

Shionogi's business: value chain

In the process of creating new drugs and delivering them to patients, a pharmaceutical company must rely on contributions from multiple business divisions. At Shionogi, every link in the value chain—from research (drug discovery and CMC), to development, manufacturing, and sales—has its own vision and formulates strategies to achieve the goals contained therein, working together when necessary to realize those objectives and in doing so consistently creating new value.

Pharmaceutical Research Division

Vision of Pharmaceutical Research Division

Innovation in drug discovery to meet societal needs

As a drug discovery-based pharmaceutical company, Shionogi considers the original pipeline ratio to be important. At the same time, we believe it is impossible to consistently create better drugs when bound by preconceived ideas. We aim to establish new approaches to drug discovery that draw on various ideas from both inside and outside the Company.

Strategy for achieving our vision

Leverage strength in small molecule drug discovery

keyword 1

Medium molecule drugs



Hopes are high that “medium molecule drugs” such as nucleic acid drugs and peptides will produce the next generation of pharmaceuticals. At Shionogi, we aim to harness the chemical technologies and expertise we have developed in the field of small molecule drug discovery, and apply these also to the discovery of medium molecule drugs.

keyword 2

Open innovation



Shionogi has sought to promote collaborative research with partners, by such means as joining the UK's Cambridge Therapeutic Consortium. We look to accelerate innovation by combining our drug discovery capabilities with the intellectual know-how of academic institutions.

keyword 3

Encouraging sense of adventure in researchers



Innovation tends to be lacking when research is just a job. To instill in our researchers a true sense of adventure, Shionogi evaluates not only research results but also the processes. Furthermore, we have established a novel program dubbed “Y Collaboration” that encourages individuals to independently search out and propose collaborative research partners.

CMC R&D Division

Vision of CMC R&D Division

Research and development of original CMC technology:
Creating valuable products meeting societal needs

The CMC R&D Division contributes from a total healthcare perspective to the creation of innovative products with potential to fulfil societal medical needs. In order to develop such innovative products, the Division undertakes CMC research and works to acquire new CMC technologies to augment its existing scientific base. By maximizing use of partnerships both inside and outside of Shionogi, the CMC R&D Division strives to bring new value to the healthcare field, transcending traditional paradigms for pharmaceutical development.

Strategy for achieving our vision

Grow the Company by developing better people, technology, and partnerships

keyword 1

Fostering well-rounded employees



Shionogi takes a proactive stance toward education aimed at building well-rounded employees, including an exchange program offering training at Shionogi Inc. in the US, and rotation between different divisions.

keyword 2

Providing new solutions for drug discovery research



Shionogi has been able to use CMC technologies to achieve breakthroughs, improving the body's absorption of chemical compounds that had a pharmacological effect but were difficult to the body to absorb. The CMC R&D Division seeks to continue providing new solutions through involvement from the drug discovery research stage.

keyword 3

Pursuing even higher levels of expertise



Shionogi seeks to create new value through the use of sophisticated CMC technologies for such tasks as developing products that are as effective as possible in meeting patient needs, identifying the synthetic routes best suited to reducing COGs*1, and developing new analytical solutions premised on cutting-edge technology.

*1 COGs: Cost of goods sold

Global Development Division

Vision of Global Development Division

Efficient and consistent development for the good of patients around the world

By 2020, we aim to have launched 10 or more products globally. To that end, we seek to maintain a high rate of success in confirmatory (Phase 3) clinical trials by swiftly and accurately identifying compound attributes during early-stage clinical trials, in order to make a science-based go/no-go decision. We furthermore plan to contribute to maximizing product value by extending our data collection horizons beyond what is needed for regulatory submissions, to also include data supporting post-launch marketing.

Strategy for achieving our vision

Build a framework for independently creating and offering pipeline products globally

keyword 1

Use of big data



Further improvement in productivity is key to realizing this vision. Shionogi works constantly on achieving greater efficiency in clinical trials, using real-world data for such purposes as identifying suitable clinical trial participants and creating influenza transmission models.

keyword 2

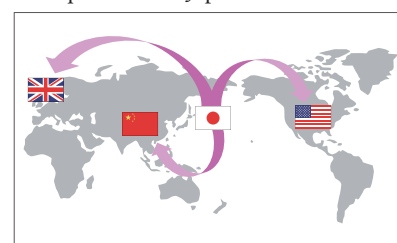
Strengthening global operations



Shionogi is building a global development framework spanning Japan, the US, and Europe, to facilitate speedy and high-quality development. Under a shared global development policy with Shionogi Inc. in the US and Shionogi B.V. in Europe, Shionogi is endeavoring to globalize its operating team.

keyword 3

Global Development Division headquartered in Japan



In an era marked by growth in global clinical trials, the Global Development Division within the parent company in Japan fulfills the important role of managing development projects across our global sites. As headquarters for Shionogi's global operation, the Division is charged with ensuring that the Company's know-how is world-class, and conducting high-quality clinical trials.

