Sales & Marketing

Japan Four Businesses Responding to Diverse Medical Needs

In Japan, with the birth rate declining and the population aging, not only the treatment of diseases, but also medical cost reduction, prevention, self-medication, and other diverse medical needs are being highlighted in line with changes in society.

The Daiichi Sankyo Group engages in 4 businesses focused around one of its strengths, the innovative pharmaceutical business,* the other 3 are the generic business, vaccine business, and OTC-related business. As the No.1 company in Japan, Daiichi Sankyo addresses a wide range of medical needs of society, making comprehensive contributions to medicine in the country.

* Pharmaceuticals protected during the exclusivity period granted by reexamination period and patents

Innovative Pharmaceuticals Business: Sales & Marketing Unit

Japan is an important market for the Daiichi Sankyo Group in terms of its revenue generated on a regional basis. The Sales & Marketing Unit delivers a wide range of innovative pharmaceuticals to patients in Japan, ranging from the anticoagulant *LIXIANA* and other products in the primary care area*1 to oncology products, among others, in the specialty care area.*2 Taking the perspective of total care centered on patients, we aim to meet the needs of each customer and to contribute to healthcare in Japan by providing relevant information correctly, quickly, and carefully to all healthcare professionals who treat patients with diverse symptoms and conditions.

*1 Drugs mainly prescribed by general practitioners
*2 Drugs mainly prescribed by hospitals/specialists

Strength and Challenge

Based on the BRIDGE's*1 concept of serving as a bridge between patients, their families, and healthcare professionals by emphasizing the connection between people, and providing proper information and products, we develop medical representatives (MRs) activities with the aim of being recognized as a reliable medical partner by everyone involved in healthcare. These activities have been highly evaluated by healthcare professionals. In a survey conducted by an external organization, we have been ranked No.1 for MR evaluation for 8 consecutive years.*2

In order to maintain our sales capabilities, we have developed and improved internal training programs and worked to foster a corporate culture of self-improvement. As a result, all MRs have passed the certificate test for 10 consecutive years. Going forward, we will place a new focus on developing MRs with oncological expertise, considering the increasing importance of oncology products. We intend to encourage MRs to enhance their sales capabilities so that they can respond to a wide range of ever-changing information needs at the right time, in the right way, and in a manner tailored to each and every healthcare provider.

*1 Bright Days Together
*2 Based on survey conducted by INTAGE Healthcare Inc.

Progress of Major Initiatives

Growth of *LIXIANA*

LIXIANA (*edoxaban tosilate hydrate*) is an oral anticoagulant developed by Daiichi Sankyo.

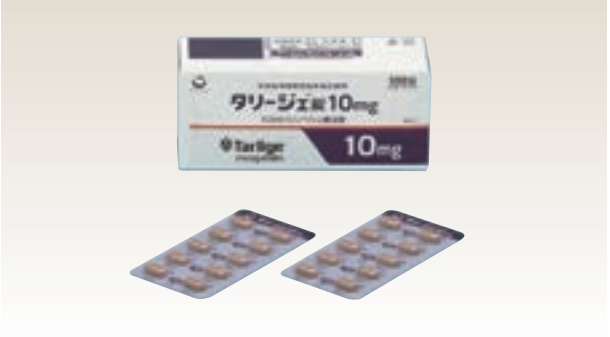
With its excellent usefulness and high convenience of once-daily dosing, we work to make a medical contribution and promote the proper use of *LIXIANA*, with the hope of helping the prevention of thromboembolism in many patients who need anticoagulant therapy.

In fiscal 2020, *LIXIANA* will overcome the impact of special expansion re-pricing and maintain the No.1 market share as the Group's mainstay product. We will promote and support the growth of OD tablets (orally disintegrating tablets) by leveraging its strength, which is highly regarded for its ease of use particularly in elderly patients.

Growth of *Tarlige*

Tarlige (*mirogabalin besilate*) is a domestic peripheral neuropathic pain*1 treatment developed by Daiichi Sankyo. The drug binds strongly and continuously to the calcium channel $\alpha 2\delta$-1 subunit*2 and exerts analgesic effects.

*1 Pain resulted from damage or dysfunction of peripheral nerves arising from a variety of causes. Typical examples include diabetic peripheral neuropathic pain and postherpetic neuralgia.
*2 The subunit is involved in the development and maintenance of peripheral neuropathic pain



Sales & Marketing

We make a contribution to patients and healthcare professionals by offering the new treatment option in the field of peripheral neuropathic pain. In addition, we promote the proper use of *Tarlige*.

In fiscal 2019, which was the first year of *Tarlige* being distributed, the drug was prescribed to patients who have concerns about peripheral neuropathic pain in everyday life. As a result, we expanded our market share. In March 2020, the limitation on the duration of treatment with the drug was lifted. We will continue to promote the proper use and work to further grow *Tarlige*.

Launch of *ENHERTU*

In May 2020, Daiichi Sankyo launched the treatment for malignant tumors, *ENHERTU* (*fam-trastuzumab deruxtecan-nxki*). *ENHERTU* is a promising new product in the field of oncology.

We make a contribution to patients and healthcare professionals by offering the new treatment option to patients with HER2 positive unresectable or recurrent breast cancer who have been previously treated with chemotherapy (limited to the use to patients who are refractory or intolerant to standard treatments). In addition, we promote the proper use of *ENHERTU*.

Generic Business: Daiichi Sankyo Espha Co., Ltd.

The Government of Japan is promoting the use of generic drugs to reduce the burden on patients and improve the national health insurance finances.

With the increasing need for generic drugs and high expectations from society, Daiichi Sankyo Espha takes pride in being as an innovator in the domestic generic pharmaceutical industry and to contribute to increasing medication adherence*1, provides authorized generics (AG)*2, or a new standard for generics featuring formulation, labelling, and packaging innovations that are easy to swallow but hard to swallow accidentally. In this way, Daiichi Sankyo Espha works to meet diverse needs of patients, their families, and healthcare professionals.

*1 The extent to which patients actively follow a medication regimen as prescribed by their health care providers

*2 Generic drugs that are the same as their original drugs in drug substances, additives, manufacturing method, and other aspects, and are marketed with permission from brand-name pharmaceutical companies

Strength and challenge

Daiichi Sankyo Espha's AGs are generic drugs that take over the asset of trust accumulated by original drugs in clinical practice and contribute to patients and healthcare professionals. With these AGs, Daiichi Sankyo Espha offers trust and confidence that it has fostered as a manufacturer of new drugs.

With a steady increase in the use of generic drugs in Japan, the role of generic drug companies that serve as an infrastructure supporting healthcare is becoming increasingly important. In addition to ensuring the quality of a large number of products, a long-term stable supply of them is demanded by society.

Daiichi Sankyo Espha operates with the goal of offering generic drugs that are reliable in terms of quality assurance, stable supply, information provision, and economy, which are the most important factors for pharmaceuticals.

Progress of key initiatives

Expand the lineup of oncology drugs

A number of huge seller AGs launched to date (i.e., *telmisartan* family, *olmesartan*, *rosuvastatin*, *silodosin*), as well as subsequent educational activities for physicians and pharmacists, among others, have built up trust of Daiichi Sankyo Espha of AG.

However, the company never remains the same and is currently enhancing its product portfolio to evolve from Daiichi Sankyo Espha of AG to Daiichi Sankyo Espha of AG with competitive advantage in oncology. In accordance with its policy to ensure information sharing with physicians in medical institutions, medical representatives dedicated to medical institutions are assigned to promote the 4 ingredients of *gefitinib*, *bicalutamide*, *anastrozole*, and *tamoxifen*.

Packaging that reduces the risk of accidental ingestion

There are cases where the family members of patients, especially small children, take relatively high risk medicines such as anticancer drugs by mistake. Daiichi Sankyo Espha developed outer packaging for PTP sheets (C-Guard/Child Guard) for the purpose of preventing people from accidentally touching drugs and drugs from falling out, with the added feature that it prevents accidental ingestion by small children.

Vaccine Business

The global 2009 H1N1 influenza pandemic triggered a surge in interest in vaccines to prevent infectious diseases in all countries around the world, including Japan. The recent outbreak of COVID-19 has had a significant impact on the economy and people's daily lives and further intensified the need for vaccines to unprecedented levels.

The Daiichi Sankyo Group is fully aware of its social responsibility as a domestic pharmaceutical company running a vaccine business. With the aim of enhancing the environment surrounding preventive care in Japan and improving health and hygiene as an integral part of the national security, the Group promotes the vaccine business.

Strength and challenge

Some of the vaccines produced by Daiichi Sankyo are used for routine vaccination. Therefore, the Company is responsible for providing society with a stable supply of the required amount of vaccines. Daiichi Sankyo introduces state-of-the-art equipment and improves its production technology and efficiency on a constant basis to maintain a system for stable supply to society. To prepare a pandemic influenza outbreak, we works to build a system to supply necessary vaccines to the public with our proprietary cell culture technology. This is part of our efforts to achieve a sustainable society.

