Delivering Innovative Pharmaceuticals to Patients around the World

We have provided many patients around the world with innovative products created in-house by combining our strengths in Science & Technology, the source of our value creation, to realize our Purpose: "Contribute to the enrichment of quality of life around the world."
In this section, we will introduce our strengths in Science & Technology and our concerted efforts throughout the value chain to deliver *Enhertu*®, the culmination of our efforts, to patients around the world.

Our strengths Science & Technology (S&T)

The greatest strength of our Group is Science & Technology (S&T), which combines our human resources core technologies, and corporate culture. We have continuously created innovative pharmaceuticals based on the technologies and experience that we have cultivated over many years as a drug discovery-oriented pharmaceutical company based on our highly specialized human resources with high level of scientific assessment capabilities and our free and open corporate culture. Moreover, the passion that our researchers pour into drug discovery, their perseverance of not giving up nor being afraid of failure and their willingness to keep challenging themselves by believing in innovation are the driving force behind our ability to create innovative new drugs. We believe it is essential to pursue cutting-edge science and further strengthen S&T in order to continue to create pharmaceuticals.

Our Pipeline

Drawing on our strengths in S&T, we have built a substantial R&D pipeline in a variety of therapeutic areas, including oncology, based on our "3 and Alpha" strategy (see Materiality ▶ P.29). 3ADCs that we have developed using our proprietary DXd-ADC technology, anti-cancer agent *Enhertu* (development code: *DS-8201*), *Dato-Dxd* (development code: *DS-1062*), and *HER3-DXd*, have been highly praised internationally and have won the World ADC Award for the "Most Promising Clinical Candidate" for three consecutive years. In addition, we have confirmed efficacy signals of *DS-7300* and *DS-6000*, which incorporate DXd-ADC technology, in early clinical trials, and we are developing them as "Rising Stars" to make them into the next growth driver following 3ADCs. In the non-oncology disease area, we are also making progress in expanding indications for *Lixiana*®, *Efient*®, and *Tarlige*®, which have supported our recent growth. We will continue to further strengthen our Group's unique pipeline to provide optimal treatment options for patients with unmet medical needs.

For details, click below:
https://www.daiichisankyo.com/files/rd/pipeline/index/pdf/FY2022Q1_Pipeline_E.pdf

Business Innovations Driven by New Drugs

The innovation resulting from the new drugs created through our strengths in S&T is not limited to research, but also drives further innovation and new opportunities throughout each function of the value chain and the business as a whole.

For example, in order to maximize product value by accelerating the pace of development of *Enhertu* and *Dato-DXd*, we are collaborating with AstraZeneca, a company with a strong presence in oncology, to cultivate new experience and expertise in conducting clinical trials, filing applications, and supplying investigational drugs on a global scale. In addition, we are taking various new initiatives under our global safety management system to ensure strict side effect management. In countries and regions where our products, including *Enhertu*, are not yet approved, we are taking new initiatives through the Expanded Access Program (EAP) to ensure access to patients in need of treatment in accordance with local regulations.

In addition, manufacturing biopharmaceuticals is a new challenge for our Group, as our mainstay products have been small molecule drugs. In order to make the manufacturing of biopharmaceuticals such as ADCs more efficient, we have established proprietary technologies for each process of cell creation, cultivation, and purification. Furthermore, we are refining our cell and gene technologies with the aim of creating next generation modalities. As for our supply chain, we are actively working to build a more robust production and supply system for biopharmaceuticals by expanding facilities at domestic and overseas plants, strategically utilizing contract manufacturing organizations (CMOs), and training and acquiring highly specialized biotech talents. At the same time, we are also focusing on promoting a new "smart supply chain" that leverages digital technology in all aspects of our operations and visualizes and integrates data. Going forward, we aim to build a process that enables continuous innovation through a series of company-wide advancements.

Interview Our S&T strengths demonstrated in *DS-5670*

Katsuyasu Ishida
Clinical Development Department III, Development Function, R&D Division

Three years have passed since the outbreak of COVID-19, an infectious disease caused by SARS-CoV-2, and the pandemic is still ongoing worldwide. At Daiichi Sankyo Group, we have been continuing research on LNP-mRNA vaccines, and in April 2020, we established the *DS-5670* Global Project Team (GPT) with the aim of promptly developing a SARS-CoV-2 vaccine in response to the COVID-19 pandemic to join the fight to contain the pandemic. In addition, the Japanese government also had high expectations for vaccine development of our Group, as we have an integrated system for research, development, manufacturing, and marketing in Japan.

