5-Year Business Plan Overview and Progress

The 5-year business plan covers the period from fiscal 2016 to fiscal 2020, which has been positioned as a period for transformation leading up to the 2025 Vision. However, we made revisions to some targets in October 2018, owing to a wide range of environmental changes. Currently, we are studying new targets in light of our strategic alliance with AstraZeneca.

Fiscal 2022 Target

- Revenue: ¥1,100.0 billion
- Operating Profit: ¥165.0 billion
- ROE: 8.0% or more
- Increase value of late-stage pipelines
  Expected total revenue at peak: ¥500.0 billion or more

Six Strategic Targets for Accomplishing Our Performance Targets

**Grow Edoxaban**

- Expanded global revenue (fiscal 2018 revenue: ¥117.7 billion)
- Ranked No.1 in market share within Japan (as of 4th quarter, fiscal 2018)
- Significantly expanded the market share in many countries within Europe and Asia

**Grow as the No. 1 Company in Japan**

- Ranked No.1 in market share of domestic ethical drugs for three consecutive years
- Ranked No.1 in MR evaluation for seven consecutive years
- Continually launching new products (Tarlige and MINNEBRO)

**Establish Oncology Business**

- Accumulated promising clinical data on DS-8201 and working ahead of schedule for the target date to submit an application for approval
- Present positive clinical data on U3-1402 and DS-1062
- Submitted an NDA for Quizartinib and Pexidartinib

**Continuously Generate Innovative New Medicine changing Standard of Care (SOC)**

- Ventured into many different modalities
- DS-1647 (oncolytic virus) NDA submitting planned
- Progressed on open innovation

**Expand U.S. Businesses**

- Expanded American Regent business (fiscal 2018 revenue: ¥117.8 billion)
- Expanded Injectafer revenue (fiscal 2018 revenue: ¥44.2 billion)
- Re-examined strategy for the pain franchise of Daiichi Sankyo, Inc.

**Enhance Profit Generation Capabilities**

- Optimized Sales & Marketing structure in the U.S. and EU (total 550 position cuts in fiscal 2016 and 2017)
- Optimized global R&D structure (four locations closed)
- Optimized global manufacturing structure (two locations closed and decided to sell one location)

**Growth Investments and Shareholder Returns**

- Reduced cross-shareholding shares (33 different stocks for a total amount of ¥6.0 billion over three-year period)
- Sold properties (¥25.0 billion over three-year period)
- Gain on sales of business transfers (¥6.3 billion)
- Issued super-long-term unsecured corporate bonds (¥100.0 billion)
- Acquired own shares (¥100.0 billion over three-year period)
- Maintained a total return ratio of 100% or more (114.8% over three-year period)
I would like to begin by thanking all of our stakeholders for the ongoing support to Daiichi Sankyo. Along with the explanation of our 5-year business plan, reasons for its revision, and its current state, I would like to introduce examples of specific initiatives I am working on to improve the corporate value as CFO.

5-Year Business Plan, Reasons for Its Revision, and Its Current State

1. 5-Year Business Plan (Presented in March 2016)
Since the development of 5-year business plan (fiscal 2016 to 2020) in March 2016, we are committed to establish a foundation for sustainable growth mainly consisting of the achievement of six strategic targets to transform ourselves along our 2025 Vision of becoming a “Global Pharma Innovator with competitive advantage in oncology.” Daiichi Sankyo has set revenue of ¥1,100.0 billion, operating profit of ¥165.0 billion, and return on equity (ROE) of more than 8% for fiscal 2020 as key numerical targets. In addition, for fiscal 2020, we aim to have three to five late-stage pipeline products that can be launched within the next five years with the potential to generate annual revenue exceeding ¥100.0 billion each at peak.