Progress of major initiatives

Stable supply of vaccines

Seasonal influenza vaccines are used for vaccination before an epidemic period in winter. Thus, we need to ship the required amount of vaccines targeting the strains of a virus becoming prevalent on a timely manner. In order to prepare for a "twindemic" of influenza and COVID-19, Daiichi Sankyo works to improve production efficiency through an effort to reduce lead time by utilizing a flexible shift production structure in order to achieve faster shipping and more increased production before an influenza pandemic.

Production system for a possible pandemic

Daiichi Sankyo is working to maintain and manage a system whereby the Company can supply novel influenza vaccines reliably in the event of a pandemic. We have put into place a system capable of supplying vaccines for approximately 23 million people. In addition, we are working on action plans and training in the event of a pandemic.

Promote new vaccine development

Daiichi Sankyo is pursuing research and development of vaccines that will transform the standard of care (SOC) based on its strength in Science & Technology. The vaccines under development include a 3-valent combination vaccine containing three live attenuated viruses of measles, mumps, and rubella (MMR vaccine).

In response to COVID-19, Daiichi Sankyo is actively engaged in research and development of new vaccines by utilizing its new modalities and through collaboration between industries, governments, and academic institutions.*

For details of actions against COVID-19, refer to page 43

Cell and virus culture with large tanks

OTC Related Business: Daiichi Sankyo Healthcare Co., Ltd.

In Japan, although the average life expectancy has been one of the highest in the world, not only the length of life but also its quality matters in this day and age. Taking care of your health on a daily basis to prevent disease, or self-care, leads to increasing your healthy life expectancy. In addition, the concept of self-medication has gained acceptance. Self-medication is a practice of using over-the-counter (OTC) drugs to relieve symptoms of mild cold, fever, headache, menstrual pain, and other similar conditions. This trend is becoming more and more pronounced, and the needs are diversifying.

In addition to OTC drugs*1, Daiichi Sankyo Healthcare handles a wide range of products including skin care cosmetics and oral care products. Among the Daiichi Sankyo groups, Daiichi Sankyo Healthcare is a unit that is closer to customers more broadly. Through the contact and communication with customers, we will continue to create products and services with a high level of customer satisfaction and contribute to improving the quality of life (QOL) of people who wish to be healthier and more attractive.

* Over-the-counter drugs available in pharmacies, drug stores, etc.

Strength and challenge

By leveraging its R&D and marketing capabilities originated from a pharmaceutical company, Daiichi Sankyo Healthcare aims to become a "total healthcare" company beyond the boundaries of the traditional OTC business. To this end, we intend to develop new growth areas and sales channels and expand our business overseas, rather than to remain within the current scope of our business.

Progress of major initiatives

Sustainable growth of OTC business

Daiichi Sankyo Healthcare pursues sustainable growth of OTC-related business by strengthening its mainstay brands including the cold remedy *Lulu*, which has been familiar to many families for many years since its launch in 1951, and antipyretic analgesic *Loxonin*, an OTC drug using *loxoprofen* sodium hydrate developed by Daiichi Sankyo.

Accelerate growth of skin care and oral care business

Skin care and oral care are promising areas for future growth. Daiichi Sankyo Healthcare is working to accelerate the growth of its skin and oral care products. The skin care products include *MINON*, a series of body cleaning products developed based on dermatology for people with sensitive/dry skin, and *Transino*, which contains tranexamic acid developed by Daiichi Sankyo and is the only OTC drug approved for the indication of melasma, a type of discoloration. The oral care products include the medicinal toothpaste *Clean Dental* and the new brand *Breath Labo*.

Expand direct marketing business

The direct marketing business is an important sales channel for delivering our products to more customers. Through the marketing business company Im Co. Ltd., Daiichi Sankyo Healthcare operates its mainstay brand *RICE FORCE* and new aging care brand *BRIGHTAGE* developed by the company.

Overseas business development

With a focus on *MINON Amino Moist series*, Daiichi Sankyo Healthcare is also strengthening its overseas business operations in China, Hong Kong, and Taiwan. In China, Daiichi Sankyo Healthcare performs sales and marketing activities through Daiichi Sankyo China (DSCN), a member of the Daiichi Sankyo Group.

Overseas Overseas Businesses with "Global Products" and "Regional Value Products"

Daiichi Sankyo Group currently does overseas businesses through Daiichi Sankyo Inc. and American Regent, Inc., in the U.S., Daiichi Sankyo Europe in European countries and ASCA* company in Asia, South & Central America regions. We aspire to grow our overseas businesses not only through the delivery of "Global Products" such as *LIXIANA* and *ENHERTU*, but also through "Regional Value Products" matched to the specific needs of patients and healthcare providers in our various regions and countries

*Asia, South & Central America

Daiichi Sankyo, Inc.

Given that Daiichi Sankyo Group aspires to be a global enterprise, growth in the U.S. market, the world's largest market for pharmaceuticals, is of critical importance. Daiichi Sankyo, Inc. has a history of success having grown *Benicar* (antihypertensive agent) into a blockbuster medicine in the U.S.

Strengths and challenges

The core business of Daiichi Sankyo Group has begun to shift from the primary care field to the specialty field, which centers on hospital/specialty healthcare providers. We have taken great strides toward achieving our goal of becoming a leader in oncology in the U.S. by attracting new, talented, creative and experienced colleagues to join us in our mission. The U.S. commercial teams, including sales, managed markets, marketing and more, have deep and broad cancer expertise and work collaboratively to bring value and patient-focused information to those providers who treat cancer.

Progress of major initiatives

Launch of *TURALIO*

TURALIO (*pexidartinib*) is the first and only approved therapy for adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery, and is now available by prescription in the U.S.

TGCT is typically a non-malignant tumor that can be locally aggressive. There were no approved systemic treatment options other than surgery before the approval of *TURALIO*.

TURALIO is prescribed through a Risk Evaluation and Mitigation Strategy (REMS) Program in order to mitigate the risk of serious liver injury seen with *TURALIO* in our clinical trials.

Launch of *ENHERTU*

ENHERTU (*fam-trastuzumab deruxtecan-nxki*), a HER2 directed antibody drug conjugate, became available by prescription in the U.S. in January 2020.

ENHERTU is a new treatment option for adult patients with unresectable or metastatic HER2 positive breast cancer who have received two more prior anti-HER2-based regimens in the metastatic setting.

In 2019, Daiichi Sankyo entered into a global development and commercialization agreement (excluding Japan) concerning *ENHERTU* with AstraZeneca. Together, Daiichi Sankyo and AstraZeneca are able to accelerate the growth of *ENHERTU* by leveraging the strengths of both companies.

American Regent, Inc.

American Regent, Inc. (ARI) is a leading injectable medication specialty pharmaceutical company. The company has a long history of supplying a variety of drugs including branded IV iron, high quality injectable generics, and veterinary medicines primarily to the US marketplace. The company employs over 1,000 people in New York, Ohio and Pennsylvania.

Strength and challenge

ARI's product portfolio is comprised of an iron injection franchise with two leading products, *Venofer* and *Injectafer*, for the treatment of iron deficiency anemia, a generic injectable franchise with a portfolio of difficult-to-manufacture, sole-sourced, and competitively differentiated products.

Taking advantage of our capabilities to develop difficult-to-manufacture and complex products, we continue to expand our portfolio of competitive products. Our broad portfolio of more than 30 marketed products is constantly evolving to meet our customers' needs and stay ahead of the dynamic generic marketplace.

Progress of major initiatives

Iron injection franchise

The iron injection franchise focuses on two products; *Venofer*, which is used to treat iron deficiency anemia (IDA) resulting from chronic kidney disease, and *Injectafer*, which is indicated to treat IDA resulting from chronic kidney disease, as well as from various other causes, but cannot be used in patients undergoing dialysis.

Due to its ability to treat a wide range of conditions and the convenience of being able to completely dose patients in only two administrations, *Injectafer* has enjoyed a rapid growth in market share since it was launched.

To achieve further growth, *Injectafer* has increased its share of voice to meet GI and OB/GYN customer needs and continued awareness among dissatisfied oral iron patients.

These two products boast a combined share of the U.S. iron injection market of more than 70%, making ARI the undisputed leader in this market. With regards to life cycle management and expanded indications, *Injectafer* is currently enrolling a HEART-FID clinical study. This study will assess the efficacy and safety of iron therapy using *Injectafer* relative to placebo in treating patients with heart failure, iron deficiency, and a reduced ejection fraction.

Generic injectable franchise

ARI manufactures, markets, and supplies generic injectable products in vial and ampule presentations. The company has been launching new products continuously and successfully to achieve sustainable growth. ARI is focused on product development and successful submission of multiple supplemental and new drug applications in FY2020 and beyond.

ARI is also in the process of executing a significant capital investment in plant manufacturing capacity to become one of the top suppliers in the U.S. generic injectable market.

New Albany factory in the U.S

Daiichi Sankyo Europe

Daiichi Sankyo Europe (DSE) currently has affiliates in 13 European countries. Through licensing and sales agreements, our products are available in almost every European country. Our European headquarters is in Munich, Germany, and close by, in Pfaffenhofen, is one of our global production plants.