The GPT began preparations with the goal of conducting a First in Human (FIH) trial as quickly as possible, even though the vaccine antigens had not yet been determined. We were able to take the multi-year process to begin clinical trials — which involves screening antigens, developing a manufacturing process, then conducting the required non-clinical studies once the antigens are determined while simultaneously manufacturing the investigational drug to be used in the clinical trials — and shorten it to just one year. This is a good example of how we leveraged our strengths in S&T.

We are currently conducting the final stage of clinical trials for commercialization. GPT and every member involved in our Group are working together to promote R&D while flexibly responding to major changes in the external environment over the past three years (repeated increases and decreases in the number of infection, changes in vaccination rates, etc.). We are also working to establish manufacturing processes, manufacture investigational drugs, and establish a commercial production system to support these processes safely at the fastest pace. We hope *DS-5670* will be a vaccine that will help end the pandemic.

Our New Challenges in the Value Chain to Maximize the Value of *Enhertu*

Enhertu is the first drug we developed using our proprietary ADC technology, which leverages our strengths in S&T, and addresses substantial unmet medical needs within breast and gastric cancers. *Enhertu* is the embodiment of our strengths in S&T, demonstrating our scientific assessment capabilities and our technological capabilities to refine drugs. We are working to maximize the value of *Enhertu* by collaborating across organizational boundaries and making a concerted effort throughout the value chain to bring the drug to market quickly, driven by our strong commitment to delivering new treatments to as many patients as possible as quickly as possible. In addition, through the use of new digital technologies, we will innovate the processes of value chain functions to strengthen the competitiveness of our overall business.

High quality and agile clinical development

The global R&D of *Enhertu* demonstrates our strengths in science-driven, high quality clinical trials and flexibility in regulatory strategy. For the gastric cancer indication, *Enhertu* received US FDA approval based on the results of clinical trials conducted in Asia. In addition, the US FDA granted five Breakthrough Therapy designations. The data from our clinical trial for the second-line treatment of HER2-positive metastatic breast cancer supported *Enhertu* becoming the new standard of care in previously treated patients with HER2-positive metastatic breast cancer, and we filed for approval in Japan, the United States, Europe, China, and other countries, and received approval in the US in May 2022 for the second-line treatment indication. Furthermore, our clinical trial for HER2-low unresectable or metastatic breast cancer was the first in the world to demonstrate statistically significant and clinically meaningful improvements in progression-free survival (PFS) and overall survival (OS) over chemotherapy, the current standard of care, for patients with HER2-low metastatic breast cancer with hormone receptor (HR)-positive disease or HR-negative disease. With the results of this trial, we expect that *Enhertu* will create a paradigm shift in the treatment of patients with HER2-low metastatic breast cancer and potentially become the new standard of care.

Reliably supplying investigational drugs

The demand for *Enhertu* for investigational use has been increasing due to numerous clinical trials and investigator-initiated studies to expand the application of *Enhertu* after its launch, in addition to the commercial demand for *Enhertu*. ADC was a new modality for us, and we have faced a great challenge in supplying investigational drugs and establishing a commercial production system. We overcame various technical and regulatory challenges by working together with our plants, CMOs, and supply chain department and simultaneously launched multiple manufacturing sites at the time of market launch, approximately four years after starting clinical trials. Even after launch, we are working to scale up and take other measures to expand production to ensure a reliable manufacturing network.

Building a resilient supply system

We are working on a wide variety of measures to ensure a stable global supply of *Enhertu*, such as diversifying manufacturing sites in Japan and overseas, finding the optimal balance between in-house production and CMO production, and securing multiple suppliers and transportation routes in order to remain heavily resilient against any environmental changes surrounding our supply chain.

