

# Science & Technology

## Superior Pharmaceutical Technologies for Creating Innovative Pharmaceuticals

### Daiichi Sankyo's Proprietary Antibody Drug Conjugate (ADC) Technologies

#### DS-8201 and following projects in ADC franchise

DS-8201 was created through Daiichi Sankyo's proprietary science and technology. The antibody portion of this drug was created by applying the antibody research and protein engineering capability of the former Sankyo, while the drug payload and linker were born out of the research capabilities of the former Daiichi Pharmaceutical. Research and development on ADC started in 2010, though it was met with considerable opposition internally because the preceding HER2-ADC already existed in another company at the time. Amid that context, researchers were selected for a cross-functional project team involved in technological development on ADC. In order to thoroughly examine the merits and issues regarding the preceding drug and to solve the issues regarding the preceding drug, the researchers in this team screened and optimized over several hundred combinations of antibodies, linkers, and payloads to ultimately produce the current DS-8201. They systematically researched and resolved all critical aspects necessary to create a truly best-in-class technology. Daiichi Sankyo's ADC technologies have substantial potential to contribute to the development of an ADC franchise, as it may be possible to attach the payload and linker to other antibodies.

### Diverse Modality Technologies

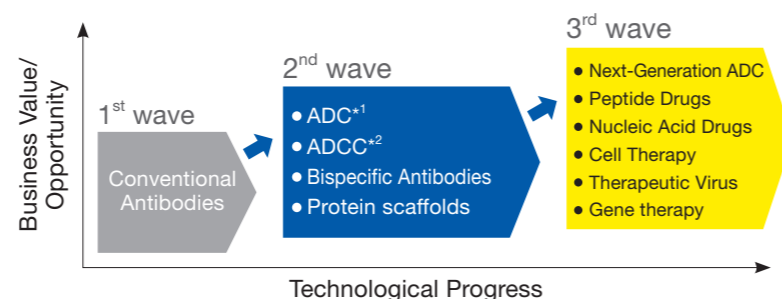
Daiichi Sankyo is working on the development of competitive drug discovery by developing innovative modality technologies for the creation of innovative pharmaceuticals. Diverse modality technologies, such as next-generation ADC, nucleic acid drugs, therapeutic viruses and cell therapy are utilized to broaden the possibilities for drug discovery.

### Powerful Research Engines

#### Research labs in Japan combining chemistry and biology expertise

Many Nobel laureates have come from Japan to date, and Japan has shown the world its high standard of research. At Daiichi Sankyo, we hire many talented researchers from the best universities in Japan every year from a wide range of fields, including synthetic chemistry, pharmacology, pharmacokinetics, toxicology and biologics. Additionally we strive to improve the scientific level of employees after joining the company, sending many of them to study at overseas universities and prestigious research institutions.

These researchers together with cross-functional project teams consist of development division, pharmaceutical technology division, marketing division and other divisions, conducting research every day in order to create new drugs.



\*1 Antibody Drug Conjugate  
 \*2 Antibody Dependent Cellular Cytotoxicity

Modality (Molecule Type)	Strategy
<b>Conventional antibodies</b>	Create foundations for quick launches of DS-8201 and other biologics and establish innovative and competitive modality technologies for drugs such as next-generation ADCs
<b>Antibody drug conjugates (ADCs)</b>	
<b>Bispecific antibodies</b>	Utilize Daiichi Sankyo's globally competitive, original T-cell-activated agonist antibody to cultivate important platforms for conducting drug discovery in the immuno-oncology field
<b>Protein scaffolds/peptide drugs</b>	Expand range of target molecules for drug discovery that possess high specificity and affinity Target development of platform for oral administration modalities for peptides
<b>Vaccine and adjuvants</b>	Pursue preventative medicine and treatment benefits through development of adjuvants that are administered together with vaccines to augment their effectiveness
<b>Nucleic acid drugs (ENA<sup>®</sup> oligonucleotides, etc.)</b>	Continue trend of DS-5141, which utilizes Daiichi Sankyo's proprietary ENA <sup>®</sup> oligonucleotide technology, to develop pipelines targeting rare diseases
<b>Cell therapy</b>	Provide innovative treatment methods for previously difficult to treat diseases, such as utilizing autologous and allogeneic cells to treat diseases, modifying viruses for therapeutic purposes, and administering normally functioning genes to support the functioning of abnormal genes
<b>Therapeutic viruses</b>	
<b>Gene therapy</b>	

