plan to use the new formulation to improve medication adherence* and enhance the effectiveness of treatment.

Our new Medical Relations Unit will have an increasingly important role to play in advancing community-based healthcare. We will also transfer more authority to each sales area in order to fully leverage our frontline capabilities – one of Shionogi’s strengths. Going forward, we will strive to be the best medical partner for patients and healthcare providers while responding to changes in the market positively and taking on new challenges.

* A process whereby patients actively participate in decisions on treatment strategies and then receive treatment and medication based on those decisions.

Ryuichi Kume, Ph.D.
Executive Officer,
Senior Vice President,
Human Health Care Division

Domestic Business
Aiming to be the best medical partner for patients and healthcare professionals
Infectious diseases, by their nature, are a transmission risk to all people. As borders become more porous and globalization gathers pace, we also face the risk of emerging and re-emerging infectious diseases and antimicrobial resistance – issues that have to be addressed by society as a whole.

At Shionogi, antimicrobial stewardship means selecting the most appropriate antimicrobial agent, dose and administration method and ensuring treatment ends at the optimal time in order to make treatments safe and reliable, control the spread of drug-resistant bacteria and viruses, and support the effective use of healthcare resources. We organize and provide relevant information to promote appropriate use of antimicrobial agents. This involves using antimicrobial susceptibility surveillance programs to gather accurate epidemiological data, rigorously analyzing industry guidelines and improving understanding about pharmaceutical profiles.

Infectious diseases are a threat to human life and can have a major impact on economic activity. Aiming to be the best medical partner for patients and healthcare providers, we are working to counter that threat by providing information about all aspects of infectious diseases, from prevention through to recovery.

Pain is something we all have to deal with in our lives. Shionogi has established a Pain Management Unit to provide broad support for pain treatment. The unit aims to transform Shionogi into a "pain concierge company." Under this model all Shionogi personnel will work together to provide information and medicines to individual patients for the best pain treatment, which should also encourage more healthcare providers to select Shionogi’s products and services.

In fiscal 2015, Cymbalta was approved for the additional indications of pain associated with fibromyalgia and chronic low back pain. Cymbalta is currently being assessed for the additional indication of pain associated with osteoarthritis and we have submitted an NDA for Naldemedine for the treatment of opioid-induced constipation (OIC). We are also seeking approval for an abuse-deterrent OxyContin formulation and additional indications for OxyContin in the area of non-cancer pain.

We therefore have a number of new pain treatment-related drugs lined up for approval and launch in fiscal 2016 and beyond. We aim to use these and other products to develop the best possible pain treatment plan for each patient and help relieve the suffering of as many people as possible.

Shionogi’s operating environment is undergoing far-reaching change. The Japanese government has launched a community-based healthcare policy and is promoting the creation of a comprehensive local healthcare system and home healthcare services. That means Shionogi will have to address advanced patient and healthcare needs. In October 2015, we established the Medical Relations Unit to build a business model that can contribute to community healthcare. Since its launch, the unit has made contact with prefectural agencies responsible for promoting community healthcare, healthcare providers, healthcare associations and other groups to gather information about the current situation and issues in each area. This information will be used to develop Shionogi’s local healthcare activities. The Medical Relations Unit, Distribution Management Department, other related groups inside Shionogi and medical representations will share this information and work together to help resolve issues in community healthcare settings.

Shionogi is a founding member of the Palliative Care Consortium, an industry body that promotes and raises awareness of cancer pain treatments.
Progress in Fiscal 2015
In the US, we have been working to expand sales of postmenopausal vulvar and vaginal atrophy (VVA) treatment Osphena (generic name: ospemifene). Our strategy is focused on technical activities to raise awareness among medical professionals about the importance of continuing with Osphena for a minimum of 90 days to ensure effectiveness. We are also using DTC* activities to influence consultation behavior and are channeling significant resources into increasing health insurance coverage for Osphena treatments. In the second half of fiscal 2015, we launched a purchasing support scheme to reduce the out-of-pocket cost for patients, based on conditions in their private health insurance plans. This drove a clear upturn in prescriptions, with Osphena currently the only drug to register sales growth in the sluggish US market for VVA treatments. We also steadily rolled out ospemifene in Europe, launching it under the Senshio brand name in Italy in October 2015 and Spain in January 2016. We are now working to secure approval for ospemifene in Singapore. Our Chinese subsidiary, C&O Pharmaceutical Technology (Holdings) Limited, is currently building a business base to transform itself into a highly profitable company through the launch of new drugs.