2. Revision of Targets (Presented in October 2018)
In October 2018, we revised the 5-year business plan. Although edoxaban, an oral anticoagulant that is one of our global mainstay products, strongly increased its market share in Japan and Europe, achievement of the targets initially set for fiscal 2020 has become challenging. This is due to the sense of uncertainty over future growth of Japan business as result of a radical reform of the NHI drug price system in the country, the unsuccessful development of new drugs in the U.S. pain business, and so on.
On the other hand, we decided to expand our investments to maximize the potential for our ADC franchise with DS-8201 listed first, and based on several strong data for the ADC franchise. Accordingly, we decided to delay our initial fiscal 2020 target (revenue of ¥1,100.0 billion, operating profit of ¥165.0 billion, and return on equity (ROE) of more than 8%) for two years to fiscal 2022. Meanwhile, as for returns to shareholders, we have decided to maintain the initial commitment calling for a total return ratio of 100% or more until 2022.
As for our oncology business, we decided to set a revenue target of ¥500 billion in fiscal 2025, exceeding the initial target of ¥300 billion by increasing and focusing our investment in the oncology business.

3. Revision Based on Impact of Strategic Alliance with AstraZeneca
After the revision of numerical targets for the current 5-year business plan in October 2018, Daiichi Sankyo decided to form strategic alliance with AstraZeneca for DS-8201 in March 2019. Currently, we are having discussions with AstraZeneca on the details of the development and commercialization plan. Once we reach agreement, we will present Daiichi Sankyo’s updated numerical targets including revised resource allocation for the other development projects such as U3-1402.

Examples of Initiatives for Improving Corporate Value
Here, I will explain our specific ROE improvement and capital cost reduction initiatives as part of our initiatives for improving corporate value, following (1) to (6) in the figure below.
Message from the CFO

(1) Realize Process Excellence

In order to improve the profit ratio as well as expand sales, we have taken steps to achieve further cost reductions and to streamline Daiichi Sankyo Group through activities called “Realize Process Excellence.” Major initiatives include enhancement of the procurement function and optimization of operating structures for manufacturing, marketing & sales, and R&D. Concerning the optimization of operating structures, in the past three years to fiscal 2018 since the start of the current 5-year business plan, we have sold, closed, or transferred three sites within our supply chain organization, and closed four sites within our R&D organization. We have also implemented optimization within our marketing & sales organization in Europe and the United States. We will further accelerate initiatives to enhance profit generation capabilities in the future.

We assumed our cost of shareholders’ equity to be approximately 6% and set forth the goal of more than 8% ROE, which is approximately 2% above the cost. Although we anticipate the WACC, the weighted average of our cost of shareholders’ equity and cost of debt, to be 5 to 6%, we use an 8% hurdle rate for investment decisions, by adding 2 to 3% to the WACC. In addition, we make investment decisions based on discount rate for each region that takes into account the characteristics of each market.

(2) Optimize Business Portfolio

In terms of investment, our focus is to optimize business portfolio by reinforcing financial investment decisions with capital cost in mind and taking synergies into consideration.

When making investment decisions for the business or capital expenditure, which has significant impact on future profit, we will support such decision through reading the future business environment, vision, and strategy, and by setting the hurdle rate, discount rate and other factors in response to market and business risks.

(3) Streamline Non-core Assets

We streamline non-core assets through pursuing optimization in assets and enhancing our total asset turnover ratio, while working to create free cash that will lead to improvement of corporate value. With regard to assets including real estate, we implement liquidation of non-core assets at the appropriate timing while considering not only the necessity of the assets for business activities and the ability to be replaced, but also life-cycle costs (maintenance costs needed to maintain functions subject to deterioration and renovation costs required to improve performance) and business continuity plans (BCPs). We sold real estate worth ¥11.0 billion in fiscal 2018 and ¥25.0 billion in total so far. In fiscal 2019, we also sold our Nihonbashi Building. As a rule, we are aggressively streamlining cross-shareholdings in accordance with Daiichi Sankyo’s policy of not holding listed stocks, except in cases where holding such stocks will maintain or strengthen long-term business relationship and contribute to improving our corporate value. We sold 10 stock brands for a total amount of ¥14.3 billion in fiscal 2018, and an aggregated total of 33 stock brands for a total of ¥146.0 billion so far. We will pursue further cost reductions in the future to achieve an appropriate level of capital efficiency.

In order to make prioritized investment of resources in the field of oncology, we decided to set some of the long-listed products in Japan and recorded ¥6.3 billion in fiscal 2018. Going forward, we will continue to review our business portfolio to streamline our assets.

