S&T

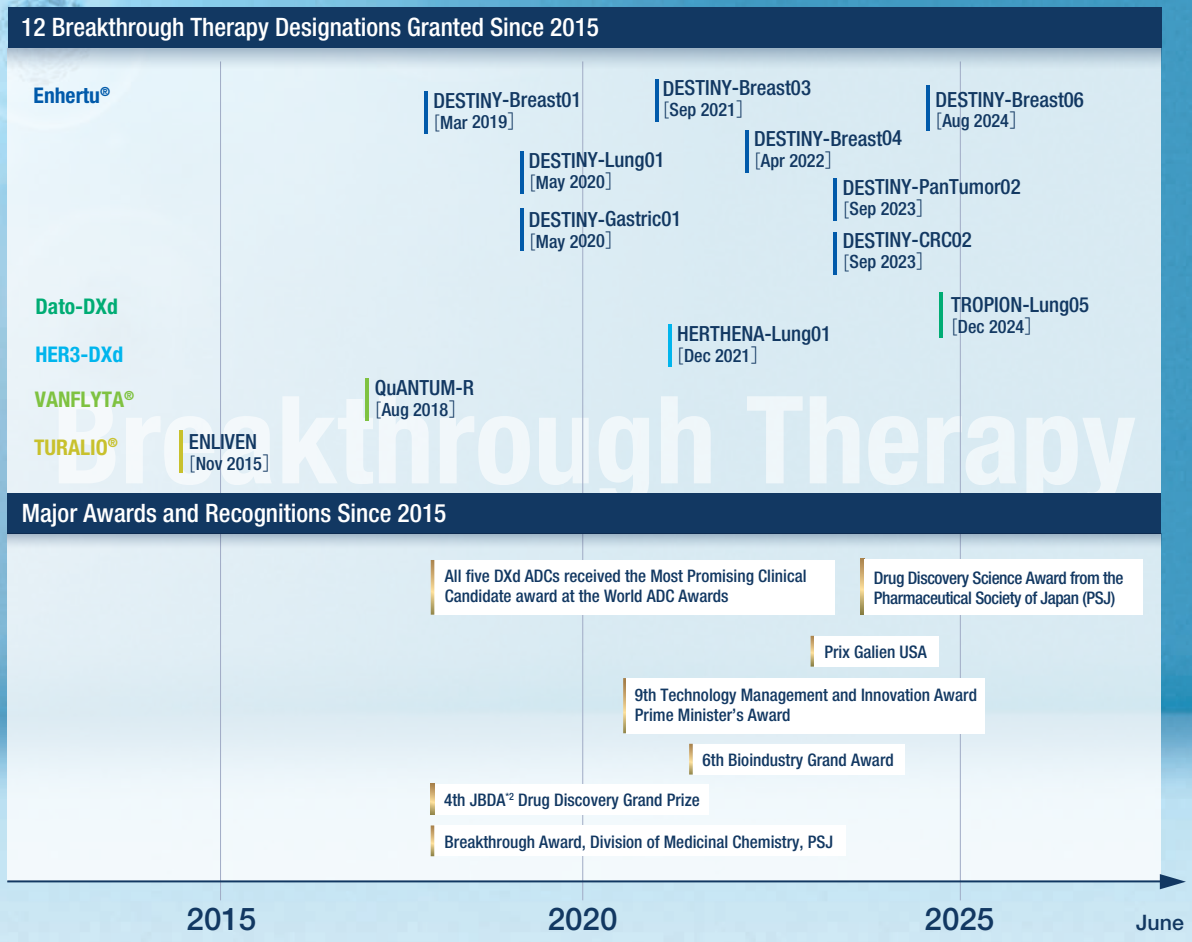
Science & Technology

Drug Discovery Capability that Drives Innovation, and a DNA of Inherited Challenge

Over the past decade, the Daiichi Sankyo Group's Science & Technology has earned high acclaim, including 12 Breakthrough Therapy Designations*1 by the FDA and numerous prestigious drug discovery awards, such as the 2024 Prix Galien USA Award, the equivalent of the most prestigious award in the pharmaceutical industry.