Strengths and challenges

Europe is an important market for the Daiichi Sankyo Group, following Japan and the United States.

The current mainstay of DSE is the anticoagulant *Lixiana*. Focusing on maximizing the product potential of *Lixiana* by growing market share, we will expand our business by adding further cardiovascular products to our portfolio as well as oncology products such as *ENHERTU*.

Progress of major initiatives

Growth of *Lixiana*

Since we launched *Lixiana* in 2015, most countries in Europe have introduced it in their local markets.

DSE is marketing *Lixiana* in more than 10 European countries. In countries where DSE does not have its own affiliates, e.g. Northern or Eastern European countries, *Lixiana* is commercialized via partners such as Servier or MSD.

The market share has been growing to almost 16% in the European countries where DSE has its own affiliates (excl. France and Turkey). The sales revenue in Germany is the second highest after Japan

To achieve further growth we have defined a single-minded proposition for *Lixiana*: "Your choice for the elderly NVAF patient" which is rolled-out across all European markets.

Approvals for NILEMDO and NUSTENDI

NILEMDO (*Bempedoic acid*) and *NUSTENDI* (Fixed dose combination tablet of *bempedoic* acid and ezetimibe) in-licensed from Esperion, have been approved by the European Commission in March and April 2020 respectively for cholesterol-lowering treatment. The new products are an ideal fit to the capabilities we have developed over the last years. They can build on and use synergies with *LIXIANA* and thus enhance our value as a business in Europe.

Preparing for oncology

Besides getting ready for new products in the cardiovascular space, Daiichi Sankyo in Europe is also diligently preparing for the future oncology business.

We have hired talented professionals for medical, market access, marketing, field force and other functions. The European commercial organization is set up well to successfully launch our oncology products.

Sales & Marketing

ASCA Company

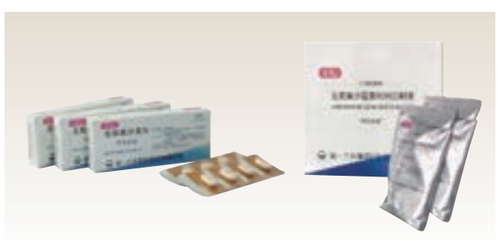
The ASCA*1 Company is responsible for operations in Asia, South & Central America, and other regions. In addition to performing sales and promotional activities through its 7 subsidiaries (in China, Korea, Taiwan, Thailand, Hong Kong, Brazil, and Vietnam*2), the ASCA Company also exports its bulks and products to licensees. The ASCA Company owns its formulating plants in China and Brazil and performs production operations there. The ASCA Company employs approximately 2,100 people at its business bases. The company has rolled out its business optimized to market and customer needs in each country and region (regional value), contributing to healthcare in each place.

*1 Asia, South & Central America
*2 Currently representative office

Strength and challenge

China is an important market for the ASCA Company because revenue from its China business accounts for the largest share of its total revenue. With its mainstay products, including the antihypertensive agent *olmesartan*, synthetic antibacterial agent *Cravit*, and hypercholesterolemia treatment *Mevalotin*, the ASCA Company operates in the market. While the China market is large, regulations are complex, and the ASCA Company is focusing on building and expanding its sales structure to maximize its potential.

The anticoagulant *LIXIANA*, one of the Group's global products, is also an important product for the ASCA Company. Since its launch in Korea in 2015, *LIXIANA* has been marketed in Taiwan, Hong Kong, Thailand, Brazil, and China via the ASCA Company's own sales organization. The ASCA Company takes full advantage of the customer base it has built for *Mevalotin* and *olmesartan*, which are also cardiovascular products, to further expand the market share of *LIXIANA* in each country. In countries where the ASCA Company does not have subsidiaries, such as Indonesia and the Middle East countries, the company will work to maximize product value by selling products through its partners.



Progress of major initiatives

Strengthen the operating structure in China

In the past, the ASCA Company has sought to expand sales through active sales alliance with local companies. Currently, the company is working to expand its own marketing territories while improving profitability, taking into account regulatory changes such as health insurance and bidding system reforms, as well as changes in the market environment.

Expand *LIXIANA*

The market share of *LIXIANA* is steadily increasing as a result of product strategies tailored to the market environment and other conditions in each country. In Korea, *LIXIANA* has maintained the largest DOAC* monthly share. In Taiwan, various marketing promotion activities have resulted in increased market share. In China, the ASCA Company is working to have *LIXIANA* listed on the National Reimbursement Drug List (NRDL) and making other efforts for sales growth in the future.

* Direct oral anti coagulant

Build an operating structure to launch oncology products

In the ASCA regions, the ASCA Company also works on building an operating structure and preparing for market launch, among other activities, in order to deliver *ENHERTU* and other oncology products to patients as soon as possible.

A new operating structure is being built with focus on designing functions and organizations as well as promoting talent acquisition required for oncology business.

Shanghai factory in China

Research & Development (R&D)

The mission and role of Research and Development (R&D) is to continue to contribute to establishing global standard of treatment and prevention methods to improve human health. This can be achieved by creating high-value-added novel therapies continuously by leveraging our accumulated knowledge and experience of high-quality and innovative drug discovery and development.

Our inquiring mind and desire to contribute humanity drive our R&D. We are supported by our passionate desire to create new medicines that contribute to the health and enriched lives of people around the world and deliver them to patients as soon as possible. We will continue to take on the challenge of creating innovative medicines.

Strength and challenge

Strength Cutting-edge science & technology cultivated over years of operation as a drug discovery-oriented company

Challenge On-track delivery of large-scale clinical trials in oncology, as well as research, development, and regulatory submissions for regenerative medicines. Further evolution of research and development using new technologies such as ICT, AI, and RWD*

* RWD (Real World Data): Data collected in the daily clinical environment (Real World), not in the experimental environment (Ideal World) like clinical trials.

Revised R&D strategy

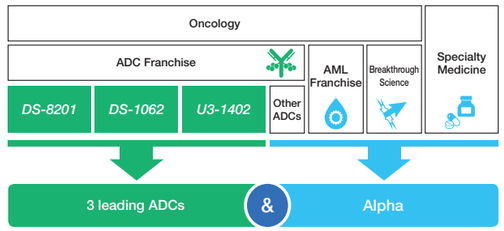
For R&D 2025 Vision, three pillars were established in the oncology field: Antibody Drug Conjugate (ADC) Franchise, Acute Myeloid Leukemia (AML) Franchise, and Breakthrough Science. Of the three, ADC Franchise, in particular, saw steady progress in clinical development of three ADCs, starting with *DS-8201*, and the potential of each ADC has increased to the point where it can be called a major pillar. Since these ADCs products use the same platform technology, with a view to going forward to "post-ADC," new drug discovery platform technologies that will drive Daiichi Sankyo's sustainable growth and creation of novel products that will transform the standard of care have become important themes to tackle.

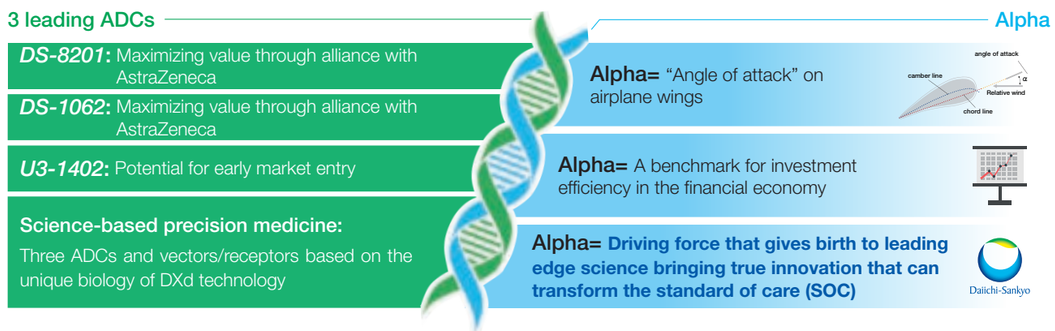
Thus, we decided to adopt our new R&D strategy as "3 and Alpha."

The number "3" refers to the three ADCs, for which we will continue to focus on our spending in R&D expenses and human resources to maximize their product values. The word "Alpha" signifies the driving force that gives birth to leading edge science bringing true innovation that can transform the SOC*. With Alpha, we intend to contribute to supporting Daiichi Sankyo's sustainable growth, with the goal of new innovation ahead of the world not only in the oncology field, but also in rare diseases, CNS diseases, and other disease areas with high unmet medical needs.

Going forward, we will pursue for more agile and flexible resource allocation and to facilitate collaboration between organizations. We hope that this revised strategy will lead to an improvement in efficiency under resource constraints, as well as to a cascade of further innovation.

* SOC (Standard of Care): Universally applied best treatment practice in today's medical science





Progress of major initiatives

3 ADCs

Characteristics of Daiichi Sankyo's ADC

In order to examine the benefits and issues of the preceding antibody drug conjugates (ADCs) and solve these issues, our researchers screened and optimized combinations of antibodies, linkers, and payloads to ultimately produce the Daiichi Sankyo's ADC technology. Daiichi Sankyo's ADC has been established as a platform technology where the payload-linker can be combined with a variety of antibodies, and we are currently developing seven DXd-ADCs loaded with a payload, a new derivative of the DNA topoisomerase I inhibitor *DX-8951* (DXd). The main characteristics of this technology are summarized in the figure below.