(4) Realize Optimal Ratio of Capital to Liability, Enhance Shareholder Returns

In order to support sufficient investment to develop oncology projects including DS-8201, we will work to streamline our assets as well as to maintain our strong financial base. With the current equity ratio of around 60% as a guide, Daiichi Sankyo will continue to pay stable dividends and flexibly implement share buy-back.

(5) Extensive Risk Management, Initiatives for Sustainability

Extensive risk management and initiatives for ESG are crucial in order to eliminate the risk of declining corporate value.

As for extensive risk management, I oversee group-wide risk management as the CFO and risk management officer. I operate the risk management system in conjunction with an annual cycle for formulating and implementing business plans. Based on assessment of impact and the likelihood of occurrence, risks with the potential to significantly impact the management of the Company are identified through the Global Management Committee Meeting and the Board Meeting. Risk response measures are enacted as well as corrected and revised as necessary.

In Closing

Daiichi Sankyo Group aims to realize its 2025 Vision of striving to become a “Global Pharma Innovator with competitive advantage in oncology.” In light of the strong progress in oncology development with focus on ADC, we formed a strategic alliance with AstraZeneca for DS-8201, which is our first ADC project. In March 2019 and have been making steady progress in development.

From a mid-term perspective, prior investment in preparation for the launch of oncology products is anticipated in each region. With respect to business development, demand for funds is expected to increase further to obtain pipelines, products, and businesses that meet the strategy. In addition, strategic investment from a long-term perspective is also essential. As such, I understand the role of CFO is extremely significant.

Going forward, I will continue to improve corporate value by enhancing shareholder returns while paying attention to the balance between investment and profitability.
5-Year Business Plan Overview and Progress: Grow Edoxaban

Strategic Target

Grow Edoxaban

Brand name: LIXIANA (Japan, Europe, Asia), SAVAYSA (U.S.)

Edoxaban, direct oral anticoagulant (DOAC) is a mainstay product in place of olmesartan, a treatment for hypertension that has expired exclusivity. Since it’s marketed, the Company has steadily expanded its market share, particularly in Japan, Europe, and Asia. Going forward, we will strengthen our initiatives for life-cycle management and further raise awareness of product information. We also aim to maximize product value by successfully marketing this product in China.

Edoxaban’s “Edo” means that this product was born from a research institute in Tokyo. As the only made-in-Japan product in this area, we are reminded of the desire to save patients not only in Japan but also around the world.

1 5-Year business plan

The annual global revenue of edoxaban has steadily increased from ¥37.3 billion in fiscal 2016 to ¥77.1 billion in fiscal 2017 and ¥117.7 billion in fiscal 2018. We forecast ¥149 billion in revenue in fiscal 2019 that will be more than the initial target for fiscal 2020, ¥120 billion ahead of schedule. Edoxaban is growing at a much faster pace than the initial expectation.

2 Progress to date

(1) Growth in Japan

Since the third quarter of fiscal 2018, we have become the No. 1 share in Japan by leveraging our product characteristics of once-daily administration and high levels of safety, as well as our high-quality marketing capabilities, which have been highly evaluated by external organizations.

Going forward, we will promote OD tablet (orally disintegrating tablet) by leveraging its strength, which is highly appreciated by doctors, saying that it is especially easy for elderly patients to take. Penetrating new evidence obtained from life-cycle management, we will try to make sure that doctors and patients will feel more reassured by anticoagulant therapy with edoxaban.

(2) Growth in each country

Since it’s marketed, steadily increasing the number of countries in which edoxaban has been marketed, it has been on the market in more than 30 countries and regions globally. In addition to steady growth in Asian region like South Korea and Taiwan, as well as in European region like Belgium and Germany, it was marketed in Brazil in August 2018 and was approved in China in December 2018. Going forward, we aim to achieve further growth by successfully marketing it in China.

(3) Life-cycle management initiatives

Currently, we are engaged in many clinical studies and lifecycle management activities, collectively referred to as EDOSURE™ that create data on how edoxaban is used in clinical settings.

The efficacy and safety data for patients undergoing catheter ablation*1 was presented in a Late Breaking Session of the European Heart Rhythm Association (EHRA) in March 2019.