## Strong Ties with Leading-Edge Academic Institutions (Open Innovation Activities)

At Daiichi Sankyo, we strive to conduct research and development on treatments that will change SOC, the universally applied best treatment practice in today's medical science. We are collaborating with various organizations, including in academia and companies, in order to further enhance our portfolio of competitive pipelines. In fiscal 2016, we started a lung cancer-related research alliance with

the Dana-Farber Cancer Institute. In fiscal 2017, we made a leukemia-related research and development alliance with The University of Texas MD Anderson Cancer Center, and we made efforts in alliances in the field of oncology to incorporate cutting-edge science, including the Memorial Sloan Kettering Cancer Center.

<p><b>Lung cancer-related research alliance</b></p> <p><b>Dana-Farber Cancer Institute</b></p> <ul style="list-style-type: none"> <li>Located in the state of Massachusetts in the U.S., this is one of the world-leading institutions in cancer research and treatment for adults and children</li> <li>Requested physician at this site to be the Principal Investigator for clinical trials of U3-1402 in lung cancer</li> </ul>	<p><b>Research and development alliance for AML treatments</b></p> <p><b>The University of Texas MD Anderson Cancer Center</b></p> <ul style="list-style-type: none"> <li>Located in the state of Texas in the U.S., this is one of the world's largest and most important academic research centers on leukemia</li> <li>An ideal partner for accelerating the development of new drugs for the treatment of acute myeloid leukemia (AML)</li> </ul>	<p><b>Research alliance for DS-8201</b></p> <p><b>Memorial Sloan Kettering Cancer Center</b></p> <ul style="list-style-type: none"> <li>Located in the state of New York in the U.S., this institution provides treatments and conducts research and education in the field of oncology at a global, cutting-edge level since its foundation in 1884</li> <li>Requested physician at this site to be the Principal Investigator for clinical trials of DS-8201 in breast cancer.</li> </ul>
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## Strong R&D DNA Cultivated Over Years of Operation as a Drug Discovery-Oriented Company

The roots of Daiichi Sankyo's R&D DNA can be traced back to the founding of the company. Our journey began with the extraction of *adrenaline*, the discovery of *orizanin* and the domestic production of *salvarsan*, and we have since developed numerous drugs that lead the drug discovery in Japan. We have also created and delivered innovative products that have had a global impact such as *pravastatin* and *levofloxacin* to people around the world.

*Edoxaban*, which is currently continuing to grow as one of our mainstay products, also leverages Daiichi Sankyo's inherent R&D DNA. Starting with research and development on the antiplasmin medicine *Ipsilon<sup>®</sup>*, we subsequently developed *tranexamic acid*, which is still used today as a hemostatic agent worldwide, and *ticlopidine*, which opened the doors for antiplatelet therapies. Anticoagulants became our next target. Although *warfarin* already existed at the time, it had various issues such as its varying efficacy

between individuals, and adverse interactions with other drugs and food. Many companies therefore were engaged in research and development for a new drug to solve these issues. It was amid these circumstances that Daiichi Sankyo succeeded for the first time in the world in synthesizing a compound with FXa inhibiting properties, which later gave rise to *edoxaban* with the improved absorption as an oral medicine.

*Olmesartan* was also created by Daiichi Sankyo, aiming for a superior profile among many other preceding drugs. DS-8201 was also similarly supported by ADC technologies, achieved by overcoming issues one by one in preceding drugs.

Utilizing this strong R&D DNA, honed and cultivated over years of operation, Daiichi Sankyo is committed to the development of innovative medicines that will change SOC.