1 Introduction: S&T's Strengths and Path to Growth

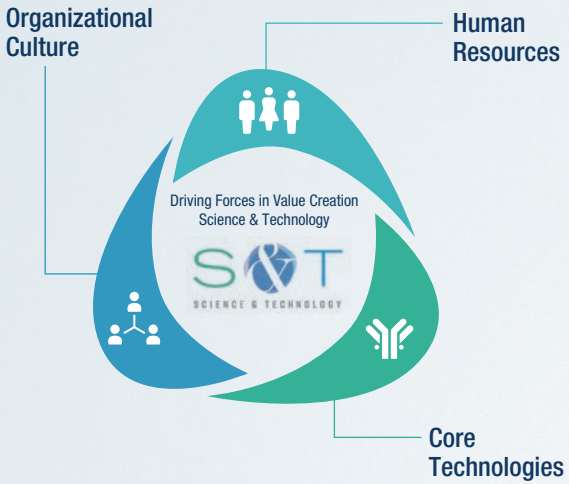
Daiichi Sankyo's greatest strength lies in its Science & Technology (S&T) capabilities. Built over many years, our unique research and development expertise is fully integrated across the entire pharmaceutical value chain, including manufacturing and supply. This foundation has enabled the creation of innovative medicines such as Enhertu® and Datroway®, allowing us to deliver differentiated value in the global market.



*1 Breakthrough Therapy Designation: A program established by the FDA to accelerate the development and review of drugs intended to treat serious or life-threatening conditions. The designation enables pharmaceutical companies to work closely with the FDA, receiving intensive guidance throughout the development process. This close collaboration can significantly shorten the time required for regulatory approval, allowing innovative therapies to reach patients faster.

*2 Japan Bioindustry Development Association

2 Competitive Advantages Based on Research & Development (S) and Proprietary Technologies (T)



● Strengths in Drug Discovery Activities

Our drug discovery activities are based not only on the successful experiences with our proprietary products, but also in the wealth of knowledge gained from extensive research and development (R&D) experiences that did not lead to new drugs. This accumulated expertise is shared across generations, fostering a culture in which researchers continuously deepen their work through mutual learning and collective growth.

Products such as Enhertu and Tarlige® are the culmination of research and development efforts that pursued drugs capable of transforming standard of care. In drug discovery, where the probability of success is extremely low, it is essential to respect the creativity and original thinking of researchers and clinical members. Daily work is carried out in a free and open manner within a culture where even failures are regarded as valuable lessons. For example, in the development of Enhertu, the discovery of DXd as a superior payload—building on past learnings, including Exatecan and the discontinued DE-310—led to the creation of our proprietary DXd ADC platform.

At the heart of our drug discovery activities is a strong desire to deliver medicines that are truly needed by patients. In selecting research themes, we place great importance on both scientific validity and medical significance, examining them from the perspectives of feasibility and potential therapeutic impact. Only those that meet the high criteria set through this rigorous evaluation process proceed to clinical development. Many themes, however, are discontinued for not meeting the criteria and projects are halted during the development stage. Even in such cases, we establish opportunities for reflection by conducting a lessons learned exercise and maintaining a system for sharing valuable insights from these experiences that are shared and applied to future R&D efforts. Where appropriate, and following a formal review process, these insights are also presented externally to help ensure the credibility and transparency of our research.

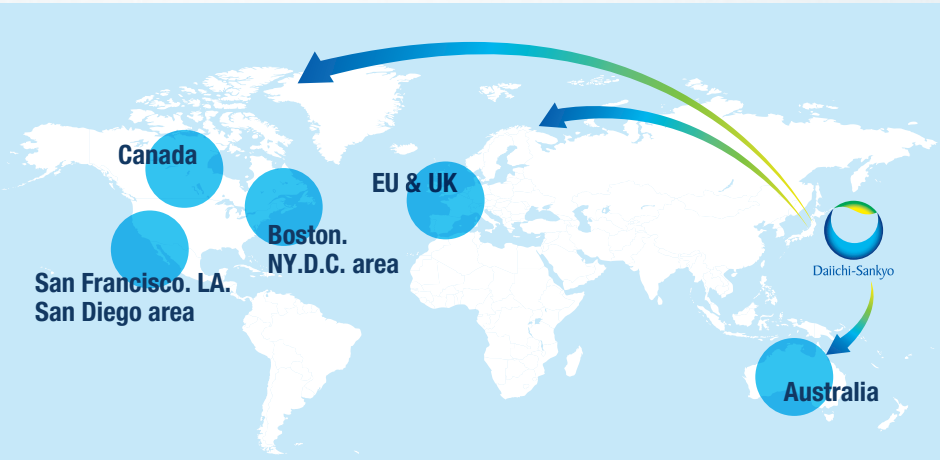
● Strengths of R&D Organization and Culture

Our R&D organization operates under a culture that values creativity and autonomy. A bottom-up environment that encourages open and candid discussions unconstrained by seniority or position has taken root, empowering researchers and clinical members to take initiative.