Taiwan Shionogi & Co., Ltd. has established a dedicated division to promote the appropriate use of infectious disease treatments in order to address the serious global public health issue of drug-resistant bacteria, and Beijing Shionogi Pharmaceutical Technology Limited has created a similar organization to actively tackle the issue in Asia.

*Direct-to-consumer: Providing information about pharmaceutical products directly to consumers.

Objectives for Fiscal 2016
In the US, one of our priority markets in SGS2020, we plan to expand sales of Osphena by implementing highly targeted sales strategies for each regional market based on sales performance to date. We will also put in place structures to drive rapid sales growth for Naldemedine after launch, which is scheduled for fiscal 2017.

In Europe, we will continue to develop new drugs and promote Senshio. In Asia, we will implement initiatives to promote the appropriate use of infectious disease treatments and make preparations to launch new products.
Aiming to grow as a drug discovery-based pharmaceutical company

We launched SGS2020 with the aim of “growing as a drug discovery-based pharmaceutical company,” focusing on the two core therapeutic areas of infectious diseases and pain / CNS disorders. Our decision to focus on those two fields reflects our long track record of developing drugs to treat infections and pain.

Infectious diseases are an inseparable part of the human condition and have affected people since the dawn of time. With Alexander Fleming’s discovery of penicillin in 1928, we finally gained a tool to control infections. Since then, it has been a constant battle to develop drugs that are effective against various pathogens, which then build up resistance to survive, requiring renewed efforts to discover effective new medicines. Shionogi has played an important role in the global fight against infections, including emerging infectious diseases and the resurgence of existing diseases. This is a Shionogi strength that we have to maintain and develop further.

In pain and CNS disorders, demand for treatments is rising worldwide as societies age rapidly. New drugs and other improvements in healthcare have helped to extend average life expectancy around the world. Now attention is turning to ways of using healthcare to increase healthy life expectancy from the perspective of QOL. Pain and deteriorating cognitive functions can have a major negative impact on QOL. By providing drugs that extend healthy life expectancy, we can make life better for many people.

To achieve that objective, we are leveraging our strengths in small-molecule drug development to create accessible and affordable medicines in our two core therapeutic fields of infectious diseases and pain / CNS disorders. Collaborating with other companies and external research bodies will be crucial to achieve one of our core principles – to supply the best possible medicine to protect the health and wellbeing of the patients we serve. Strong alliances are built on the best possible partners using the best possible methods to maximize innovation. That thinking is behind our efforts to reinforce Shionogi’s presence through partnerships with pharmaceutical companies and academic centers of excellence in Japan and overseas.
Prescription Drugs

Major Products

Shionogi will work steadily to expand its share in the Japanese market, focusing on seven strategic products.

**Crestor® tablets**
*Hyperlipidemia treatment*
- Crestor® tablets launched April 2005
- Crestor® OD tablets launched June 2016

Shionogi-developed statin therapy Crestor has been proven highly effective in lowering LDL cholesterol and is a leader among dyslipidemia treatments in Japan and overseas. It reduces the risk of atherosclerotic diseases, and affords physicians and patients a greater sense of satisfaction and reliability. Crestor OD tablets were developed using Shionogi technology to improve patient adherence. The tablets are hard yet disintegrate rapidly.

**Cymbalta® Capsules**
*Treatment for depression, depressive condition, diabetic neuropathic pain, fibromyalgia pain and chronic lower back pain*
- Launched April 2010

Cymbalta is a serotonin and noradrenaline reuptake inhibitor approved as an anti-depressant in more than 100 countries. It is recommended as the first-line treatment for diabetic neuropathic pain (DNP) in domestic and international guidelines.

Cymbalta received approval in Japan for the additional indication of pain associated with fibromyalgia in May 2015 and for the additional indication of pain associated with chronic lower back pain in March 2016.

**Irbetan family of drugs**
**Irbetan® Tablets**
**AIMIX® Combination Tablets**
**IRTRA® Combination Tablets**
*Antihypertensive*
- Irbetan® Tablets launched July 2008, AIMIX Combination Tablets launched December 2012, **IRTRA® Combination Tablets launched September 2013**
- Irbetan is a long-acting angiotensin II receptor blocker (ARB) with a powerful hypotensive effect lasting 24 hours and anti-metabolic organ protecting effects. Shionogi also sells the drug as part of combination formulations, such as **AMIX Combination Tablets** with calcium antagonist amlodipine, and **IRTRA Combination Tablets** with diuretic trichlormethiazide, contributing to the treatment of hypertension through a family of Irbetan products.