Achievements in fiscal 2018: Progress of our next growth drivers and expansion of pipeline and technology through investment toward sustained growth

R&D is an integral part of being a drug discovery-based pharmaceutical company, and in this respect we positioned fiscal 2018 as a year in which to develop growth drivers for 2020 and beyond. Overall, we made steady progress in R&D, aided by active investment in eight high-priority projects. Over and above our typical budget for R&D, we set aside a special budget of ¥20 billion for strategic R&D investment, entering into 10 new strategic collaborations with a view to building a stronger development pipeline for the medium and long term.

Please refer to page 29 for details of strategic collaborations.

Steady progress with eight high-priority projects (as of March 31, 2019)

	Eight high-priority projects	Achievements in fiscal 2018
Infectious Disease	Novel HIV drug candidate	Conducted pre-clinical studies before the start of clinical trials in fiscal 2019
	S-004992 (Tuberculosis)	Conducted pre-clinical studies before the start of phase I clinical trials (China)
Pain/CNS	S-600918 (Refractory/unexplained chronic cough)	Phase II trials confirmed effect on refractory, unexplained chronic cough (Japan)
	S-637880 (Neuropathic pain)	Phase I clinical trials and a micro-dosing study (Japan)
	S-812217 (Depression)	Phase I clinical trials began in October 2018 (Japan)
Others	S-540956(Nucleic acid adjuvant)	Conducted pre-clinical studies before the start of clinical trials in fiscal 2019
	S-770708 (Idiopathic pulmonary fibrosis)	Phase I clinical trials completed (Japan)
Peptide	Peptide projects	Began five new discovery programs (Infectious disease: 1, Pain/CNS: 2, Others: 2)

Discovery Research: Continuous generation of new development candidates

In fiscal 2018, Shionogi's efforts toward the continuous generation of new development candidates resulted in two discovery success stories. In the field of infectious diseases, we created a novel flu drug candidate, while in frontier areas (disease areas other than the core therapeutic areas of infectious diseases, pain, and CNS disorders), we created a drug candidate for non-alcoholic steatohepatitis (NASH).

CMC Research: Contribution to maximizing value of new development candidates

In CMC research, we succeeded in improvement of API purity and formulation stabilization for cefiderocol, a candidate for the treatment of multidrug-resistant gram-negative bacterial infections, accelerating its development ahead of a planned launch in the US. We also pursued development of a commercial inhalation device in preparation for the launch of S-770108 (pirfenidone inhalant), a treatment candidate for idiopathic pulmonary fibrosis. In trials, our inhaler demonstrated competitive results relative to rival devices from other companies.

Steady advances by development products

In fiscal 2018, Shionogi also progressed development of late-stage development products, achieving steady advances both domestically and overseas.

Most notably, we filed for approval of the flu drug *Xofluza* in the US and obtained approval on October 24, two months earlier than planned. As a result, alliance partner Roche was able to begin marketing before the start of the flu season. In addition, positive results were obtained in Phase III clinical trials in influenza patients at high risk for complications, and Roche filed a supplemental New Drug Application in the US.

There was also favorable progress in development of new two-drug HIV regimens licensed out to ViiV Healthcare: *Juluca*, *Dovato*, and cabotegravir + rilpivirine.

Progress with late-stage development pipeline and other compounds (as of March 31, 2019)

<i>Xofluza</i> Influenza virus infection	US: NDA submission-Approval (October 2018) Japan: Approval of 20mg granule formulation, phase III clinical trial for pediatric granule formulation, phase III clinical trial for prophylaxis
Cefiderocol Multidrug-resistant gram-negative bacterial infections	Accepted for review: US (February 2019), Europe (March 2019) Global phase III clinical trial gram-negative carbapenem resistance in progress, phase III clinical trial for hospital-acquired pneumonia in progress
<i>Rizmoic</i> Opioid-induced constipation	Europe: Approval (February 2019)
<i>Mulpleta</i> Thrombocytopenia	Approval: US (July 2018), Europe (February 2019)
<i>Intuniv</i> ADHD	Japan Additional NDA for use in adult patients (August 2018)
<i>Vyvanse</i> ADHD	Japan: Approval (March 2019)
S-005151 Acute ischemic stroke, Epidermolysis bullosa	Japan: Phase I clinical trial began (acute ischemic stroke, FY2018 Q1)

Pipeline (as of March 31, 2019)