Characteristics 1	New payload	Characteristics of Payload
Characteristics 2	High potency of payload	
Characteristics 3	Bystander antitumor effect	
Characteristics 4	Payload with a short half-life in the blood	
Characteristics 5	Stable linker	Characteristics of Linker
Characteristics 6	Selectively cleaved linker in cancer cells	
Characteristics 7	High drug-antibody ratio	

Characteristics 1 New payload

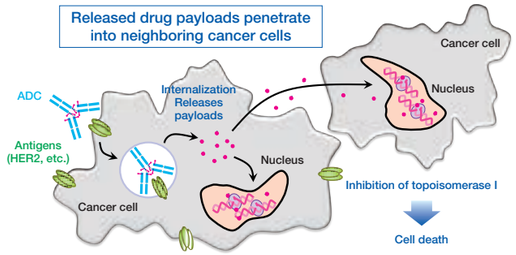
The payload of Daiichi Sankyo's ADCs is DXd, a novel derivative of the DNA topoisomerase I inhibitor *DX-8951*, which was created by former Daiichi Pharmaceutical.

Characteristics 2 High potency of payload

DXd is approximately 10 times as potent as *SN-38* (the active metabolite of irinotecan featuring the same mechanism of action). Providing further rationale was the pre-clinical pharmacology finding that demonstrated that DXd is effective in cancer cells that are less sensitive or resistant to the payload of *T-DM1*, the standard of care for certain type of HER2-positive breast cancer. Effectiveness has been confirmed clinically, as well.

Characteristics 3 Bystander antitumor effect

The "bystander antitumor effect" means a process where after the ADC binds to an antigen expression-positive cancer cell (HER2-positive, for example) and being taken up into the cell, the payload is released from the ADC in the cancer cell, transfer to extracellular by penetrating the membrane, and exerts cytotoxic effects on neighboring antigen expression-negative cancer cells (HER2-negative, for example). The DXd payload is designed to have higher lipophilicity and membrane permeability. In general, antigen expression-positive and -negative cancer cells are present concomitantly in the tumor microenvironment. Through this bystander antitumor effect, it is hypothesized that the drug also has impacts on tumors with a high proportion of cancer cells that are antigen expression-negative.



Characteristics 4 Payload with a short half-life in the blood

Immediately after intravenous administration, an increased blood concentration of drug payloads released all at once from an ADC has the potential to cause side effects. Daiichi Sankyo's drug payload is less likely to be released while in the blood because of its stable linker, and the drug payload is designed to be eliminated quickly from the blood (easily metabolized and has a short half-life) following release.

Characteristics 5 Stable linker

For ADC technology to exhibit cancer cell-specific efficacy, the payloads must be reliably delivered to cancer cells, and here the linker plays an important role. If the linker is unstable, the ADC may degrade after administration and the payloads will be released in the blood. This can reduce efficacy before the payloads are carried to the cancer cells, and can potentially cause side effects if the payloads affect normal cells. Pharmacokinetic analysis of the phase 1 study has confirmed the stability in human blood of Daiichi Sankyo's ADC construct.

Characteristics 6 Selectively cleaved linker in cancer cells

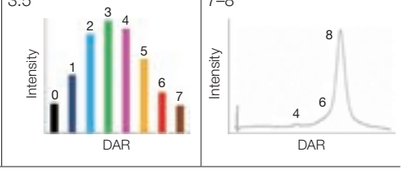
The ADC must be stable in the blood and yet readily release its payload once internalized into the cancer cell following binding to the cancer-cell antigen. The linker of Daiichi Sankyo's ADC is cleaved by enzymes including cathepsins, which are highly expressed in cancer cells, causing payload release. Therefore, the possibility of the linker being cleaved in parts other than cancer cells is minimized. In addition, the cleavage site is situated at an appropriate location for efficiently releasing the payload inside cancer cells.

Characteristics 7 High drug-antibody ratio

The drug-antibody ratios (the number of payloads held on a single antibody) for currently approved ADCs range unevenly between two and seven, whereas Daiichi Sankyo's ADC can load a maximum of eight payloads with high uniformity. Historically, ADCs bearing more payloads per antibody cause aggregation after being formulated. But Daiichi Sankyo's ADC construct and its formulation minimizes aggregation, even with the high DAR. Furthermore, we possess technology to control the drug-antibody ratios optimally according to antigen expression and internalization rates. For example, *DS-8201* and *U3-1402* have a DAR of eight and *DS-1062* has a DAR of four.

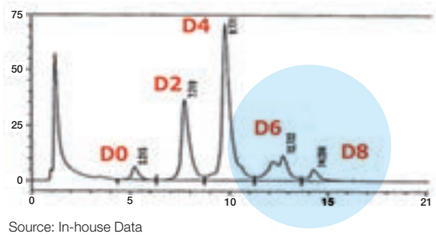
▶ **Distribution of binding payload**

	*T-DM1**	*DS-8201*
Antibody	*Trastuzumab*	Anti-HER2 Ab
Payload	Tubulin inhibitor (*DM1*)	Topoisomerase I inhibitor
DAR	3.5	7–8



* *Kadcyla BLA*
Source: Ogitani-Y et al., Clin. Cancer Res. 2016; 22:5097-5108, Marcoux-J et al., Protein Science 2015; 24:1210-1223

▶ ***DS-1062*: Distribution of the number of payload**



Source: In-house Data

Below is an overview of our pipeline. For detailed data (safety, efficacy, etc.) presented at scientific conferences, please see "IR Library" for investors on our website.

Read more here **IR Library for investors**
https://www.daiichisankyo.com/investors/library/

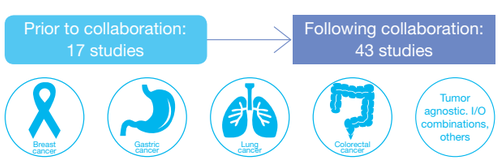
Trastuzumab deruxtecan / DS-8201 (anti-HER2-ADC)

DS-8201 is an anti-HER2 antibody drug conjugate (ADC) comprising Daiichi Sankyo's proprietary linker and payload (DXd) covalently combined with an anti-HER2 antibody.

Strategic Collaboration with AstraZeneca

In order to maximize the value of *DS-8201*, we entered into a global joint development and commercialization agreement in March 2019 with AstraZeneca, a company with a wealth of experience and resources in oncology. Under the agreement, the two companies are jointly developing monotherapy/combination therapy for HER2-expressing cancers, and the development costs will be shared between the two companies. As for commercialization, the two companies will undertake co-promotion in regions other than Japan and share profits and losses. In Japan, Daiichi Sankyo will be the sole marketer and will pay royalties to AstraZeneca.

Our collaboration with AstraZeneca is progressing well. Before the agreement was signed, we were planning 17 clinical studies, but the number has increased to 43 after the agreement. These studies will start in sequence from fiscal 2020.



Research & Development (R&D)

▶ **The list of *DS-8201* studies (as of August 2020)**

	Cancer type	Phase	Study name	Description	Status
1		Phase 1	N/A	First-in-human study HER2-positive breast cancer, HER2-low breast cancer, HER2-positive gastric cancer, and other cancers	Has results
2	Breast cancer	Phase 2	DESTINY-Breast01	HER2-positive breast cancer post *T-DM1*	Has results
3		Phase 3	DESTINY-Breast02	HER2-positive breast cancer 3L, vs. phys choice of SOC	Data expected in FY2021 H2
4		Phase 3	DESTINY-Breast03	HER2-positive breast cancer 2L, vs. *T-DM1*	Data anticipated in FY2021 H1
5		Phase 3	DESTINY-Breast04	HER2-low breast cancer, 2L/3L vs. phys choice of SOC	Data anticipated in FY2021 H2
6		Phase 3	DESTINY-Breast05	HER2-positive breast cancer, post-neoadjuvant	In preparation
7		Phase 3	DESTINY-Breast06	HER2-low hormone therapy refractory breast cancer, vs. phys choice of SOC	In progress
8		Phase 1b/2	BEGONIA	TNBC, combination with *durvalumab*	In progress
9	Gastric cancer	Phase 2	DESTINY-Gastric01	HER2-positive gastric cancer 3L~ vs. phys choice of SOC (HER2-low gastric cancer in exploratory cohort)	Has results
10		Phase 2	DESTINY-Gastric02	HER2-positive gastric cancer 2L	In progress
11		Phase 1b/2	DESTINY-Gastric03	HER2-positive gastric cancer, 2L~/1L	In progress
12	Lung cancer	Phase 2	DESTINY-Lung01	HER2m NSCLC, HER2-positive NSCLC	Data anticipated in FY2021 H1
13		Phase 2	HUDSON	NSCLC, combination with *durvalumab*	In progress
14	Colorectal cancer	Phase 2	DESTINY-CRC01	HER2-positive colorectal cancer 3L (HER2-low colorectal cancer in exploratory cohort)	Has results
15	Other	Phase 1	N/A	Breast cancer, bladder cancer, combination with *nivolumab*	In progress
16		Phase 1	N/A	NSCLC, breast cancer, combination with *pembrolizumab*	In progress
17		Phase 2	DESTINY-PanTumor02	HER2-expressing cancer (bladder, biliary tract, cervical, endometrial, ovarian, pancreatic, and other rare cancers)	In preparation

1 First-in-human Phase 1 Study

Phase 1 study, started in September 2015, has been conducted mainly on patients with breast, gastric, lung, or colorectal cancer. Interim results of the study were presented at the past conferences of the American Society of Clinical Oncology (ASCO), the European Society for Medical Oncology (ESMO), the San Antonio Breast Cancer Symposium (SABCS), the World Conference on Lung Cancer (WCLC), and other academic conferences.