Incorporated as drug discovery-oriented companies originating from Japan	Creation and cultivation of leading pharmaceuticals in Japan	Research capabilities for creating innovative pharmaceuticals globally	Development capabilities contributing to success in large-scale global clinical trials
<p><b>1902</b> Launched <i>adrenalin</i> (Product name: <i>Adrenalin</i>), the world's first adrenal cortex hormone agent to be extracted successfully</p>	<p><b>1965</b> Launched <i>tranexamic acid</i> (Product name: <i>Transamin</i>), an antiplasmin medicine</p>	<p><b>1989</b> Launched <i>pravastatin</i> (Product name: <i>Mevalotin</i>), a drug that was developed by applying biological fermentation technologies and revolutionized the world of medicine as an antihyperlipidemic agent</p>	<p><b>2002</b> Launched <i>olmesartan</i> (Product names: <i>Olmotec</i> and <i>Benicar</i>), an antihypertensive agent that became a blockbuster drug on the global market (Japanese launch took place in 2004)</p>
<p><b>1910</b> Made the world's first discovery of vitamin B1 (<i>orizanin</i>) in rice bran and established a foundation for the theory of vitamins</p>	<p><b>1981</b> Launched <i>ticlopidine</i> (Product name: <i>Panaldine</i>), which opened the doors for antiplatelet therapies</p>	<p><b>1993</b> Launched <i>levofloxacin</i> (Product name: <i>Cravit</i>), a broad-spectrum oral antibacterial agent that left a mark on the history of not only Japan but also the entire world with its broad spectrum of antibacterial activity</p>	<p><b>2009</b> Launched <i>prasugrel</i> (Product name: <i>Eliant</i>), an antiplatelet agent developed for the global market</p>
<p><b>1915</b> Realized domestic production of <i>salvarsan</i>, a treatment for syphilis, which was a common disease in Japan</p>	<p><b>1986</b> Launched <i>loxoprofen</i> (Product name: <i>Loxonin</i>), an anti-inflammatory analgesic which has now come to be sold as an OTC</p>		<p><b>2011</b> Launched <i>edoxaban</i> (Product names: <i>LIXIANA</i>, <i>SAVAYSA</i>), an anticoagulant developed for the global market</p>

# Global Organization & Talent

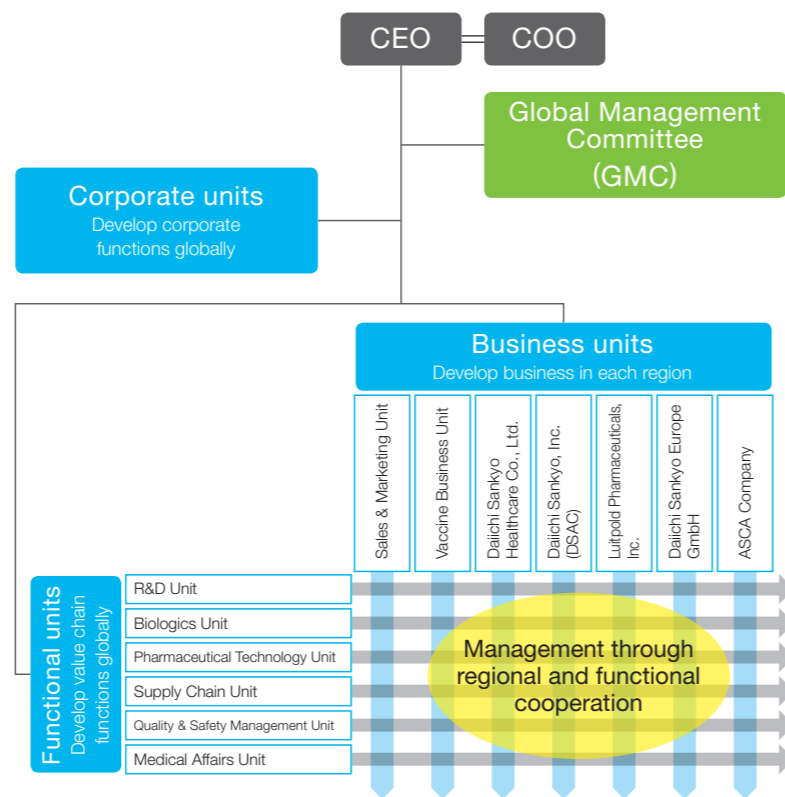
## Global Management System Uniting Intellects from Around the World

### Global Management Committee Facilitating Swift and Accurate Decision-Making

In order to conduct management and decision-making from a global perspective, we established the Global Management Committee (GMC), joined by the head of each unit. In the GMC, the CEO speedily and accurately grasps trends in the market and environment through discussions with people responsible for major regions and functions, and engages in strategic decision from a global perspective.

