Creating Innovative Pharmaceuticals

Among the four material issues on business, "creating innovative pharmaceuticals" is the basis of our value creation and our top priority. Together with the other three material issues, we believe that creating innovative pharmaceuticals will lead both to the resolution of unmet medical needs, and to the realization of our Purpose.

3 and Alpha

In research and development, we have adopted "3 and Alpha strategy" to meet our FY2025 target and achieve our 2030 Vision. The "3" in 3 and Alpha refers to *Enhertu* ®, *Dato-DXd*, and *HER3-DXd*, our three pillars in oncology, to which investment and resource allocation are prioritized. *Enhertu* is our key 3ADCs product. Our goal is for it to transform treatment and outcomes for patients with HER2-targetable tumors and become the first agent of choice. *Enhertu* is currently undergoing clinical trials for a variety of lines of treatment and indications—including HER2 positive breast cancer, and HER2 low expression breast cancer—and we are working to expand its applications. Large numbers of people continue to suffer from cancer, and we are striving to deliver new pharmaceutical therapies to both patients and healthcare professionals as quickly as possible.

In "Alpha," which is our projects other than 3ADCs, we also aim to provide innovative pharmaceuticals to patients with cancer or rare diseases without effective treatment or sufficient treatment by using existing therapeutic drugs. We are aiming to commercialize the mRNA vaccine for COVID-19, *DS-5670*, as soon as possible; clinical trials to verify the booster effects of additional doses and the effects on non-vaccinated patients are currently ongoing. Confident that our strength in Science & Technology will lead to the development of new drugs in unknown fields, we will continue to embark on new challenges.

Expand 3ADCs in Broader Cancer Types and Indications

	Breast cancer	Gastric cancer	Non-small cell lung cancer (NSCLC)	Colorectal cancer
Enhertu				
DESTINY - Breast03*1	HER2-positive breast cancer 2L, vs. *T-DM1*			
DESTINY - Breast04*1	HER2-low breast cancer post-chemotherapy, vs. physician's choice			
DESTINY - Breast06	HER2-low / HR-positive breast cancer chemotherapy-naïve, vs. physician's choice			
DESTINY - Gastric04		HER2-positive gastric cancer 2L, vs. standard of care		
DESTINY - Lung01/02*1			HER2 mutated NSCLC, HER2-overexpressing NSCLC 2L ~ / HER2 mutated NSCLC 2L ~; 2 doses (5.4, 6.4mg/kg)	
DESTINY - CRC01/02				HER2-expressing colorectal cancer 3L / HER2-expressing colorectal cancer 3L; 2 doses (5.4, 6.4mg/kg)
Dato-DXd				
TROPION - Lung01			NSCLC, 2/3L	
HER3-DXd				
HERTHENA - Lung01			EGFR mutated NSCLC, 3L	

*1 Extremely succeeded in FY2021

Diverse Modalities

Pharmaceuticals include various types of drug molecules—such as small molecules and antibodies—which are collectively called "modalities." Advances in science have led to the formation of a variety of modalities, and these have allowed us to work on drug discovery targets that have previously proven challenging. Indeed, using ADC technologies we have created our own ADC modality, to go alongside our small molecule drugs. We believe that after 3ADCs, our next growth drivers will come from one of four areas: the DXd-ADC family, second-generation and new-concept ADCs, modified antibodies, or the ENA® family. In addition, our work on *DS-5670* has enabled us to advance our development of LNP-mRNA technologies, and we have also accumulated development and production know-how. These technologies will undoubtedly prove useful for the public health of countries around the world during future pandemics. In addition, we are also conducting research of various modalities and advancing research and development to increase treatment possibilities for unmet medical needs related to cancer, rare diseases, etc.

Growth Drivers to Follow 3ADCs

DXd-ADC Family
- DS-7300: efficacy being verified in Ph1
- DS-6000: efficacy being verified in Ph1
- DS-3939: preparations in progress for FIH*2
- DS-xxxx: preparations in progress for FIH

Second-generation and New-concept ADCs
- Second-generation ADC, DS-9606
  - ▶Ph1 in progress
- New-concept ADC
  - ▶Preparations in progress for FIH

Modified Antibodies
- DS-1055 (immuno-oncology)
  - ▶Ph1 in progress
- DS-1103 (immuno-oncology)
  - ▶Preparations in progress for FIH
- Bispecific antibodies
  - ▶Preparations in progress for FIH

ENA® family
- Multiple projects using ENA technologies
  - ▶DS-5141, DS-5144, DS-5150, DS-5151, DS-5153, DS-4108, etc.

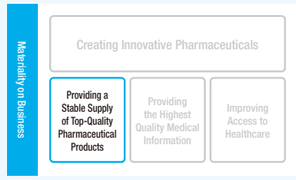
*2 "FIH" stands for "first in human." In FIH clinical trials, drugs, procedures, or treatments are tested on humans for the first time.