*1 Derived from two words, edoxaban and Assurance. It signifies our hope that doctors and patients will feel more reassured by anticoagulant therapy with edoxaban.

*2 A procedure used to ablate abnormal electrical pathways in the heart tissue by inserting a thin tube (catheter) through the blood vessels to the heart in order to restore normal rhythm of the heart of patients with AF.

What are direct oral anticoagulants?

A blood clot usually forms to stop bleeding and will eventually dissolve and shrink. However, should a blood clot grow larger rather than dissolving, and consequently come to block a blood vessel, it could result in a lack of blood flow to areas of the body beyond the clot, potentially even leading to the death of the tissue therein. This condition is known as thrombosis.

Warfarin has long been the standard treatment to prevent blood clots. However, there are many restrictions to which attention needs to be paid when using warfarin such as periodic monitoring with blood tests, a variety of drug interactions, and dietary restrictions. Direct oral anticoagulants including edoxaban have been developed to significantly improve the inconvenience of warfarin as mentioned above.

Value Report 2019 Daiichi Sankyo Group Value Report 2019

---

**Table: Trends in sales share of DOACs in Japan**

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Fiscal 2014</th>
<th>Fiscal 2015</th>
<th>Fiscal 2016</th>
<th>Fiscal 2017</th>
<th>Fiscal 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>25%</td>
<td>20%</td>
<td>15%</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>Lixian</td>
<td>1%</td>
<td>2%</td>
<td>3%</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>75%</td>
<td>78%</td>
<td>85%</td>
<td>90%</td>
<td>95%</td>
</tr>
</tbody>
</table>

Copyright © Created based on 2019 IQVIA, MIDAS Sales Data Reprinted with permission

**Graph: Global Revenues of Edoxaban (Billions of yen)**

- FY2015: ¥37.3 billion
- FY2016: ¥77.1 billion
- FY2017: ¥117.7 billion
- FY2018: ¥149 billion

Copyright © Created based on 2019 IQVIA, MIDAS Sales Data Reprinted with permission

---

**What is a blood clot?**

A blood clot usually forms to stop bleeding and will eventually dissolve and shrink. However, should a blood clot grow larger rather than dissolving, and consequently come to block a blood vessel, it could result in a lack of blood flow to areas of the body beyond the clot, potentially even leading to the death of the tissue therein. This condition is known as thrombosis.

---

**What are direct oral anticoagulants?**

A blood clot usually forms to stop bleeding and will eventually dissolve and shrink. However, should a blood clot grow larger rather than dissolving, and consequently come to block a blood vessel, it could result in a lack of blood flow to areas of the body beyond the clot, potentially even leading to the death of the tissue therein. This condition is known as thrombosis.

Warfarin has long been the standard treatment to prevent blood clots. However, there are many restrictions to which attention needs to be paid when using warfarin such as periodic monitoring with blood tests, a variety of drug interactions, and dietary restrictions. Direct oral anticoagulants including edoxaban have been developed to significantly improve the inconvenience of warfarin as mentioned above.
By continually launching and expanding sales of proprietary developed products, we grew the innovative pharmaceuticals business. At the same time, we utilize the Company’s superior sales capabilities to acquire licenses for promising products in order to sustain a virtuous cycle driving further growth. Through these efforts, we are working to strengthen Daiichi Sankyo’s presence in Japan. During the 5-year business plan, we have successfully achieved many feats seen below, including Vimpat, an epileptic agent, and CANALIA combination tablet, a treatment for type 2 diabetes mellitus, growing with a sales revenue target of ¥10 billion or more for fiscal 2019. Furthermore, Daiichi Sankyo has ranked No.1 both in MR evaluation*, which is an important foundation for sustainable growth, for seven consecutive years, and in revenue from pharmaceutical products in Japan for three consecutive years.

* Based on survey conducted by ANTERIO Inc.

In fiscal 2019, we will add to our product portfolio our in-house developed drugs, Tarigel for pain treatment and Minnebro for hypertension, and Vanéria, a promising new cancer treatment. We will aim to quickly nurture these new products.