### Execution of Global Matrix Management Comprised of Regional Business Units and Functional Units

Each global entity organically, working to maximize value at a group level from a functional perspective, including research and development, pharmaceutical technology and production. These global entities also work to maximize regional value, operating in alignment with unmet needs and regulations in each country.



### Global R&D Structure Enabling Swift Decision-Making

GEMRAD\*, the top decision-making body in R&D, is composed of members representing various domestic and overseas divisions, including those responsible for R&D, pharmaceutical technology, biologics, marketing, business development and finance. The multi-functional memberships enable GEMRAD to make appropriate decisions based on active discussions with a global perspective and comprehensive assessments covering everything from science to business starting at the research and development stage.

Moreover, establishing R&D project teams under GEMRAD and granting each team considerable authority enables the acceleration and improvement in efficiency in research and development.

\* Global Executive Meeting for Research And Development

### Dynamic Global Organization for Responding Promptly to Operating Environment Changes

In recent years, there has been a strong cry for speed in global research and development in the oncology area. Daiichi Sankyo integrated its oncology R&D organizations and introduced the Cancer Enterprise, a unique concept originated in Daiichi Sankyo. The Cancer Enterprise works in cancer drug developments as well as marketing toward product launches, with functions going beyond research and development such as with pharmaceutical technology, Global Oncology Marketing, Global Medical Affairs and supply chain. Related functions work together to obtain information on market needs and for differentiating from competitor products, as well as in responding promptly to environmental changes.



## Robust, Global Pool of Talent

### Proactive Employment of Global Talents from Around the World

We employ many talented individuals with diverse backgrounds from across the globe and we enhance our global organization and talent while working to achieve synergy by having such talent from around the world work together with our highly capable talents in Japan.

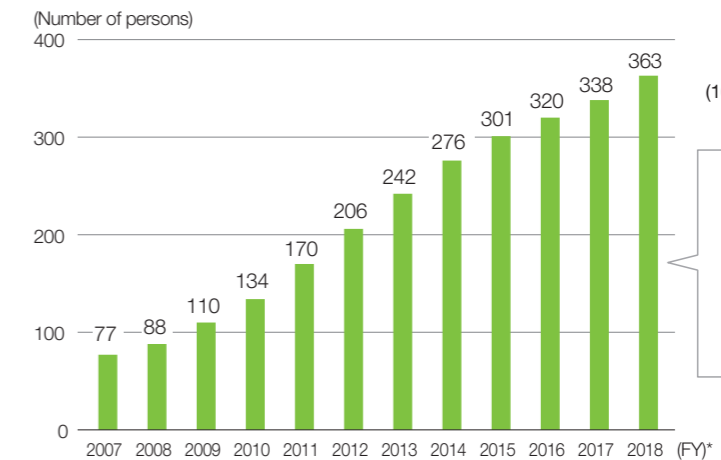
As one example of this, we have hired excellent global talent leaders in research and development, marketing, and other functions in the oncology area, accelerating research and development and conducting preparation for launches, in order to become a "Global Pharma Innovator with competitive advantage in oncology."

<b>Oncology R&amp;D</b> Antoine Yver Global Head Tom Held ADC Franchise Leader Arnaud Lesegretain AML Franchise Leader Eric Richards Oncology Regulatory Leader Gilles Gallant Global Team Leader DS-8201 Masato Murakami Biomarker Leader	<b>Global Oncology Marketing</b> Thierry Gruson Global Oncology Marketing Head	<b>Global Market Access &amp; Pricing</b> Juan-Carlos Jaramillo Market Access & Pricing Global Head
<b>Global Oncology Medical Affairs</b> Dalila Oulid-Aissa Global Oncology Medical Affairs Head	<b>Quality &amp; Safety Management</b> Vikram Dev Global Medical Safety Lead	

### Human Resources Development Programs Taking Advantage of Global Experience

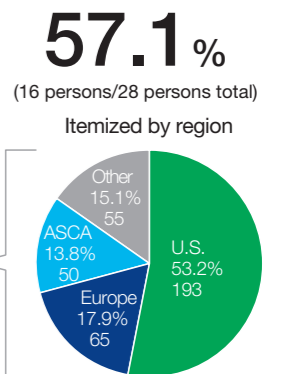
Daiichi Sankyo considers its people to be its most important asset. In human resources development programs taking advantage of global experience, Daiichi Sankyo identifies positions that are key to the accomplishment of its management vision and the goals of its mid-term business plan on a global basis, and develop people through duties with challenging goals and high difficulty or through relocations overseas. As such, we proactively promote global talent management that offers opportunities for further contributions.