	Phase I	Phase II	Phase III	Submission
Global	S-004992* ¹ Tuberculosis	S-120083 Inflammatory pain	Cefiderocol Multidrug-resistant Gram-negative bacterial infections	Cefiderocol (US) Complicated urinary tract infections, including pyelonephritis
	S-117957 Insomnia	S-707106 Type2 diabetes		Cefiderocol (EU) Multidrug-resistant Gram-negative bacterial infections
	S-237648 Obesity	S-488210 Head and neck squamous cell carcinoma		Baloxavir Marboxil(Taiwan) Influenza virus infection
	S-588210 Solid tumor	epertinib Malignant tumor		
		S-588410 Bladder cancer		
In Japan	S-812217 Depression	Cefiderocol Multidrug-resistant Gram-negative bacterial infections	Cefiderocol Multidrug-resistant Gram-negative bacterial infections	<i>Intuniv</i> ADHD (adult)
	S-600918 Neuropathic pain	S-600918 Refractory/unexpected chronic cough	<i>Xofluza</i> Influenza virus infection (prophylaxis)	
	S-637880 Neuropathic pain	S-237648 Obesity	<i>Xofluza</i> Influenza virus infection (New dosage for children)	
	S-010887 Neuropathic pain	S-525606 Allergic rhinitis caused by Japanese cedar allergen	<i>Cymbalta</i> Depression (pediatric)	
	S-005151 Acute ischemic stroke	S-588410 Bladder cancer	<i>Oxycodone</i> Moderate to severe chronic pain	
	S-770108 Idiopathic pulmonary fibrosis	SR-0379 Cutaneous ulcer	S-588410 Esophageal cancer	
		ADR-001* ² Decompensated liver cirrhosis		
Out-licensed	GSK3342830 Multidrug-resistant Gram-negative bacterial infections		<i>Dovato</i> Treatment for HIV infection TANGO study (maintenance)	<i>Xofluza</i> Influenza virus infection (High risk patients)
			CAB* ³ Long-Acting Parenteral formulation Treatment for HIV infection	
			CAB* ³ +RPV* ⁴ Long-Acting Parenteral formulation Treatment for HIV infection	
			<i>Xofluza</i> Severe influenza virus infection	
			<i>Xofluza</i> Influenza virus infection (pediatric)	

Infectious diseases
 Pain/CNS
 Others

*1 In preparation for Phase I *2 In preparation for Phase I/II *3 CAB: Cabotegravir *4 RPV: Rilpivirine

Human Health Care Division

Vision of Human Health Care Division

Contribute to healthcare through patient-focused collection and provision of information

As a drug discovery-based pharmaceutical company, Shionogi contributes to better health by effectively communicating the value of new products to medical professionals. By endeavoring to do so in a far more productive manner, Shionogi can secure a future for our drug discovery research and development activities. Shionogi strives to meet the nation's increasingly diverse medical needs by supporting the government's community-based healthcare approach through the provision of information tailored to specific communities.

Strategy for achieving our vision

Build highly efficient sales model while at the same time strengthening organization and human resources

keyword 1

Incorporation of IT into sales activities



Basic information on drugs is accessible to all, via channels such as the internet. As such, medical professionals rely on MRs to provide more specialized knowledge. Shionogi strives to enhance the quality of information provided through use of IT to monitor, analyze, and verify MRs' daily activities, to aid in identifying customers' needs in advance.

keyword 2

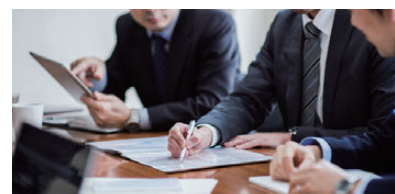
Support for MRs' provision of information



For MRs to respond to customers' increasingly diverse needs, they require not only information and knowledge, but also the ability to convey this appropriately. At Shionogi, we have established a code of practice for information dissemination, based on new guidelines on ethical drug detailing activities issued by the MHLW in 2018. We are also using these guidelines and code of practice to identify opportunities for improvement, in order to better serve our customers' needs.

keyword 3

Human resource development



In order to develop the human resources needed to facilitate Shionogi's future growth, the Human Health Care Division uses various activities both inside and outside the company to instill in employees critical thinking skills and the ability to take action. We are now seeing employees draw on that experience in their engagement with local communities and customers.