In fiscal 2019, data was published in prominent scientific journals; the primary analysis results of the study were published in *the Lancet Oncology* for HER2-positive breast cancer and gastric cancer, *the Journal of Clinical Oncology* for HER2-low breast cancer, and *CANCER DISCOVERY* for other HER2-expressing or -mutated cancers.

Breast cancer

2 DESTINY-Breast01 study

The primary analysis results of this study were presented orally at the SABCS in December 2019. The results were also published in *the New England Journal of Medicine*. Based on the results, we submitted BLA in the U.S. in August 2019, obtained approval in December 2019 and launched in January 2020. In Japan, we submitted NDA in September 2019, obtained approval in March 2020 and launched in May 2020. In Europe, approval application was accepted in June 2020 and is being review under accelerated assessment.

6 DESTINY-Breast05 study

This is a head-to-head comparative study of *DS-8201* versus *T-DM1* in patients with residual invasive HER2-positive breast cancer following preoperative chemotherapy who are at high risk for recurrence. Preparations are underway to initiate the study in the second half of fiscal 2020.

Gastric cancer

9 DESTINY-Gastric01 study

The primary analysis results of this study were presented at the ASCO in May 2020. The result was also published in *the New England Journal of Medicine*. In Japan, sNDA was filed in April 2020. Since the SAKIGAKE designation has been granted to this indication, the review duration is expected to be 6 months or less. In May 2020, the drug received the Breakthrough Therapy and Orphan Drug Designations from the U.S. Food and Drug Administration (FDA), despite the study having been conducted only in Japan and South Korea. Going forward, we plan to proceed with discussions with the FDA so that we can submit sBLA in the U.S. as soon as possible.

Lung cancer

12 DESTINY-Lung01 study

Interim data from the HER2-mutated cohort were presented at the ASCO in May 2020. In May 2020, *DS-8201* received the Breakthrough Therapy Designation from the U.S. FDA based on the interim data.

Colorectal cancer

14 DESTINY-CRC01 study

The primary analysis results from the HER2-positive cohort were presented at the ASCO in May 2020.

DS-1062 (Anti-TROP2-ADC)

DS-1062 is an anti-TROP2 ADC comprising our proprietary linker and payload conjugated to the anti-TROP2 antibody.

Strategic Collaboration with AstraZeneca

In order to maximize the value of *DS-1062* through accelerated development, and to allocate resources to the subsequent DXd-ADC and Alpha projects, in July 2020 Daiichi Sankyo entered into a global joint development and commercialization agreement for *DS-1062* with AstraZeneca, a company with a wealth of experience in lung cancer. The form of the agreement is almost the same as that for *DS-8201*.

▶ **The list of *DS-1062* studies (as of August 2020)**

	Cancer type	Phase	Study name	Description	Status
1		Phase 1/2	N/A	First-in-human study NSCLC, TNBC	In progress
2	Lung cancer	Phase 2	N/A	NSCLC (with mutation)	In preparation
3		Phase 1	N/A	NSCLC, combination with *pembrolizumab*	In preparation

1 First-in-human phase 1 study (NSCLC, TNBC)

The phase 1 study, begun in February 2018 included patients with non-small cell lung cancer (NSCLC). Last year, interim data on NSCLC were presented at the WCLC in September 2019 and at the ASCO in May 2020. In June 2020, a triple-negative breast cancer (TNBC) cohort was added to this study.

3 Phase 1 study (NSCLC, combination with *pembrolizumab*)

In May 2020, Daiichi Sankyo entered into an agreement with Merck for clinical study to evaluate the combination of *DS-1062* and *pembrolizumab*. Preparations are underway to initiate the study in the second half of fiscal 2020. In addition, we are planning to test *DS-1062* in combination with other immune checkpoint inhibitors (I/O agents). We are considering developing *DS-1062* in combination with I/O agents for the 1st-line treatment of NSCLC.

Patritumab deruxtecan / *U3-1402* (Anti HER3-ADC)

U3-1402 is an anti-HER3 ADC comprising our proprietary linker and payload conjugated to the anti-HER3 antibody patritumab.

▶ **The list of *U3-1402* studies (as of August 2020)**

	Cancer type	Phase	Study name	Description	Status
1	Breast cancer	Phase 1/2	N/A	First-in-human study HER3-positive breast cancer	In progress
2	Lung cancer	Phase 1	N/A	NSCLC	In progress
3		Phase 1	N/A	EGFR-mutated NSCLC, combination with *osimertinib*	In preparation
4	CRC	Phase 2	N/A	Colorectal cancer	In preparation

1 First-in-human phase 1 study (HER3-positive breast cancer)

This study has been underway since December 2016 and shown that HER3 expression detected in some patients prior to the first dose of *U3-1402* decreases following the initiation of treatment. In HER3-positive breast cancer, patient selection is key to determining the efficacy and safety of *U3-1402*. Therefore, we will focus on the development of biomarkers and review our future development plans.

2 Phase 1 study (NSCLC)

At the WCLC in September 2019, interim data on the efficacy and safety of *U3-1402* were presented for the dose-escalation part.

3 Phase 1 study (EGFR-mutated NSCLC, combination with *osimertinib*)

In August 2020, Daiichi Sankyo entered into an agreement with AstraZeneca for clinical study to evaluate the combination of *U3-1402* and *osimertinib*. With the aim of developing *U3-1402* as a 2nd-line treatment of EGFR-mutated NSCLC, preparations are underway to initiate the phase 1 study in the second half of fiscal 2020.

Alpha

Oncology

Quizartinib (FLT3 inhibitor)

Quizartinib is an FLT3 inhibitor with a potent inhibitory activity against mutated gene called FLT3-ITD, which is present in around 30% of acute myeloid leukemia (AML) patients.

In Japan, the Ministry of Health, Labour and Welfare approved *quizartinib* for the indication of relapsed/refractory FLT3-ITD AML in June 2019. The drug was launched in October 2019 under the brand name of *Vanflyta*.

In the U.S., we received a Complete Response Letter in June 2019. In Europe, we received a negative view on approval from the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) in October 2019.

Phase 3 study of 1st-line treatment (QuANTUM-First study) is currently underway globally.

Pexidartinib (CSF-1R/KIT/FLT3 inhibitor)

Pexidartinib is a receptor tyrosine kinase inhibitor showing specific inhibitory activity against CSF-1R/KIT/ and FLT3.

Pexidartinib was approved by the FDA for the indication of tenosynovial giant cell tumor (TGCT) in August 2019, and was launched under the brand name of *Turalio*. In Europe, we received a negative view on approval from the EMA's CHMP in June 2020.

We are also discussing a development in the Asian region, including Japan.

Axicabtagene ciloleucel (anti-CD19 CAR-T cell)

Axicabtagene ciloleucel is a cell therapy (chimeric antigen receptor T cell: CAR-T cell) product licensed-in from Kite Pharma, Inc., a subsidiary of Gilead Sciences, Inc. in the U.S. The product targets the CD19 antigen expressed on the surface of B-cell lymphoma.

Daiichi Sankyo submitted NDA in Japan in March 2020 based on the results from a global phase 1/2 clinical study (ZUMA-1 study) conducted by Kite Pharma and a phase 2 study in Japan conducted by Daiichi Sankyo. The agent has been designated as an Orphan Regenerative Medicine Product by the Ministry of Health, Labour and Welfare.

DS-1647/G47Δ (oncolytic HSV-1)

DS-1647(G47Δ) is a cutting-edge (third-generation) oncolytic virus created by Professor Tomoki Todo of the Institute of Medical Science of the University of Tokyo, by using genetic modification technologies to modify herpes simplex virus type 1 so that it only multiplies inside cancer cells.

We plan to submit NDA in Japan based on the results from the investigator-initiated clinical study undertaken by Professor Todo. The SAKIGAKE designation has been granted to *DS-1647* by the Ministry of Health, Labour and Welfare.

Valemetostat/DS-3201/EZH1/2 inhibitor

DS-3201 is an inhibitor of the histone methyltransferases *EZH1* and *EZH2*. Some cancer cells show *EZH1/2*-dependent proliferation.