Number of Persons Newly Relocated from Japan to Overseas Group Companies (Cumulative)



\* Cumulative number as of April 1 of each year

Percentage of corporate officers with experience being assigned overseas



# Presence in Japan

## No. 1 in Terms of Pharmaceutical Revenue in Japan for 2 Consecutive Years

**Extensive product lineup**

- Selling products with a wide range of areas of disease, including the cardiovascular, endocrine system, central nervous system, infectious diseases and anti-inflammation.

**Acquire valuable new products**

- Continually acquiring valuable new products including *denosumab*, *NEXIUM*, *TENELIA* and *VIMPAT*.

**Strong cooperative relationship with wholesalers**

- Strengthening cooperative relationships through close coordination with MS\* who are highly trusted by healthcare professionals.
- \* Marketing specialists at wholesalers

**Rated No. 1 in terms of inquiry response**

- Ranked No. 1 in inquiry responses to pharmacists working in pharmacies
- Introduced artificial intelligence (AI) technologies to reinforce inquiry response functions

As a drug discovery-oriented company originating from Japan, Daiichi Sankyo established a firm position in Japan, and has developed *Mevalotin*, *Cravit* and others to become leading products in Japan.

As in other developed countries, it is common for first-in-class drugs to become market leaders in the Japanese market, and shares grow by order of launch in many segments.

*Olmetec* was the fifth ARB\*1 to enter such a market environment, though with Daiichi Sankyo's collective strength in medical affairs and post-marketing studies in addition to sales capabilities, *Olmetec* grew to ultimately gain the No.1 share. Similarly, *NEXIUM* was the fourth PPI\*2 to enter the market, though *NEXIUM* grew to gain the No. 1 share in three years. The currently growing *LIXIANA* was also fourth to enter the market with additional indication, though it is running at a close second in market share. In light of these accomplishments, we think that Daiichi Sankyo has a competitive advantage in the Japanese market, which resulted in us being No. 1 in terms of pharmaceutical revenue for two consecutive years.

By continually launching and expanding sales of our proprietary products, we will grow an innovative pharmaceuticals business through a robust product lineup. At the same time, we will utilize the Company's superb sales capabilities to acquire licenses for promising products in order to sustain a virtuous cycle driving further growth.

\*1 Angiotensin II Receptor Blocker  
\*2 Proton Pump Inhibitor

- ▶ ***Olmetec***: Fifth to enter the market, went to No. 1 share
- ▶ ***NEXIUM***: Fourth to enter the market, currently No. 1 share
- ▶ ***LIXIANA***: Fourth to enter the market, currently No. 2 share

In order to complement this virtuous cycle, we have strengthened our cooperative relationship with wholesalers, and have closely cooperated among all internally related departments in earnestly and appropriately responding to inquiries from healthcare professionals and to medical affairs functions. As a result, we have achieved No. 1 in terms of revenue.

**Continuous launch & sales growth of own products**

- Launching and achieving sales growth in our proprietary products *Efient* and *LIXIANA*
- Currently applying for approval for our proprietary products *mirogabalin* and *esaxerenone*



## No.1 MR Evaluation

### MRs Ranked No. 1 by Physicians for 6 Consecutive Years

With changes in the environment such as integrated community medical systems in Japan, the needs of healthcare professionals change and diversify all the time. In this context, based on the thoughts of each healthcare professional, we have contributed to medicine by faithfully developing activities according to customer functions and needs by mainly MRs in multichannel approach\*1. We believe that these activities have been highly appreciated.