Through aggressive in-licensing activities, we will win promising in-licensing products to overcome the challenging market environment.

Pharmaceutical Market in Japan

The pharmaceutical market in Japan is worth approximately ¥10 trillion, of which approximately 90% is comprised of prescription pharmaceuticals that require prescriptions from physicians with the remainder of the market being accounted for by general pharmaceuticals and over-the-counter (OTC) drugs that can be freely purchased in pharmacies and drug stores. Moreover, the use of generic drugs has been increasing in the prescription pharmaceutical market, and these drugs have recently come to represent about 73% of the market on a sales-volume basis* in September 2018.

* Generic drugs = (original drugs for which generic drugs have been released + generic drugs)

Growth of Japan Business

- Domestic pharmaceutical revenue No.1 for three consecutive years
- Top class brand capabilities in quality and safety
- MR evaluation from healthcare professionals: No.1 for seven consecutive years
- Survey conducted by ANTERIO Inc.

Fine-tuned sales capabilities

- Acquire valuable new products
- Antiepileptic agent, Vimpat (UCB Japan)
- Biosimilars [Amgen]
- CANALIA combination tablet (Type 2 diabetes mellitus treatment) [Mitsubishi Tanabe Pharma Corporation]
- Minnebro for hypertension, Launched in May 2019
- Tarigel for pain treatment, Launched in April 2019
- Verlipat for the treatment of resistant refractory FLT3-ITD AML, Approved in Jul. 2019

COLUMN

Pharmaceutical Market in Japan

- (Total of the 6 products above, including the impact of IV drug price revisions.)
- Requires prescriptions from physicians
- Has official set prices (NHI drug prices)
- Includes all original drugs
- Includes generic drugs
- Includes combination tablets
- Purchasing pharmacies and drug stores
- Can be advertised as individual brands
- Share of market based on monetary value

2 Progress to date

In addition to LÖKANA, an anticoagulant developed for the global market, the innovative pharmaceuticals business is developing its operations centered around six major products: NEXIUM, an ulcer treatment; Memary, an Alzheimer’s disease treatment; PRALIA, a treatment for osteoporosis that prevents the progression of bone erosion associated with rheumatoid arthritis; RANMARK, a treatment for bone complications caused by bone metastasis from tumors; Efient, an antiplatelet agent; and TENELIA, a type 2 diabetes mellitus treatment.

Of these, NEXIUM, Memary, PRALIA* and RANMARK have achieved the No.1 shares in their respective markets.

* No.1 in the bone resorption inhibitor market

Total revenue from the six major products has steadily expanded, from ¥197.3 billion in fiscal 2016 to ¥212.8 billion in fiscal 2017. However, in fiscal 2018, revenue remained almost unchanged at ¥211.5 billion, due to factors such as significant reduction in the drug price of NEXIUM, which are more severe than expected at the time of the 4th mid-term business plan announcement. In fiscal 2019, revenue are expected to increase ¥y-y to ¥217.0 billion, despite the impact of the drug price revision. Although the market environment is becoming increasingly challenging, we will leverage our extensive product portfolio and excellent sales capabilities to achieve our fiscal 2020 target of ¥243 billion in revenue.

1 5-Year business plan

In addition to LÖKANA, an anticoagulant developed for the global market, the innovative pharmaceuticals business is developing its operations centered around six major products: NEXIUM, an ulcer treatment; Memary, an Alzheimer’s disease treatment; PRALIA, a treatment for osteoporosis that prevents the progression of bone erosion associated with rheumatoid arthritis; RANMARK, a treatment for bone complications caused by bone metastasis from tumors; Efient, an antiplatelet agent; and TENELIA, a type 2 diabetes mellitus treatment.

Of these, NEXIUM, Memary, PRALIA* and RANMARK have achieved the No.1 shares in their respective markets.