Achievements in fiscal 2018: Growth in domestic business

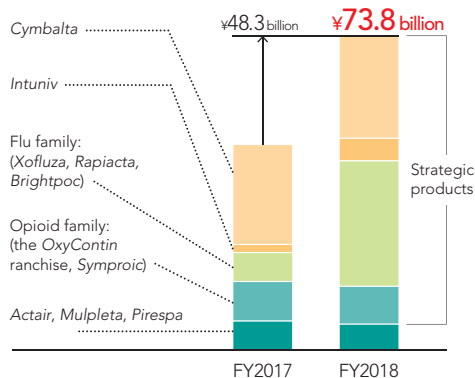
Concentration of management resources led to increased sales of strategic products, driving domestic sales higher
 In domestic sales of prescription drugs, Shionogi focused its management resources on strategic products, primarily *Cymbalta*, *Intuniv*, *Xofluza*, the *OxyContin* franchise and *Symproic*. As a result, sales of strategic products were ¥67.8 billion (rising 63.1% year on year) and sales of new products amounted to ¥73.8 billion (rising 52.8% year on year). Sales of *Xofluza*, the flu drug launched in March 2018, were ¥26.3 billion.

Sales growth turned positive on a year-on-year basis in the third quarter because of growth in the aforementioned strategic products along with a diminishing impact from the launch of generic versions of *Crestor* and *Irbetan* in the previous fiscal year.

During fiscal 2018, Shionogi reorganized its domestic sales operations, and set up a "Specialty Product Office" for specialty products which require high-level expertise—namely, *Actair*, *Mulpleta*, *Pirespa*, and the HIV franchise. With that reorganization, Shionogi established a structure that will enhance its expertise in specialty products and allow management resources to be further focused on strategic products with a large market size.

Sales of new products

Increased 52.8% YoY

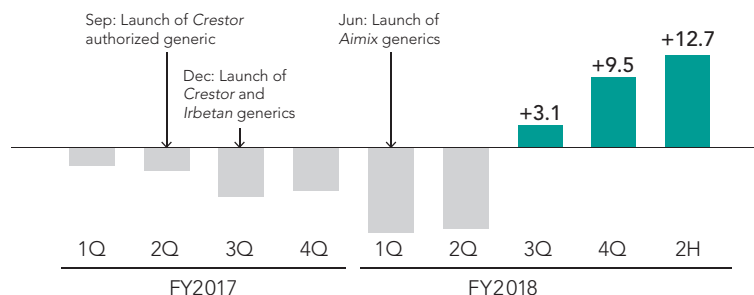


Sales of prescription drugs in Japan (YoY comparison)

(Billions of yen)

The impact of share capture by generic competitors hit a plateau in 1H FY2018

➔ Sales-growth phase by our own earnings power



Global Business Division

Vision of Global Business Division

To serve the health of people around the world by bringing Shionogi's products to them in the most effective way

At Shionogi, we seek to bring the benefits of Shionogi's innovation to as many people as possible across the globe, either through our own sales capabilities in certain regions, or in partnership with influential local companies.

Strategy for achieving our vision

Maximize product value through a combination of in-house sales, business alliances, and export operations

keyword 1

Operational and strategic support for Group companies overseas



The Global Business Division offers operational support and strategic guidance to our overseas Group companies, with presence in the US, Europe, China, Taiwan, and Singapore, resulting in strong alignment and increased efficiency while encouraging the effective pursuit of the goals of each region.

keyword 2

Support of business alliances in Asia



In China and elsewhere in Asia, Shionogi contributes to better health by actively pursuing alliances with partners with complementary strengths, in order to expedite the development and approval process for our innovative drugs and to encourage their broad availability and accessibility.

keyword 3

Export of drug active ingredients, and bulk and finished products



Shionogi exports products in API, bulk, and finished form, providing patients with access to our products across much of the world.

Achievements in fiscal 2018: Growth of overseas business

Maximizing product value through both in-house sales and alliances

In the US, in April 2019, Shionogi entered a new marketing agreement for *Symproic* with BioDelivery Systems International (BDSI). On our own, Shionogi Inc. launched *Mulpleta* in the US, a treatment for thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.

In Europe, Shionogi obtained regulatory approval for both *Rizmoic* (sold under the brand name *Symproic* in Japan and the US) and *Mulpleta*.

We have entered into multiple sales alliances for *Rizmoic*, with Sandoz responsible for sales in Germany, the UK, and the Netherlands, Molteni Farmaceutici covering Italy and Poland,

and Ferrer as our partner in Spain.

In China, too, Shionogi has forged new alliances, licensing both *Mulpleta* and the anticancer agent eperitinib to the Edding-pharm Group.

By combining in-house sales with a range of alliances with highly respected partners with complementary capabilities, the Global Business Division seeks to maximize the value of Shionogi products. Our overseas sales have shown growth above the prior-year in all major regions, and rigorous cost management has brought the US business into the black in 2018 after years of operating losses.

Globally speaking, we are continuing to build a foundation for business expansion, with the next key step being progression of cefiderocol through the regulatory approval process in the US and Europe.