In human resource development, we prioritize a long-term perspective. To support the continuous growth of our researchers and clinical members, we have established a framework for nurturing “masters of drug discovery & development” by building clear career paths and promoting the transfer of skills and expertise through senior-to-junior mentoring. We also offer diverse growth opportunities, such as support for obtaining doctoral degrees, overseas study and assignments, fellowships, broad learning and development programs, cross-functional rotations within and beyond R&D, and strategic placement that leverages individual expertise.

Through our R&D activities, we have cultivated serial drug inventors—researchers who have created multiple successful medicines—as well as R&D leaders who drive research initiatives. Many inventors on the patents for Enhertu have been involved with other compounds that have successfully reached the market. Engagement in multiple projects enables the accumulation of knowledge and experience, which in turn drives the continuous creation of innovation. The presence of leaders with such experience and track records also serves as a strong source of motivation for junior R&D personnel.

Overseas Study Program



To develop researchers with doctoral degrees, we actively provide opportunities to study outside Japan. Through this program, Japan-based researchers deepen their understanding of cutting-edge science and technology while building networks within the global research community. They are expected to leverage their experiences by proposing new research themes and taking on leadership roles as team leaders. More than 150 researchers in total have been dispatched since FY2007.

Nearly all leaders who drive R&D possess scientific expertise, and deep understanding and respect for science, which is firmly embedded in our organizational culture. This shared mindset enhances trust and teamwork among R&D personnel, forming the foundation for achieving both scientific creativity and effective organizational leadership.

Furthermore, with discovery research and clinical development within the same organizational unit, collaboration between the two functions takes place regularly. This allows the intentions of both teams to be quickly integrated and reflected when setting research and clinical development criteria, enabling seamless execution of R&D.

Our R&D structure also possesses strong adaptability to external changes. During the era of the former Sankyo and Daiichi Pharmaceutical,small molecule drug discovery was the mainstream; however, following their integration, we expanded our area of research to the biologics field under a multimodality strategy. In 2013, we established the Biologics Oversight Function to strengthen our research capabilities and production technologies in new modalities such as antibodies, ADCs, and nucleic acid medicines. Furthermore, in 2016, we appointed R&D leader from global pharmaceutical companies to enhance our development capabilities in the oncology area. Since then, we have significantly expanded our global development capability in oncology by hiring many physician scientists as development leaders. The number of clinical members who have relocated from Japan to the United States and are playing key roles in global development has also increased. These changes are clearly reflected in the transformation of our major pipeline between FY2014 and FY2024.

What enables these transformations is the continuous investment in R&D from a long-term perspective, along with strong leadership that sets a clear direction while respecting the expertise of R&D personnel. By clearly articulating R&D policies and balancing them with creative-thinking, R&D leaders have driven the breakthrough innovations. A relationship of trust and mutual respect between management and R&D serves as the foundation for an organization capable of responding flexibly and agilely to a rapidly changing external environment.

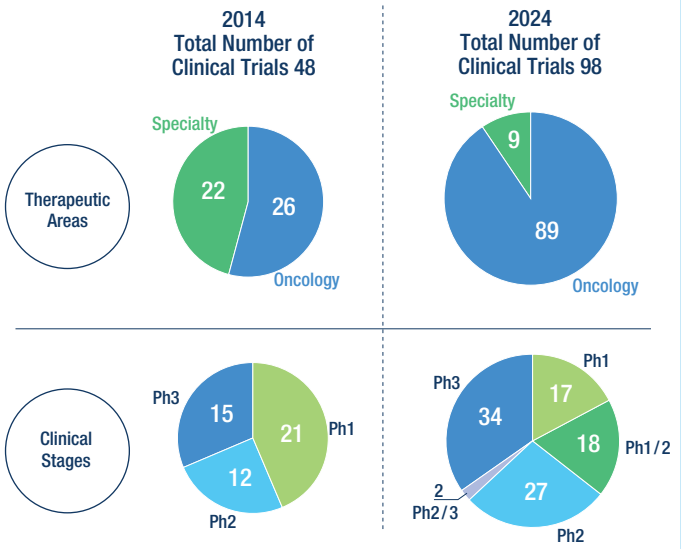
Dedication to quality and careful craftspersonship that has been passed down for over 120 years. It refers to careful coordination of techniques and attention to detail. By combining knowledge, experience, and skills, teams work with perseverance and collaboration to bring new drugs to completion.