The following studies are currently underway: phase 2 study in patients with adult T-cell leukemia-lymphoma in Japan; global phase 1 study in patients with non-Hodgkin's lymphoma, including relapsed/refractory peripheral T-cell lymphoma (PTCL); and phase 1 study in patients with acute myeloid leukemia/lymphoma in the U.S.

In April 2019, the SAKIGAKE designation was granted to *DS-3201* by the Ministry of Health, Labour and Welfare for the treatment of PTCL.

DXd-ADC

Of the seven DXd-ADCs are currently under development at the Company, four are being developed as part of "Alpha". For *DS-7300* and DS-6157, phase 1 studies are underway. *DS-6000* (target not disclosed) and *DS-3939* (anti-TA-MUC1-ADC) are in preclinical phase.

DS-7300 (anti-B7-H3-ADC)

DS-7300 is an anti-B7-H3-ADC using DXd-ADC platform. B7-H3 is a type I transmembrane protein belonging to the B7 family.

Since October 2019, phase 1/2 study have been performed in patients with solid tumors (head and neck, esophageal, non-small cell lung, and other cancers) in Japan and the U.S.

DS-6157 (anti-GPR20-ADC)

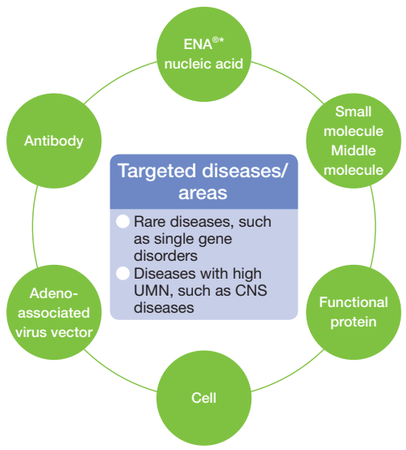
DS-6157 is an anti-GPR20-ADC using DXd-ADC platform. GPR20 is an orphan G protein-coupled receptor (GPCR) that is expressed specifically in gastrointestinal stromal tumors (GISTs).

Since May 2020, phase 1 study have been performed in patients with GIST in Japan and the U.S.

Specialty Medicine

In the Specialty Medicine area, Daiichi Sankyo has set forth a medium-to-long-term vision of delivering innovative pharmaceuticals to patients suffering from diseases for which no effective treatment is available or for which existing treatments are insufficient. Daiichi Sankyo's immediate goal is to become a world-class innovator with competitive advantage in rare diseases by taking advantage of our strengths in science and technology and pursuing innovation. Our ultimate goal is to become a world-class innovator in the Specialty Medicine.

We will make the maximum use of a wide range of our modalities to develop drugs for rare diseases, such as single gene disorders, or other diseases with high unmet medical needs (UMN), such as diseases of the central nervous system (CNS).

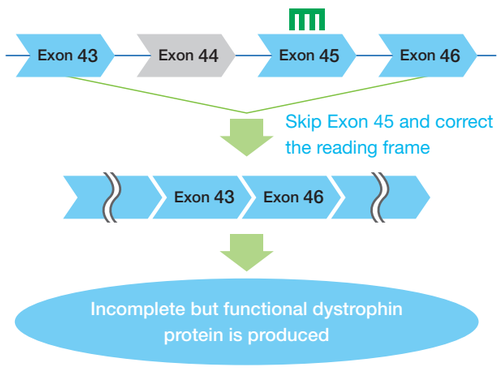


* 2'-O,4'-C-Ethylene-bridged Nucleic Acids. A modified nucleic acid made using proprietary technology owned by Daiichi Sankyo. ENA® is a registered trademark of Daiichi Sankyo.

DS-5141 (nucleic acid drug)

DS-5141 is a nucleic acid drug using our proprietary nucleic acid modification (ENA®). ENA® is an ethylene-bridged nucleic acid in which ethylene is bridged at the furanose sugar ring at 2'-O and 4'-C ends. ENA® demonstrates high binding force with DNA and RNA as well as superior thermal and nuclease resistance.

Duchenne muscular dystrophy (DMD) is an X-linked recessive muscular disorder that is caused by a dystrophin gene abnormality that results in the production of no dystrophin protein. *DS-5141* is expected to improve the symptoms of DMD by skipping exon 45 and producing an incomplete but functional dystrophin protein in the splicing process where messenger RNA is produced from the dystrophin gene in patient's myocytes.



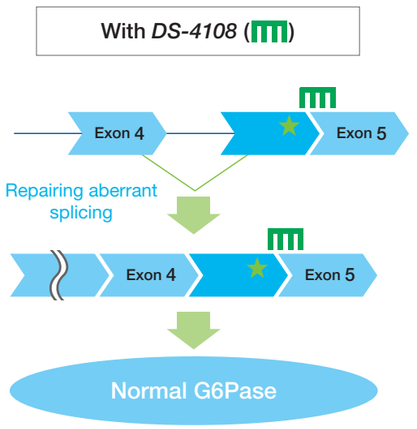
In a phase 1/2 study that has been performed in Japan since October 2015, results of a 12-week treatment with *DS-5141* have shown that Exon 45 skipping during splicing was confirmed in all 7 patients, and the dystrophin protein was observed in one patient. Following the results, a subsequent 48-week study has been in progress, the results of which will become available at the end of 2020.

DMD projects using ENA® nucleic acid modification include those for *DS-5144* (exon 44 skipping), *DS-5150* (exon 50 skipping), *DS-5151* (exon 51 skipping), and *DS-5153* (exon 53 skipping) and these projects are in pre-clinical phase.

DS-4108

DS-4108, a nucleic acid drug, which uses ENA® technology similar to that for *DS-5141* to control splicing, has been created from a joint research with Kobe Gakuin University, the National Center for Child Health and Development, and Hiroshima University. *DS-4108* is being developed as a treatment for glycogen storage disease type Ia (GSDIa) caused by specific gene mutation. GSDIa is a rare disease with the incidence of 1 in 100,000 that causes fasting hypoglycemia, hepatomegaly, and other conditions due to a congenital deficiency of sugar-producing enzyme (glucose-6-phosphatase, G6Pase). No drug therapy has been approved for GSDIa and the disease is managed with strict diet therapy.

ENA® has thus expanded beyond the DMD projects and is expected to become a new platform technology following the DXd-ADC platform technology.



Correct the aberrant splicing by ENA® oligonucleotide and induce production of normal G6Pase

DS-1211

The TNAP inhibitor *DS-1211* has been developed as a treatment for pseudoxanthoma elasticum. In this disease calcification of blood vessels and connective tissues occur gradually and causes skin lesions, decreased visual acuity, and cardiovascular complications, among others, due to genetic mutations in ABCC6. For pseudoxanthoma elasticum, no drug therapy has been approved, and the estimated number of patients is 18,000 in Japan, the U.S., and five European countries. Currently, phase 1 study have been completed, and phase 2 study are in preparation.

DS-6016

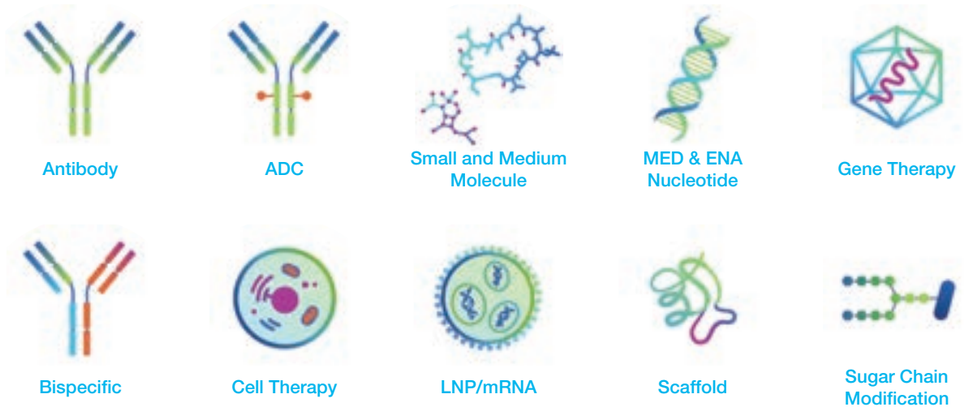
The anti-ALK2 antibody *DS-6016* has been under a collaborative research effort with Saitama Medical University, which was selected for AMED's CiCLE program in August 2017. *DS-6016* targets fibrodysplasia ossificans progressiva (FOP), a disease characterized primarily by heterotopic ossification in which bone is formed in tissues that are not normally formed due to genetic mutations in ALK2, a key receptor in the transmission of osteogenic signals. It has been reported that area of heterotopic ossification expands with age, and total assistance becomes necessary for almost all patients who are aged 40 years and older. Currently, no approved drug therapy is available. FOP is very rare, and the number of patients is estimated to be little less than 80 in Japan and little less than 300 in the U.S. Preparations are underway to initiate a phase 1 study.