Diverse Modalities

Nucleic acids / LNP-mRNA / 2nd generation ADCs / Bispecific antibodies / Advanced chemistry

New-concept ADCs / Gene therapies / Cell therapies / Digital solutions

Providing a Stable Supply of Top-Quality Pharmaceutical Products



Pharmaceutical companies have a responsibility to ensure a steady and stable supply of high-quality pharmaceutical products. Through the appropriate capital investment, we have been establishing a global production and supply system that responds to increased demand for antibody drug conjugates (ADCs) and other new-modality products.

Establishing a Robust Global Supply Chain toward an Increase in Demand for 3ADCs

The key to our transformation in the field of oncology lies in maximizing the supply of our 3ADCs and, to this end, we are promoting capital investment in Group plants. An ADC comprises three parts: 1. an antibody; 2. a drug; and 3. a linker that binds the antibody to a drug. The manufacturing process comprises four-step: 1. culture, to produce the antibody (biotechnology); 2. synthesis, to bind the drug to the linker; 3. conjugation, to bind the antibody to the drug linker; and 4. formulation, in this case freeze-drying, to create the final product.

In order to ensure a stable supply of ADCs in the future, we are strengthening our in-house production capabilities and securing production lines at contract manufacturing organizations (CMOs).

In FY2021, we made the decision to invest approximately 80 billion yen.

Production Sites Worldwide

Investment Plan to Strengthen ADC Production System

	FY2021	FY2022	FY2023	FY2024	FY2025
	Actual	Planned			
Antibody	●	●	●	●	
Drug	●	●	●	●	●
Formulation	●		●		

* ● indicates years in which investment is planned

Quality Assurance for the Supply of Top-Quality Pharmaceutical Products

In order to reduce risks related to the quality of our products, Daiichi Sankyo Group regularly audits manufacturing sites of both Group companies and external partners to ensure they have appropriate quality management systems in place. COVID-19 continued to prevent on-site audits in FY2021, so we conducted paper audits and remote audits to ensure quality control and reduce quality risks.

In light of the increasing demand for ADCs, we are in the process of planning and implementing numerous changes, such as scaling up production capacity and partnering with new overseas CMOs. Previously, CMOs were directly managed from Japan; however, in order to strengthen our foundation for quality assurance and the stable supply of ADCs, we intend to transition to a new quality management system wherein we oversee CMOs in coordination with our overseas Group companies.

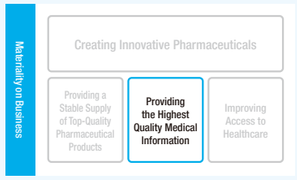
To manage these changes, as we fully comply with the pharmaceutical regulations of the countries in which we operate it is vital we do so in an efficient and effective manner. To this end, we will ensure that all relevant departments collaborate with each other, and contribute to the stable supply of our products globally. Furthermore, with the goal of establishing an even stronger global quality management system, we have also started using a new IT system, which enables us to centrally manage quality information such as change control, deviations and so on.

Addressing the Procurement Challenges to Ensure Stable Supply

COVID-19 and the ongoing situation in Ukraine have led to various procurement issues, including rising prices of raw material, delayed deliveries of manufacturing materials and equipment, and logistical disruption. However, we successfully maintained stable supply of our products in FY2021 through a variety of measures, including modifying production plans, multi sourcing, securing substitute suppliers, establishing new transportation routes, and increasing our inventories.

Difficulties in procuring raw materials and manufacturing materials persist, while logistics systems remain unstable. For these reasons, we will continue to work to mitigate and reduce risks that might prevent the stable supply of our products.

Providing the Highest Quality Medical Information



Highly reliable safety and efficacy information is essential for healthcare professionals in prescribing pharmaceutical products to treat patients with confidence. We contribute to healthcare by providing, collecting, and transmitting valuable information related to our pharmaceutical products that is rooted in established evidence, ensuring this information is communicated widely in society.

Aiming to be a Reliable Medical Partner

According to a FY2021 third-party survey for healthcare professionals in Japan, our Group was ranked No. 1 in three fields: medical affairs (MA) activities (cardiovascular field), medical representative (MR) activities, and responses to inquiries. In the field of MA, we drew on expert knowledge in medical, pharmaceutical, and natural sciences, and maintained fairness, independence, and transparency in a range of activities, including interacting with healthcare professionals, and planning and promoting clinical research aimed at resolving clinical questions (questions related to the use of drugs raised by both patients and healthcare professionals). In FY2021, we also gave numerous presentations at academic conferences and submitted large numbers of academic papers. Our activities on the provision, collection, and transmission of information by MRs were wide-ranging. We leveraged our uniquely wide-ranging line-up—which covers cardiovascular field, central nervous systems, pain, and oncology, etc.—to provide expert information related to safety and efficacy; this information is useful to healthcare professionals tasked with treating patients with various diseases. We also took care to engage in activities from a patient perspective. With regard to inquiries to our product information center, in October 2021 we started using a drug information (DI) chatbot utilizing AI, named “Itsudemo DI24,” on our website for medical healthcare professionals; this formed part of our efforts to establish a system that makes accurate information available 24 hours a day, 365 days a year.