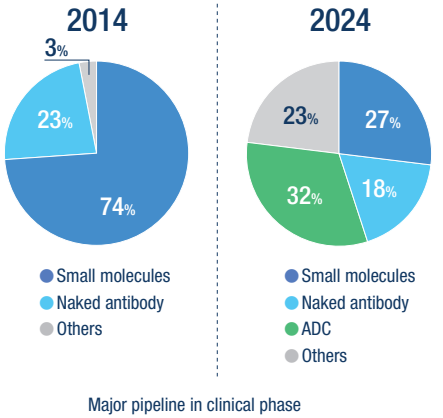
A research culture where people can freely discuss and propose ideas based on one's own thinking, regardless of position or rank

In research and development,, researchers and clinical members experience many failures as they repeatedly test and refine hypotheses to reach conclusions. Such a process, involving trial and error, is sometimes referred to as "intelligent failure" and is actively encouraged, as it contributes to scientific learning and progress.

Changes in Major Pipeline

The major pipeline has significantly expanded, with the number of clinical trials doubling.
The strategic overhaul has led to a shift in our priority disease areas.



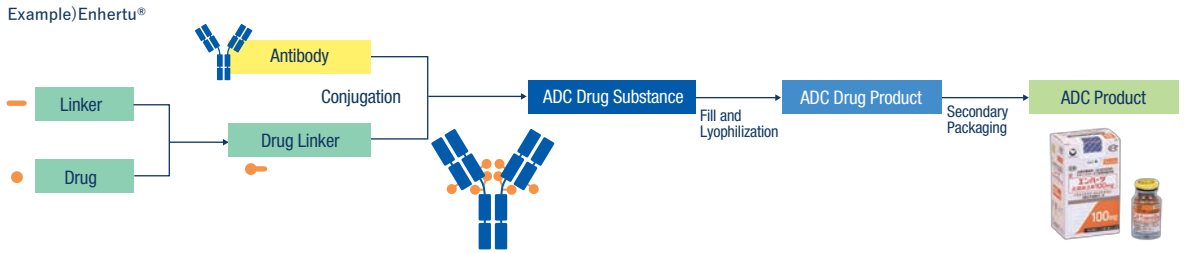


Major pipeline in clinical phase

Pipeline transformation to multimodality

The pipeline composition has shifted from only small molecules/naked antibodies to multi-modalities including ADC, bi-specific antibody, mRNA, etc.

The ADC consists of multiple components, each of which is manufactured and managed separately.



ADCs consist of an antibody, a drug, and a linker that connects the antibody to the drug. The manufacturing process of an ADC involves four main steps: (1) the antibody production process (cell culture), (2) the synthesis process for linking the drug to the linker, (3) the conjugation process that attaches the drug-linker to the antibody, and (4) the formulation process, including filling and lyophilization, to produce the final product. Daiichi Sankyo's strengths are particularly evident in the molecular design and manufacturing process development of ADCs. As the company's internal R&D focus has shifted from small molecule pharmaceuticals to biopharmaceuticals, its continued excellence in synthetic chemistry has been effectively applied to linker design and drug-linker synthesis in ADCs. In addition, the conjugation process—binding the antibody to the drug-linker—embodies our proprietary expertise in reliably producing high-quality ADC drug substances with consistency.

Currently, the Daiichi Sankyo Group is expanding its supply capacity while managing the balance between in-house production and the use of CMOs*3 as part of establishing a robust manufacturing system. Because ADC manufacturing is highly complex, building a stable production system is not an easy task. However, we have been strengthening our partnerships with CMOs that have been able to meet high-quality standards from an early stage. In addition, to prepare for future growth in product demand, we are also making capital investments on the scale of several hundred billion yen.

*3 CMO (Contract Manufacturing Organization)

As we expand our production capacity, new challenges have also emerged. Even when the manufacturing process itself remains the same, differences in production sites necessitate fine-tuning of the processes, and it is essential to make appropriate adjustments. To ensure stable product quality, such adjustments must be repeated multiple times, placing a significant burden on internal resources. However, we work closely with various stakeholders involved with the Daiichi Sankyo Group to continuously pursue further improvements in quality.