Providing information to meet diverse medical needs

The Medical Affairs Division creates new value of our products by conducting clinical research to solve unmet medical needs. The Business Division provides the value of *Enhertu* to medical professionals correctly and promptly based on established information. Since each cancer patient's condition is different, in providing information by MR*1 and MSL*2, we not only provide and collect information about the product, but also communicate with medical professionals about changes in patients who have received the drug, and the anxieties and happiness they feel, in order to provide more safety-focused and thoughtful care.

*1 Medical Representatives *2 Medical Science Liaison

Drug Discovery and Research | Clinical Development | Supply Chain | Value Delivery

Reliability and Quality Assurance

Safety Management Initiatives

Global reliability and quality assurance

We ensure the reliability of clinical trials and the quality of investigational drugs and commercial products in response to accelerated global development. In addition, we take global regulatory actions and assure product quality for additional manufacturing sites and CMC changes in response to increased demand.

Thorough risk management and delivery of high-quality safety information

In addition to contributing to the approval of *Enhertu* in each country from a safety perspective, we have formulated a common global plan to minimize safety risks of *Enhertu* and monitor side effect information (ILDs*3, etc.) collected from all over the world on a global scale to ensure thorough risk management. Furthermore, to ensure patient safety, we have formulated a common global safety message and provided it to the healthcare professionals in cooperation with other divisions in each country where we market *Enhertu*.
Through these initiatives, we are working to provide high-quality safety information.

*3 Interstitial lung disease

DX to support value chain and accelerate execution of our business strategies

High-capacity computing environment to support data-driven drug discovery support

We developed an infrastructure providing computing power with a secured IT environment that scales on an on-demand basis, with which researchers execute a self-developed problem-solving program tailored to each problem they face. This enables us to reduce the time required to test hypotheses and shorten the research period.

Implementation of IT system (eQMS) for global quality management process

We implemented an eQMS that standardizes quality management processes and enables us to centrally manage quality information such as operational changes controls, as well as information regarding quality deviations and so on, in order to establish a robust global quality management system that quickly resolves quality issues and reduces the quality risks in global GxP operations and products. We promote quality risk management across regions and GxP fields, improve operational efficiency and data integrity, and implement continuous improvement.

Building a global supply and demand system and digital twin*4 infrastructure to support a resilient supply chain

We are introducing a system designed to support *Enhertu's* global supply and demand planning and coordination, and creating optimal production plans for in-house production in Japan and overseas, as well as for CMO production, while taking into account milestones such as obtaining approvals and applying for changes in each country. In addition, we are working on implementing a manufacturing quality data management system and data concept to create digital twins for our in-house production sites.

*4 Environment reproduced in digital space based on information from the real world

Data analytics platform

We have built a data analytics platform that utilizes a variety of internal and external data, and have begun to make company-wide use of this infrastructure for safety monitoring and other purposes. In particular, we have built a user-friendly and comprehensive search and analysis tool for safety data from multiple clinical trial data and post-marketing for *Enhertu*, and are using it to implement timely safety measures and promptly provide high-quality safety information to the healthcare professionals.

MR digital tools

In Japan, we introduced a new information provision platform that enables seamless MR activities in the real and digital worlds and customer-oriented promotions leveraging digital technologies in the new hybrid workstyle during the COVID-19 pandemic, aiming to provide information that meet the needs of medical professionals.

Delivering 3ADCs to Patients around the World, starting with *Enhertu*

Most aspects of the oncology field change rapidly from diagnosis to standards of care (the established and most widely used current medical practices), and this therapeutic area will continually evolve at a fast pace. Our Oncology Business Unit (OBU) has challenged itself to transform treatment for a variety of cancers. We take proactive action to continually deepen our knowledge of the journey patients and their providers take from diagnosis through treatment and beyond so that we can provide optimal solutions to diverse medical needs as quickly as possible.

We aim to increase the number of countries and regions in which we market *Enhertu*, and with expanded indications including breast and lung cancer, while also striving to obtain additional approvals for 3ADCs. We are also working on products in other oncology fields with the goal of establishing them as new standards of care.

Furthermore, with this goal of developing new standards of care, and to ensure our innovative pharmaceuticals could reach as many patients as possible in the shortest possible time, we entered into a global collaboration with AstraZeneca for the joint development and commercialization of two of our lead ADC products, *Enhertu* and *Dato-DXd*. We are now creating a streamlined and effective organizational structure and building expertise to ensure we can optimize other promising product candidates in our pipeline following the ADCs.