**OxyContin family of drugs**
**OxyContin® Tablets**
**OxiNorm® Powder**
**OxiFast® Injection**
*Cancer pain analgesic*

A combination of 12-hour sustained-release OxyContin tablet and immediate-release OxiNorm powder enables cancer pain to be relieved more effectively.

OxiFast injection can be used for pain relief in patients with difficulty taking oral drugs.

**Pirespa® Tablets**
*Idiopathic pulmonary fibrosis treatment*
- Launched December 2008

Pirespa is the world’s first drug to be indicated for idiopathic pulmonary fibrosis. Pirespa is expected to inhibit the decrease in vital capacity and slow the progression of idiopathic pulmonary fibrosis.

**Finibax® for Intravenous Drip Infusion**
**Finibax® solution kit for Intravenous Drip Infusion**
*Carbapenem-type antibiotic*
- Finibax® solution kit for Intravenous Drip Infusion launched September 2005

Shionogi-developed Finibax is a carbapenem-type antibiotic for injection with strong antibacterial activity against *Pseudomonas aeruginosa*.

There is increasing expectation surrounding this product’s effectiveness as a treatment for serious and intractable infections such as sepsis, pneumonia, and peritonitis.

**Rapiacta® for Intravenous Drip Infusion**
*Antiviral drug for influenza*
- Launched January 2010

Rapiacta is the world’s first neuraminidase inhibitor for intravenous drip infusion. As a single-dose intravenous drip infusion, Rapiacta can be expected to produce reliable treatment benefits, enabling it to be used to treat outpatients and hospitalized patients in all age groups, from infants to the elderly.
Shionogi Healthcare established

We established Shionogi Healthcare Co., Ltd. as a wholly owned subsidiary in January 2016 to provide consumer healthcare products in Japan.

Reasons for setting up Shionogi Healthcare
As the world’s first country to face the challenges of a rapidly aging society, Japan needs to curb public healthcare expenditures, which totaled more than ¥40 trillion in fiscal 2013. The government is promoting self-medication as part of a package of measures to reduce healthcare spending. Over-the-counter (OTC) drugs are set to play a key role in this approach, including preferential tax treatment for OTC drug purchases from fiscal 2017. This is likely to lead to far-reaching changes in the healthcare environment in Japan. Against this backdrop, Shionogi Healthcare’s mission is to help extend healthy life expectancy by contributing to patient health in the field of self-medication, which will bring us into closer contact with the end-users of our products.

An independent, dynamic company
In the OTC drugs category, where consumers have the final say about which products to buy, market needs move and change all the time. Companies have to constantly stay abreast of that change by rapidly developing new products, securing marketing approval and adjusting sales promotion strategies. Responding to that kind of change on a daily business is difficult for any single business division in Shionogi, but a standalone company is more nimble, offering a significant competitive advantage. We believe an independent company will give us a better chance of success in the self-medication market.

Strategic products
Shionogi Healthcare focuses on four categories – pain, oral care, health support and infections. Oral care in particular is a promising growth market. Over the last decade, as seniors have become healthier, there has been a dramatic increase in the number of people retaining their principal natural teeth. However, at the same time, there are still many people who lose interest in food after losing some of their teeth in old age. Our Correct Series of denture adhesives, which includes three distinctive types of adhesive – cushion, stick-on and tape-type – improves the stability of dentures, making talking more fun and helping to maintain and improve appetite. The Correct Series is one of the brands in our portfolio that can make a real difference to healthy life expectancy.

A presence in all areas of the value chain – development, manufacturing and selling
Shionogi Healthcare will adhere to the Company Policy of Shionogi and work to develop, manufacture and sell OTC drugs in an integrated and efficient way, aiming to continually evolve as a company that helps extend the healthy life expectancy of as many people as possible.

Key products

**Analgesics**

*Sedes Series*

Fast-acting, effective analgesics with isopropylantipyrine for the treatment of intolerable pain.

**Multivitamin supplements**

*Popon Series*

A lineup of pharmaceutical-grade multivitamins for people prone to poor health.

**Isodine®**

Isodine® contains povidone-iodine, a powerful antiseptic that was taken on the Apollo moon mission. It can be used as a mouthwash, ointment and handwash. Shionogi began selling Isodine® in 2016 after signing an exclusive sales collaboration contract with Mundipharma. Isodine® is globally known as Betadine® brand.

Isodine® is a registered trademark of Mundipharma K.K.