We are also considering initiatives to realize the "one-stop shop" concept. Currently, each of the major manufacturing processes for ADCs—antibody production, drug-linker synthesis, conjugation, and formulation—is carried out at multiple global sites. Coordinating these processes requires combining the appropriate sites, which results in long lead times for final product delivery and necessitates complex production planning and supply chain management. By pursuing the "one-stop shop" concept, where multiple ADC processes can be carried out at a single site, we can shorten the transportation lead time between manufacturing sites and significantly improve the overall speed of manufacturing. This would also allow for greater flexibility in responding to sudden schedule or quantity changes during the development stage, thereby accelerating the overall development process.

MESSAGE

From Early-Stage Development to Commercial Production and Supply — A Seamlessly Integrated Organization Supporting our "Science & Technology"

We are continuously working to improve our manufacturing processes to deliver better medicines to patients in a stable manner and to provide products that are accessible to people around the world at appropriate prices.

In 2023, we established the Technology Unit, which integrates three functions—Biologics, Pharmaceutical Technology, and Supply Chain—which plays an important role as part of Daiichi Sankyo's "Science & Technology." The concept behind the Technology Unit is integration of clinical and commercial. By integrating and closely coordinating activities from early-stage development to commercial production and supply, we have built a system that enables the rapid and stable delivery of high-quality medicines to patients. Two years have passed since its establishment, and collaboration within the Unit has been strengthened, allowing us to examine various issues from multiple perspectives and grow into an organization capable of responding flexibly. The Technology Unit is also a large global organization with more than 4,000 members. While sharing the overarching direction of achieving a balance between global alignment and local autonomy, we aim to build an organization where each member can think and act proactively.

Executive Officer
Head of Technology Unit
Hiroto Kashiwase

3 To Generate the Next Innovation

With the aim of sustainable growth, we strive to continuously deliver new value to patients and society by consistently delivering a pipeline of products based on our proprietary technologies and strengthening the human capital base that creates and them.

●R&D Strategy Centered on Technical Superiority

We have continuously created breakthrough new drugs such as Olmesartan, Edoxaban, and Enhertu, which have supported the growth of our business. All of these products originated from our research laboratories in Japan and are signature achievements that exemplify our drug discovery capabilities. The development and launch of Enhertu marked a turning point, establishing our position as a global leader in the ADC field. In particular, ADCs based on our proprietary DXd ADC technology, are enhancing our global presence not only through five products in collaboration with partner companies but also through follow-on candidates such as DS-3939.

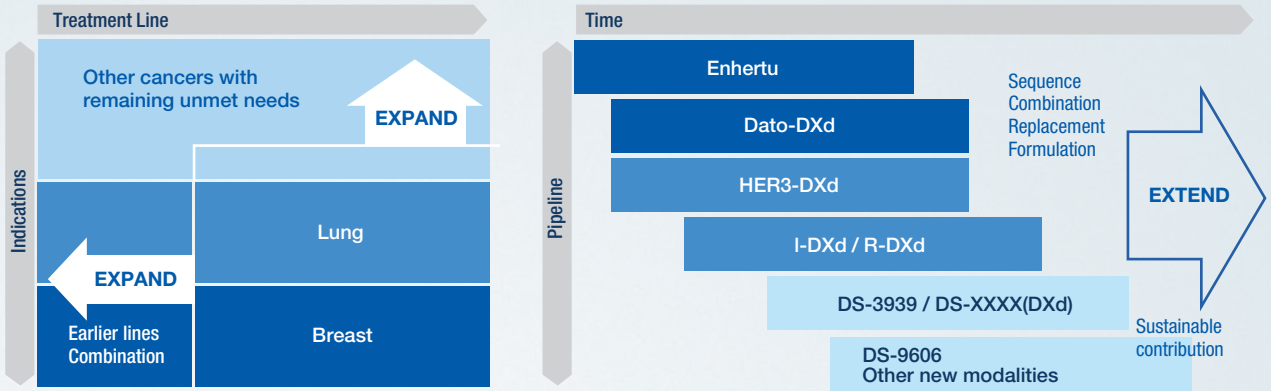
In clinical development, we are working to maximize the value of our pipeline through two strategic approaches: EXPAND, which aims to broaden indications and shift treatments to earlier lines of therapy; and EXTEND, which seeks to prolong treatment duration through sequencing and combination therapies. To sustain and further enhance our continuous creation of new drugs, we are committed to establishing highly innovative technology platforms and continuously generating multiple new products based on these platforms.