* No.1 in the bone resorption inhibitor market

Total revenue from the six major products has steadily expanded, from ¥197.3 billion in fiscal 2016 to ¥212.8 billion in fiscal 2017. However, in fiscal 2018, revenue remained almost unchanged at ¥211.5 billion, due to factors such as significant reduction in the drug price of NEXIUM, which are more severe than expected at the time of the 4th mid-term business plan announcement. In fiscal 2019, revenue are expected to increase ¥y-y to ¥217.0 billion, despite the impact of the drug price revision. Although the market environment is becoming increasingly challenging, we will leverage our extensive product portfolio and excellent sales capabilities to achieve our fiscal 2020 target of ¥243 billion in revenue.
In our 5-year business plan, we set up the target of growing oncology business revenue to ¥300.0 billion in fiscal 2025. Last year, we raised it to over 500 billion yen. The development of the ADC franchise centered on DS-8201 and AML franchise have been steadily accelerating. In fiscal 2019, we obtained approval of quizartinib and pexidartinib, and plan to submit DS-8201 for approval.

1 5-Year Business Plan

We will establish an oncology business by launching several drugs currently in late-stage development. Concurrently, we will accelerate early-stage pipeline development and evaluate the further enrichment of our oncology pipeline through the acquisition of external assets. Through the acceleration of oncology research and development, we aim to grow oncology business revenue to more than ¥40.0 billion in fiscal 2020, ¥150.0 billion in fiscal 2022 and ¥500.0 billion in fiscal 2025, when this business will function as a core business.

2 Progress to Date and Future Initiatives

Daiichi Sankyo has been promoting organizational changes and strengthening human resources in order to accelerate development in the oncology area. We have completed organizational changes and have completed recruiting excellent global leaders with long years of experience in the oncology area.

Our organizations such as research and development, pharmaceutical technology, supply chain, global marketing, and global medical affairs cooperate organically under these leaders, and all employees are working together to promote a transformation to become a “Global Pharma Innovator with competitive advantage in oncology.”

The Oncology R&D sub unit has established three pillars, antibody drug conjugate (ADC) franchise, acute myeloid leukemia (AML) franchise, and breakthrough science that we will focus on.

We are aiming to become a world-leading science organization built on these three pillars and to deliver seven valuable new molecular entities (NMEs) over eight years by 2025.

* New treatment that changes cancer treatment by applying innovative science and technology

3 About Cancer

Cancer is one of the diseases with high prevalence and mortality both in Japan and worldwide. Every year, approximately 14 million people are newly diagnosed with cancer across the world. In Japan, cancer has been the leading cause of death since 1981, while in 2018, annual cancer deaths reached approximately 410,000 people. Given these statistics, cancer has a devastating impact on human life and health.

Cancer death (all types of cancer) 2018 (Thousands/year)

<table>
<thead>
<tr>
<th>Country/Region</th>
<th>Japan</th>
<th>U.S.</th>
<th>Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newly diagnosed cancer (n)</td>
<td>9,555</td>
<td>409</td>
<td>617</td>
</tr>
<tr>
<td>5-year survival (%)</td>
<td>94.9</td>
<td>90.7</td>
<td>87.1</td>
</tr>
</tbody>
</table>

Source: GLOBCAN 2018, FACT SHEET

4 Cancer Treatment

(1) Cancer treatment

Cancer treatments are divided into two categories: systemic therapy and local therapy. Local therapy consists of surgery and radiotherapy.

Systemic Therapy

- Drug therapy: Attacks cancer cells with drugs
  - A mainstay of treatment if local therapy is inappopriate such as hematomal cancer or metastasis disease

Local therapy

- Surgery: Removes cancer surgically
  - Cancer can be cured if it remains in the primary lesion
- Radiotherapy: Eliminates cancer cells with radiation
  - Exerts therapeutic effects without surgically removing organs
  - Sometimes combined with drug therapy and surgery

2) Drug therapy (chemohterapeutic drugs and molecular targeted drugs)

Previously, chemotherapy drugs played a principal role in drug therapy. Chemotherapeutic drugs are small molecule drugs that produce therapeutic effects on highly proliferative cells. They also affect to maintain function, such as gastrointestinal and bone marrow cells. This impact on normal cells are the cause of most of the chemotherapy-induced side effects.