DX Initiatives for Maximizing Product Value and Creating New Value

Following *Enhertu's* designation in Japan's cost-effectiveness evaluation system in FY2020, we conducted a cost-effectiveness analysis using Real World Evidence (RWE)*1. This is the first cost-effectiveness analysis using RWE in Japan, and there are not many examples in other countries either. Creating reliable RWE requires bringing together data science expertise. We were able to leverage RWE by bringing together data science expertise under our DX promotion structure across our entire company. In Japan, we are also working to develop not only drugs but also DTx*2, which promotes well-being by bridging the gaps in patient care, including when patients are at home. Going forward, we will continue to maximize product value and create new value by combining the wisdom we have accumulated as a pharmaceutical company in the field of data analysis together with digital technology.

*1 Clinical evidence derived from analysis of real-world data (data relating to patient health status and/or health care routinely collected from a variety of sources)
*2 Software that performs medical interventions (treatment, management, prevention) directly to patients based on evidence of usefulness

Interview

Mission to deliver our oncology medicines to patients around the world

Ken Keller
Head of Oncology Business Unit

The Oncology Business Unit (OBU) is committed to achieving our 2030 Vision to become an innovative global healthcare company contributing to the sustainable development of society. By aligning our U.S. and European oncology businesses and global oncology functions together under the new OBU in April 2021, we are now one unified team devoted to people with cancer.

Our OBU will accelerate our decision making and increase our agility to respond to the rapid changes we see in standards of care, treatment and diagnoses patterns, and payer dynamics. Our ADC pipeline has the potential to transform the current standard of care across multiple types of cancer, including breast, lung, colorectal, gastric and more. We know the needs of the oncology community continue to rapidly change from diagnosis patterns to standards of care. We must continue to evolve and adapt — operating with agility and simplicity — to deliver for our patients and customers.

Contributing to improving the lives of people all over the world requires us to work collaboratively within the OBU as well as across the organization to deliver on Daiichi Sankyo's global ambition to bring innovative pharmaceuticals to patients, customers and society overall.

"Putting patients at the center of our efforts is critical. We will continually collaborate with patient groups, physicians, pharmacists, and insurers to provide the best possible support to our patients with the desire to leave no patient behind."

Purpose

Contribute to the enrichment of quality of life around the world

Expanded indications

HER2 positive breast cancer second and third line treatment
HER2 positive gastric cancer second and third line treatment
HER2 positive non-small cell lung cancer second line treatment
HER2 low breast cancer (post-chemotherapy)

(Approved indications as of August 31, 2022)

Number of patients treated

Appx. **8,000** patients

(As of March 31, 2022)

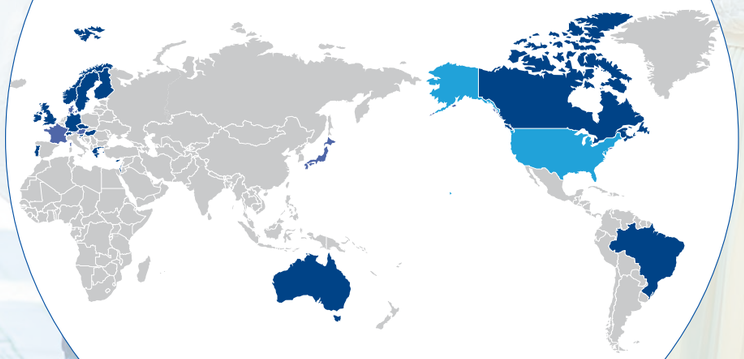
Number of trials conducted

30

(As of July 31, 2022)

Expanded number of countries and regions marketed

FY2019 FY2020 FY2021



Combining the Collective Strengths of the Daiichi Sankyo Group

Our realization that we are delivering innovative pharmaceuticals to as many patients as possible is shared throughout the company and is the driving force behind our transformation for the future. Going forward, we will continue to further enhance our strength in Science & Technology, and will maximize the value of *Enhertu* and other advanced pharmaceuticals to quickly provide treatment options and deliver innovations that create new value for patients.