Achievements with DXd ADCs are driving the acceleration of research and development of technology platforms across multiple modalities. We have a robust foundation in multi-modality research, including small molecules and antibodies. Building on this, we are developing proprietary technologies across various modalities—spearheaded by next-generation ADC technologies that leverage novel payloads—and are working to create new treatment options. Through these efforts, we aim to achieve more stable and sustainable growth.

These initiatives are expanding not only in the oncology area but also in the specialty medicine area[*4]. Multiple candidates in both fields are expected to progress to the development stage, and they are anticipated to become key pillars supporting our medium- to long-term growth.

*4 Disease areas other than oncology

EXPAND & EXTEND to deliver our technology to more patients



- Establish and expand DXd ADC therapies in Breast and Lung cancers
- Go Earlier explore early lines of therapy/ stage of diseases; replace chemotherapy
- Go Wider: into new indications beyond currently focusing areas to serve more patient needs

- Address unmet needs after Enhertu treatment
- Seek effective treatment sequencing, novel combination, or formulation to enhance efficacy and improve treatment
- Grow early pipeline following 5DXd ADCs to contribute to more patients in the future

●Strengthening Research and Development Foundation for Achieving Continuous Creation of New Drugs

To realize continuous creation of new drugs, it is essential to further enhance our R&D capabilities. A key initiative in this effort is the strengthening of our human capital base. By increasing the number of R&D personnel through expanded hiring of both new graduates and mid-career professionals, we are actively welcoming talent from diverse global backgrounds. Through this, we aim to invigorate our organization and elevate our technological capabilities, while enabling the integration of external knowledge and expertise.

We are also making progress in establishing a global-scale open innovation ecosystem. In addition to leveraging our strong presence in Japan, where our research laboratories are located, we have set up bases in Boston (DS Research Institute Boston) and Munich (DS Research Institute Munich), two of the world's leading innovation hubs[*5]. Through collaborations such as with the Tissue & Cell Research Center Munich (TCRM), we are actively exploring promising drug discovery seeds and advancing cutting-edge research that leverages the unique strengths of each region.