Continuous Improvements to our Customer Experience (Europe)

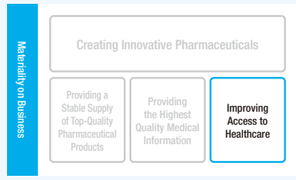
Our EU Specialty Business Unit (EUSBU) has prioritized a Customer First Mindset in the cardiovascular therapeutic area, in which it truly and systematically seeks, analyses and learns from all interactions and feedback from customers– and uses that input to deliver an outstanding experience to them. Since FY2019, our Group has used Net Promoter Score (NPS)* across our Europe operations. We have received feedback from more than 5,500 customers in nine countries, which we are using to evaluate, analyze, and improve our activities. Our NPS improved in FY2021, a reflection of the continuous improvements we have been making. We learned that customers primarily associate the Daiichi Sankyo Group with “reliability,” and that “reliability” is clearly one of our strengths. Other strengths include: communications tailored to individual customers through the adoption of an omni-channel approach; and the use of digital solutions that cater to changes in doctor-patient communication methods. By analyzing our NPS, we are working to continually improve the customer experience we provide and become a key player in the field of cardiovascular treatments.

*Net Promoter Score indicates how customers view our company in comparison to rival companies

Using Integrated Analysis Tools for *Enhertu* Safety Information

With the launch of *Enhertu*, there has been a demand for more specialized and more individualized safety information. In order to more quickly provide optimal safety information to healthcare professionals, we have introduced an integrated data analysis platform (IDAP) that enables us to carry out the integrated analysis of internal and external data. The data we analyze comes from multiple clinical trials and post-marketing side effect information respectively, and our analyses result in high-quality safety information — such as course data of side effects and frequency data of side effect occurrence in each group by patients' background — which we promptly provide to healthcare professionals. We are using the platform to carry out safety monitoring and for a wide variety of other purposes.

Improving Access to Healthcare



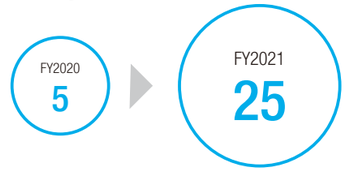
In addition to taking actions to address unmet medical needs, one of the important missions of pharmaceutical companies is addressing the problem of insufficient access to healthcare caused by various social factors. In line with the Daiichi Sankyo Group Policy on Access to Healthcare, we are continually working to address the challenge of access to healthcare across our entire value chain, based on the three pillars of “Research & Development,” “Availability,” and “Capacity Building.”

Sales of *Enhertu* Expanded to 25 Countries and Regions

In January 2020, we launched *Enhertu* in the U.S. ahead of other countries for its first indication: third-line treatment of HER2-positive breast cancer. After that, we launched the drug in Japan in May 2020, and in Europe in February 2021. Since then, in addition to accelerating the market penetration of *Enhertu* in Japan, the U.S., and Europe, we have been working on its early-access in regions other than Japan, the U.S., and Europe, and on adding further indications. In FY2021, *Enhertu* was sold in 20 countries around the world; as of March 31, 2022, sales have been expanded to a total of 25 countries. We have entered into a strategic collaboration for *Enhertu* with AstraZeneca, whose oncology business reaches over 70 countries and regions. We intend to expand access to the drug through our collaboration with AstraZeneca, which has excellent market access based on a relationship of trust with payers and oncology specialists and extensive experience and know-how in medical affairs and development, etc.

For further information regarding delivering innovative pharmaceuticals to patients around the world, please see ▶P. 19

Number of Countries/Regions in Which *Enhertu* Is Sold



Developing the *DS-5670* COVID-19 Vaccine

In order to meet our social responsibilities as a Japanese pharmaceutical company that operates a vaccine business, we aim to continue delivering a stable supply of vaccines and to contribute to improving Japan’s preventive care and its health and hygiene.

In FY2021, to fight the rapid spread of COVID-19, we began manufacturing AstraZeneca’s vaccine, and thereby swiftly realized domestic production and supply of the vaccine that had been developed overseas. This was the first COVID-19 vaccine produced in Japan and, in June 2021, it was supplied by the Japanese government to various countries in Southeast Asia. We are also using our proprietary mRNA technologies to develop the *DS-5670* COVID-19 vaccine, and we are working to establish domestic mRNA vaccine production systems at Daiichi Sankyo Biotech toward its commercialization.

We also intend to establish these mRNA technologies as platform technologies capable of being used to develop vaccines not only for *DS-5670* but for future emerging and re-emerging infectious diseases. By using these technologies to provide people with preventive care, we intend to help them carry on living their normal lives.


Kitamoto Plant

Establishing Daiichi Sankyo Sales Bases in Australia, Canada, and Singapore

In FY2021, we established wholly owned subsidiaries in Australia, Canada, and Singapore. These new companies will develop and sell pharmaceuticals and contribute to healthcare in their respective countries. The establishment of these new companies means that we now operate bases in 26 countries and regions around the world. Going forward, we will continue to strengthen our foundations for expanding sales of oncology products and other new products around the world.

Number of Countries/Regions with Daiichi Sankyo Bases

26