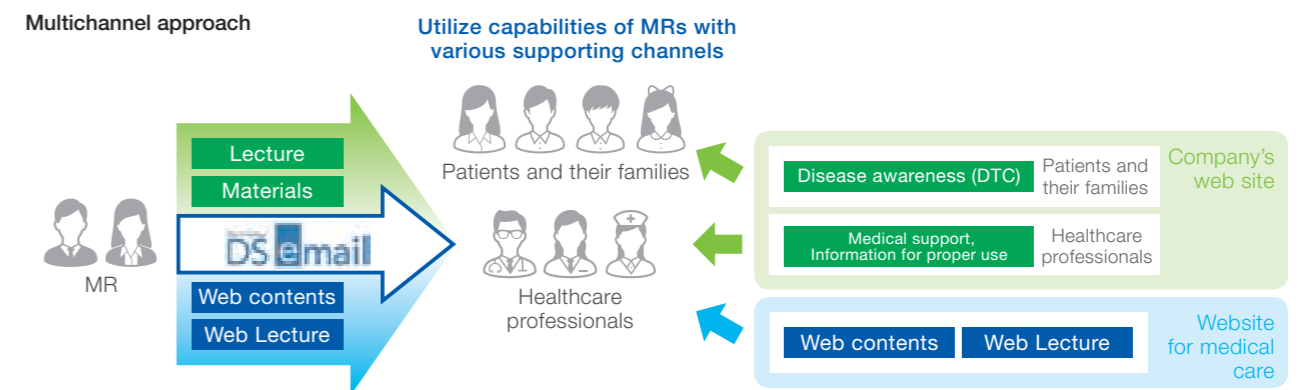
With regard to MR evaluation as well, we have been ranked highly not just for items such as knowledge and information, but also in items including human nature and responsiveness. As a result, we are comprehensively ranked No. 1.\*2

\*1 Mainly MRs utilizing lecture, web lecture and internet etc.  
\*2 Conducted by ANTERIO Inc.

### Comprehensive Training Programs

- All MRs have passed the certificate test held in December for the eighth consecutive year since fiscal 2010.
- We are strengthening training programs for MRs with a view toward the launch of specialty products centered on the oncology business. By establishing an internal oncology certification program, we are planning to raise the level of expert knowledge, and increasing and strengthening future MRs that can manage oncology.

### Multichannel approach

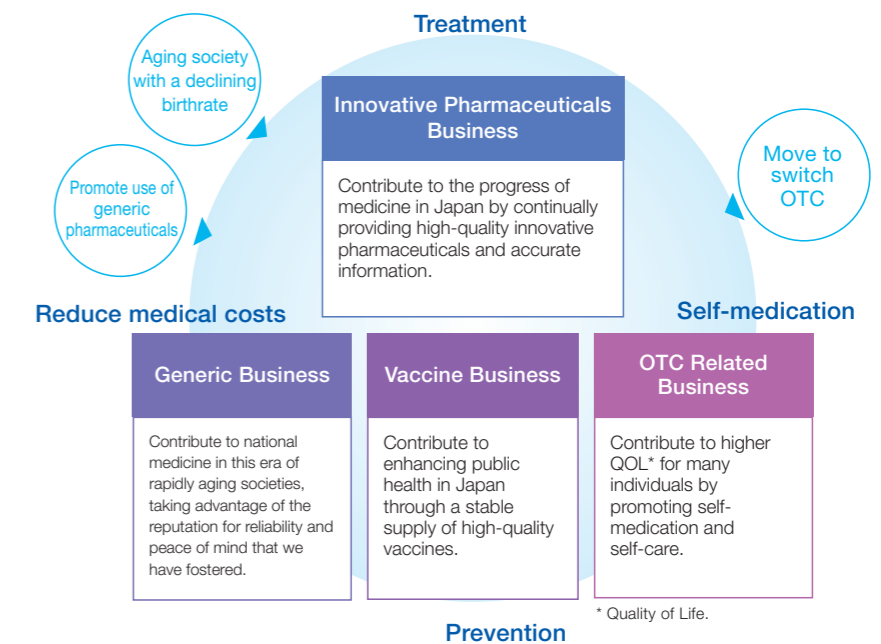


## Four Businesses Responding to Diverse Medical Needs

By leveraging the strength of its innovative pharmaceuticals\* business, Daiichi Sankyo engages in its generic business, vaccine business, and OTC related business in Japan.

As the No. 1 company in Japan in both name and substance, Daiichi Sankyo addresses a wide range of medical needs related to areas such as treatment, reducing medical costs, prevention, self-medication with these four businesses making comprehensive contributions to medicine in Japan.

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



\* Quality of Life.