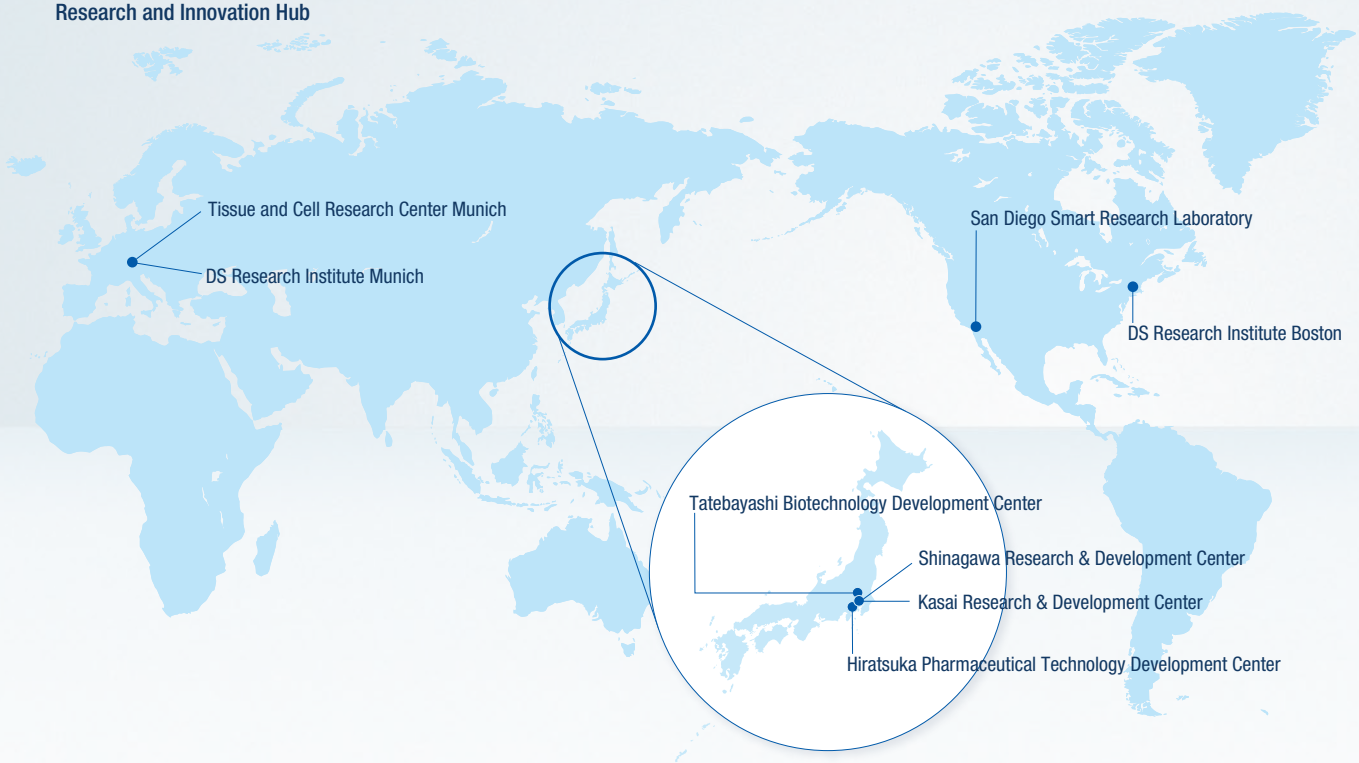
Also, we have newly established a Smart Research Laboratory in San Diego. By implementing an automated experimentation and data integration environment that utilizes robotics and our proprietary high-performance software, we have made 24/7/365 research possible, dramatically improving the reproducibility and productivity of drug discovery. Moreover, it represents an important step toward collecting the vast amount of data necessary for next-generation drug discovery processes such as AI-driven drug discovery. We are also working to create an environment where researchers can focus on intellectual and creative tasks. The results are

continuously shared with our research laboratories in Tokyo, helping to elevate the capabilities of our research infrastructure across the company.

Furthermore, these global sites play a key role not only in driving technological innovation but also in developing the next generation of leaders. Experienced researchers and management-level personnel from Japan have relocated to the research hubs in the US and Europe, where they gain hands-on experience that enhances both organizational capabilities, such as R&D execution, but also individual leadership skills, scientific assessment capabilities, and management acumen. By aligning organizational development with individual growth, we are strengthening our global framework to continuously generate innovation.

*5 Innovation Hub: Bases and mechanisms where key players in innovation, centered on companies possessing knowledge and technology across a wide range of fields gather

Research and Innovation Hub



MESSAGE

Bringing together the power of professionals — The forefront of drug discovery that Daiichi Sankyo's research and development tackles

Since joining the former Sankyo Co., Ltd., I have spent the past 28 years honing my skills both as a drug discovery researcher and in research management. Through numerous trials and errors in research, I have come to deeply appreciate the importance of teamwork above all else. During my journey, I have had the privilege of being involved in the exploratory research of Tarlige® and Enhertu. Researchers with diverse areas of expertise draw out each other's strengths and work together to create promising development candidates. These are then taken forward by clinical development teams, who provide strong leadership to drive clinical trials and ultimately bring new drugs to market. There is a profound sense of fulfillment in this entire process that words alone cannot fully express.

We are driven by a single-minded desire to deliver new treatment options to patients and healthcare providers. With this conviction, our research and development team takes on challenges with earnestness every day. I am proud to say that this unwavering commitment is one of Daiichi Sankyo's greatest strengths in drug discovery. The journey of developing new medicines involves repeatedly formulating hypotheses and testing them. Even when we face failures and setbacks, we stay focused on the needs of patients, deepen our understanding of diseases, turn the lessons learned through these challenges into shared organizational knowledge, and pass them on to the next generation.

New science is being born every day around the world. Remaining ever mindful of these developments, we make continuous efforts to gather information and collaborate—always with humility. It is our mission to conduct drug discovery activities that earn the trust of patients and to consistently deliver new innovations to the field of medicine. The true driving force behind Daiichi Sankyo's Science & Technology lies in nurturing dedicated drug discovery professionals. This unwavering strength will undoubtedly be passed on to the next generation.

Corporate Officer,
Head of RD division,
Head of Research
Yuki Abe