Research & Development (R&D)

Research

Create new modalities

Daiichi Sankyo has been advancing drug discovery research by use of a wide variety of modalities, including next generation ADCs, bispecific antibodies, nucleic acid drugs, cell therapy (including iPS cells), gene therapy, and LNP-mRNA, in addition to small molecules, *DS-8201*, and other DXd-ADCs. We have been promoting multi-modality strategy to create the optimal modality for the disease by an appropriate modality for the drug target and the disease, and by simultaneously developing a new modality.



Efforts in gene therapies

Daiichi Sankyo focuses on gene therapy using the adeno-associated virus (AAV) vector, which is considered to be the most feasible vector among gene therapies. We will initiate gene therapy research for monogenic rare diseases first and plan to start clinical studies for several projects in fiscal 2024 and beyond. In parallel, mass production technology we will be established in order to apply the gene therapy to serious common diseases for which existing treatments are insufficient.

Since we considered building in-house manufacturing capability as a major hurdle for the development of gene therapy drugs, we decided to introduce manufacturing technology from Ultragenyx Pharmaceutical Inc. Ultragenyx Pharmaceutical Inc. has developed its own AAV production system using HeLa and HEK293 cells, and has already achieved actual performances of clinical studies, ensured stable quality of products, and attained know-how on mass production and analytical techniques for quality control. Through the introduction of this technology, we will soon establish in-house manufacturing capability for gene therapy programs, and begin manufacturing investigational drugs by the mid-2020s. Daiichi Sankyo has several gene therapy drug candidates undergoing nonclinical studies. One of the focused project is for retinitis pigmentosa, for which we have undertaken a collaborative research with Nagoya Institute of Technology. Retinitis pigmentosa is a genetic disorder characterized by the loss of photoreceptors, which exist in the retinal cells of healthy people and causes severe deterioration of visual acuity as the disease progresses. In this collaborative research program, we have identified the highly active, novel photo-responsive protein. Improvement of visual acuity is expected if the protein could be expressed in retina through gene therapy. In addition to establishing manufacturing technology for gene therapy drugs, we will accelerate the research and aim to realize early practical use of innovative pharmaceuticals for patients.

Pharmaceutical Technology

The Pharmaceutical Technology works to establish technologies for the commercialization and production of new medicines created through research and development.

Through research and regulatory application activities related to drug substances, drug products, and quality evaluation, we develop commercial production processes to achieve high-quality and stable production, in addition to processes to manufacture and supply investigational drugs, whereby transferring manufacturing and analysis technologies to supply chain functions. After the launch of products, we continue to work on establishing and improving manufacturing processes in alignment with the life cycles of products, including improving usability and taking measures against counterfeit drugs, in order to increase the added value of our medicines.

Strength and challenge

Strength Capabilities to establish robust commercial production processes and quality evaluation methods for drug substances and drug products, to implement application processes steadily, and to develop products that meet the unmet needs of patients and healthcare professionals

Challenge Continued efforts to establish research and development capability for production processes adapted to a wide range of modalities following ADCs

Progress of major initiatives

Increasing production of *DS-8201* following the collaboration with AstraZeneca

With a significant increase in demand for *DS-8201* following the strategic collaboration with AstraZeneca at the end of March 2019, as well as the steady progress in the clinical studies of subsequent DXd-ADCs, we are facing an urgent need to expand our production capacity for ADCs, which is a key task. In response to the increase in demand, we have built new production bases inside and outside our Group, worked on regulatory filing of new manufacturing bases, and established a structure to support more clinical studies with a limited number of investigational drugs, thereby contributing to maximizing the value of *DS-8201*.

Going through the filing process for *ENHERTU* in the U.S. and Japan at an unprecedented speed in our history

With the mission of delivering *ENHERTU*, Daiichi Sankyo's first global oncology product, to patients as soon as possible, we worked on the filing process. To attain simultaneous filing in the U.S. and Japan , a process was established and implemented to streamline the preparation of application data on the design of drug substances, drug products, and quality. In the U.S., all data related to manufacturing process validation were submitted to the U.S. Food and Drug Administration (FDA) following the filing of application, ahead of the deadline agreed with the FDA. This contributed to the accelerated approval of *ENHERTU*. In addition, we were able to respond to inquiries from authorities in the U.S. and Japan in an on-time manner by sharing information promptly and forming timely agreements on the responses to queries with AstraZeneca. As a result of these measures, approval was obtained in an unprecedented short period of time in the Company's history.

Increasing added value through pharmaceutical technology

One of the important roles of the Pharmaceutical Technology Unit is to design formulations and packaging that are easy for patients and healthcare professionals to use and suitable for patients in terms of their diseases, as well as to develop relevant manufacturing methods. We make an effective use of our researchers' findings obtained during their visits to healthcare settings and information collected by our marketing personnel concerning the needs of healthcare professionals to promote the development of products and technologies. Examples of our past efforts include the development of *LIXIANA* orally disintegrating (OD) tablets, *Olmetec* OD tablets, and extended-release formulations of oral narcotic drugs. To provide a new treatment option for patients with COVID-19 as soon as possible, Daiichi Sankyo utilizes technology acquired through the development of anti-influenza agent *Inavir* to promote research and development of *nafamostat* inhalation formulation.

Developing highly productive expression systems in novel CHO cell* line

In the strategic collaboration with AstraZeneca for *DS-8201* and *DS-1062* and the early development of subsequent DXd-ADCs and other antibody drug pipelines, important issues for the Company have been improving antibody productivity and reducing manufacturing lead time. In the manufacturing of antibody drugs, long period of time for cell culture has been one of the reasons for the prolonged manufacturing lead time and high cost. The Company has participated in the Manufacturing Technology Association of Biologics (MAB) supported by the Ministry of Economy, Trade and Industry (METI) and the Japan Agency for Medical Research and Development (AMED), and successfully obtained novel CHO cell line with high proliferative ability. In addition, a new CHO cell expression system developed by combination with an in-house developed vector showed about three to four times higher antibody productivity than the previous system. In the future, we will be able to shorten manufacturing lead time, supply investigational drugs in a timely manner, and achieve low-cost commercial production by applying this technology to the manufacturing of subsequent DXd-ADCs and other antibody drugs.

* Chinese hamster ovary cells. Widely used in the manufacture of antibody drugs.

Future efforts

Increasing production of DXd-ADCs and future modalities

As a result of the strategic collaboration with AstraZeneca for *DS-8201* and following *DS-1062* and the steady progress in the clinical studies of subsequent DXd-ADCs, an ever-more-extensive expansion of the production capacity is required for manufacturing investigational drugs and commercial products. We facilitate on-time technology transfer to commercial production facilities, considering an option of further utilizing contract manufacturing organization (CMOs). For research on the drug substances, drug products, and quality evaluation of new modalities, such as next generation ADCs, nucleic acid, cell therapy, and gene therapy, we are working hard to develop and utilize advanced technologies, including ones derived from strategic use of specialized contract development and manufacturing organizations (CDMOs). In addition, we will work on enhancing our development/quality research structure for vaccines such as *DS-5670* (COVID-19 vaccine).

Supply Chain

A supply chain is a series of processes from the procurement of raw materials to the production, inventory control, and delivery of products. Our supply chain is shifting rapidly to oncology/biological products. In particular, in response to the rapid expansion of antibody-drug conjugate (ADC) products, we are strengthening our production and supply system by making large capital expenditures for manufacture of biological products and adding contract manufacturers worldwide, among other efforts.

Strength and challenge

Strength Launch and stable supply of products suitable for the market in each country through a global manufacturing and supply system
Capable of providing a long-term stable supply of high-quality pharmaceutical products around the world in the event of an emergency such as a natural disaster

Challenge To establish a stable supply system, taking into account development and launch schedules for the subsequent ADCs
To establish storage and transportation/delivery systems for regenerative medical products such as *DS-1647 (G47Δ)* and *axicabtagene ciloleucel* (anti-CD19 CAR-T cell)

Progress of major Initiatives

Formulate and steadily promote supply strategies in response to the increased demand for 3 ADCs

Considering a significant increase in demand for *ENHERTU* following the announcement of a strategic collaboration with AstraZeneca at the end of March 2019, demand forecast for *DS-1062*, and modification to the 5-year business plan, which was made at the end of October 2019 to clarify that the Company would place a top priority on maximizing the value of 3 ADCs, Daiichi Sankyo has strengthened its production system to maximize the capacity to supply 3 ADCs. In order to ensure stable supply in the future, the Company has increased its in-house production capacity and acquired production lines at overseas contract manufacturing organizations (CMOs).

As for *ENHERTU*, we swiftly began supplying products in the U.S. and Japan.

Contribute to generating group profits by reducing costs

The supply chain of a company plays an important role in pursuing cost reductions to generate profits. For *edoxaban*, which sustains our current revenue, we improve manufacturing methods in our plants, explore new sources of raw materials, and make other ongoing efforts to reduce costs. We have also achieved a significant cost reduction in equipment procurement by examining specifications carefully and making inquiries to competitive suppliers, under a situation where engineering operations that require a large capital expenditure are on the rise.

Global supply chain management

As the Daiichi Sankyo Group is a global supplier of products, global supply chain management is critical to ensuring a stable supply of products. We have established and worked to strengthen a tripartite global supply chain management system for the global procurement of raw materials, control of production volumes, inventory control, delivery, and resolution of supply and demand management issues in Japan, U.S., and Europe.

Future efforts

Steadily promote the establishment of a stable supply system in response to increased demand for 3 ADCs

To maximize the value of 3 ADCs, Daiichi Sankyo plans to make investments of more than ¥100.0 billion in manufacturing facilities by fiscal 2022. In addition to further strengthening its production system to maximize the capacity to supply 3 ADCs, we will build a supply system to ensure stable supply in the future. We also continue to train manufacturing personnel for biological products.

Promote reliable and stable supply during the COVID-19 pandemic

Daiichi Sankyo establishes a task force in its supply chain to achieve stable supply by continuing the operation of plants through thorough infection prevention measures and securing routes for importing raw materials for drug substances and intermediates.

Steadily promote the use and management of advanced technology

The Daiichi Sankyo Group has accelerated research and development of new modality products, such as CAR-T cell therapy, nucleic acid drug, gene therapy, and siRNA*. For its supply chain, we examine transportation/delivery methods that fit the characteristics of each new modality. Currently, we are developing a commercial logistics scheme for regenerative medical products that require transportation and delivery in the ultra-low temperature range, such as *DS-1647 (G47Δ)*, an oncolytic virus, and *axicabtagene ciloleucel*, a CAR-T cell product.

* small interfering RNA

The Medical Affairs Unit collects, analyzes, and evaluates medical information related to the Company's products; and generates and disseminates evidence, whereby contributing to treatment and maximizing the medical value of the Company's products. We identify clinical questions existing in the real clinical setting through collecting, analyzing and evaluating information on unmet medical needs and develop medical strategies to solve them. We perform clinical research activities based on the medical strategies and disseminate new evidence. Repeating this cycle of information collection, analysis and evaluation; and evidence generation and dissemination leads to improved medical value of the products. In addition, we are evolving product information functions and enhancing the quality of responses to our stakeholders.

Strength and challenge

Strength Know-how on information collection, analysis, and evaluation, and evidence generation and dissemination obtained from numerous clinical studies that we have performed mainly in the cardiovascular area
Our high capability in Japan for responding to inquiries from physicians and paramedical staff, which we were ranked No. 1 in a call center satisfaction ranking of pharmaceutical companies.

Challenge To strengthen organization/function for more sophisticated evidence generation and dissemination in the oncology area as a pharmaceutical company with competitive advantage in oncology

Progress of major initiatives

Generate and disseminate scientific evidence on *edoxaban*

Edoxaban is becoming one of the best anticoagulant therapy options for patients with cardiovascular disease worldwide, particularly in Japan and Europe. In fiscal 2019, evidence obtained through several clinical researches including ENTRUST-AF PCI study was presented in major academic conferences and journals, and the evidence was cited in 3 global and 3 Japanese clinical guidelines. Currently, we are conducting a large observational study aimed at revealing the real clinical setting data of anticoagulant therapy and prognosis in elderly patients

aged 75 years or older with non-valvular atrial fibrillation, and the study results are becoming available. We will remain committed to generating and disseminating more evidence so that *edoxaban* contributes to more patients.

Generate and disseminate scientific evidence in the oncology field on a global scale

In order to enhance the capabilities to generate and disseminate evidence for *ENHERTU* and other oncology products on a global scale, we strengthen our functions globally and in Japan and engage in a range of medical activities.

In collaboration with AstraZeneca, we have promoted the activities in line with a global medical strategy to generate and disseminate evidence on breast and other cancers after the launch of *ENHERTU*. The Medical Affairs is also responsible for the Company's publication strategy as part of evidence disseminating activities. In fiscal 2019, we made an oral presentation of the results form DESTINY-Breast01 study, which were the first pivotal study results of DXd-ADC pipelines at the San Antonio Breast Cancer Symposium (SABCS). The results were also simultaneously published in the *New England Journal of Medicine*. Through these events, we were able to disseminate the evidence effectively. As the oncology medical practice continues to advance at a fast-moving pace, it is essential to collect information on treatments and competitive products. We are conducting several activities to contribute to maximizing the medical value of products from an early stage of research and development by enhancing these functions to collect, analyze, and evaluate information, as well as by strengthening cooperation with related functions.

Future efforts

Further strengthening of evidence generation and dissemination in the oncology field

To contribute to maximizing the value of DXd-ADC pipelines and other products as a pharmaceutical company with competitive advantage in oncology, we promote developing cancer type-based medical strategies in addition to product-based medical strategies, and carry out relevant activities. In addition, we enhance the functions of medical science liaison (MSL), real world evidence (RWE), and companion diagnostics/biomarkers. Cooperating with related functions, we complement "Fast to Market strategies (meaning strategies to obtain approval and launch a product in the shortest period of time)" from a scientific and medical perspective. Through patient advocacy activities (such as support for patient groups) mainly outside Japan and the publication of patient-friendly manuscripts, we will also strengthen patient-centric information collection and evidence dissemination.

Take advantage of digital health tools/care

With the aim of improving patient's drug adherence, promoting the proper use of drugs, monitoring the efficacy and side effects that are reported from patients, supporting the diagnosis of diseases, and understanding potential medical needs, we have initiated the development of electronic patient reported outcome (ePRO)/personal health record (PHR) applications and evaluation of applying them to clinical researches for various products.

We will use ePRO/PHR as a platform to gain experiences and know-how in digital health tools/care.

Quality & Safety

Quality & Safety unit undertakes the following activities from research and development through to post-marketing phases in order to assure the quality of medicines and the reliability of information and to ensure the safety of pharmaceutical products, the: 1) ensuring the reliability of processes and data related to the manufacturing and analysis of products; 2) ensuring the reliability of data on efficacy and safety, as well as the quality of products, in terms of Good Practice (GxP) compliance; 3) promoting compliance through comprehensive management of regulatory affairs functions; 4) performing pharmacovigilance activities in an accurate manner, including collecting, assessing, and analyzing product safety information; 5) promoting the proper use of products in a timely manner to minimize risks; and 6) ensuring regulatory compliance concerning safety information.

Strength and challenge

Strength	**Experience and know-how in quality assurance and safety management that we have gained through the roll-out of various global products while responding appropriately to the requirements of each country, with standards for the quality and safety of pharmaceutical products becoming increasingly stringent at a rapid pace in many countries around the world**
Challenge	**To acquire resources needed to enhance timely quality assurance and safety management systems in response to a significant increase and acceleration of clinical studies following the strategic collaboration for *DS-8201* and *DS-1062*, as well as progress in research and development and business evolution for other products including new modalities**

Progress of major initiatives

Restructuring of organizations

Although the Daiichi Sankyo Group's past product portfolio focused on cardiovascular products, oncology pipelines have expanded in recent years, and development is also accelerating. In fiscal 2019, we launched *Tarlige*, *ENHERTU*, and many other products and performed many clinical studies of oncology products. As the oncology business is expanding, the Company has established independent safety management functions to ensure prompt and accurate decision-making concerning safety measures for oncology products for which safety management becomes increasingly complex.

Global initiatives concerning quality assurance and safety measures for oncology products

Pharmaceutical companies are required to comply with GxPs and must comply with inspections by regulatory authorities in each country in order to obtain approval. *ENHERTU* is Daiichi Sankyo's first oncology product for which approval application was filed based on global clinical studies and it was approved in December 2019 in the U.S. and March 2020 in Japan. *ENHERTU* was also the Company's first biologics product that had undergone an inspection by the Food and Drug Administration (FDA). For this reason, we formed a response team at an early stage, made sufficient preparations through mock inspections and other activities, and underwent inspections by the authorities. As a result, we were able to acquire compliance with the requirements by the FDA and the Ministry of Health, Labour and Welfare.

With regard to the safety of *DS-8201*, interstitial lung diseases (ILDs) have been defined as an "important identified risk," and a global ILD risk management system has been established. We work to swiftly obtain information on the cases of ILDs reported in various countries, and assess and analyze it in cooperation with AstraZeneca.

In Japan, in addition to formulating a drug risk management plan, we manage distribution by identifying medical institutions and physicians capable of managing ILDs,. To ensure that medical representatives can provide medical institutions with information promptly in response to their inquiries regarding safety, we have set up a safety communicator system and worked on other efforts to strengthen our support system.

We will build a similar system for *DS-1062*.

Future efforts

In addition to the global roll-out of *DS-8201*, we will accelerate and expand the development of *DS-1062* in alliance with AstraZeneca. This will result in more complex operations in quality assurance and safety management and a significant increase in information. In order to provide a stable supply and information to ensure that the product is used without uneasiness, we will promote quality assurance and safety management in light of the characteristics of anticancer drugs and ADCs.

In Japan, we will also develop the business of regenerative medical products such as *axicabtagene ciloleucel* and *DS-1647(G47Δ)*. These new modality products require measures not needed for conventional small molecule drugs and antibody products. Therefore, we will perform proper and accurate quality assurance and safety management depending on the characteristics of regenerative medical products (handling of biological samples, custom-made, etc.).