On the other hand, molecular targeted drugs target genes and proteins that are highly expressed in cancer cells. They are less likely to affect rapidly dividing normal cells. Although molecular targeted drugs have their own unique side effects, they have relatively fewer side effects than conventional chemotherapeutic drugs.
Daiichi Sankyo’s ADC (Antibody Drug Conjugate)

1 What is ADC?
An ADC, which is short for Antibody Drug Conjugate, is an agent that covalently combines an antibody with a chemotherapeutic drug, payload, through a linker. Antibody drugs and chemotherapeutic drugs each have their own advantages and disadvantages, but ADC has the potential to exploit the strengths of both while mutually compensating for the disadvantages of both drugs.

Antibody drug
- High target selectivity
- Fewer side effects, relative to chemo
- Sometimes insufficient efficacy

Chemotherapeutic drug
- Low target selectivity
- Many potential side effects
- Strong anti-tumor effects (cytotoxic activity)

2 Mechanism of Action with ADC
ADC exerts its therapeutic effects through the following steps:
(1) ADC binds to an antigen on the surface of a cancer cell
(2) Subsequently, ADC-antigen complex is internalized into the cancer cell
(3) Lysosomes cleaves the ADC linker in the cancer cell, resulting in the release of the cytotoxic payload
(4) Cancer cells undergoes therapeutic effects by the released payloads

3 Structure of Daiichi Sankyo’s ADC
Our ADC technology is applicable to various antibodies.

4 Characteristics of Daiichi Sankyo’s ADC
Daiichi Sankyo began development on ADC technology in 2010. There were already preceding products in the market that used ADC technology at that time, and our entry to the research and development was certainly not early. Daiichi Sankyo’s researchers screened over 100 types of linkers to bind the antibody to the payload. The key aim was to overcome the shortcomings of existing ADC technology. These efforts ultimately produced the ADC construct used in Daiichi Sankyo’s ADC technology is applicable to various antibodies.

5 High potency of payload
Doxorubicin (DOX) is a well-established anthracycline-based chemotherapeutic drug. It has been demonstrated that the payload released by an ADC is more effective than free DOX in killing tumor cells in vitro and in vivo. In addition, the toxic effects on normal cells are reduced.

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

7 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 in vivo stability of Daiichi Sankyo’s ADC construct.

8 Payloads with a short half-life in the blood
Payloads are critical for ADCs because the duration of drug exposure to cancer cells must be short enough to minimize systemic toxicity. The payloads of ADCs are usually designed to be eliminated quickly from the blood (a short half-life) after administration.

9 New payload
The payload of Daiichi Sankyo’s ADCs currently in the research and development stage is DXd, a new derivative of the DNA topoisomerase I inhibitor DX-8951 created by former Daiichi Pharmaceutical. As a cytotoxic in early development of DX-8951 had promising potency, but with an unacceptable risk-benefit profile.

10 High drug-antibody ratio
Bystander effect
The bystander effect means a process where after the ADC binds to an antigen expression-positive cancer cell (HER2 positive, for example), the payload is released from the ADC in the cancer cell, penetrates the membrane, and exerts cytotoxic effects on neighboring cancer cells.

11 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 in vivo stability of Daiichi Sankyo’s ADC construct.

Pharmacokinetics profile of DS-8201 Phase 1 6.4mg/kg
DS-8201: Payload: Total antibody (incl. DS-8201)

Payloads Half-life in rats (hours)
- DXd*: (payload of Daiichi Sankyo’s ADC) 6.9
- DM1†: (payload of 7 DM1) 3.3-10

Overview and progress of 5-Year Business Plan: Establish Oncology Business

Daiichi Sankyo’s ADC Franchise

At present, Daiichi Sankyo has seven ADC projects for different antibody targets with the same linker and payload. Clinical trials began for DS-8201, U3-1402, and DS-1062 are in progress, with data presented at numerous medical conferences. Phase 1 studies are slated to start in fiscal 2019 for DS-7300 and DS-6157.

1 DS-8201 (anti-HER2-ADC)
DS-8201 is an anti-HER2 antibody-drug conjugate which our proprietary linker and payload are conjugated to anti-HER2 antibody. This project is most advanced of our ADC franchise, with clinical studies underway in breast cancer, gastric cancer, lung cancer, colorectal cancer, and bladder cancer.

(1) What is HER2?
HER2 is an antigen found on the cell surface. It has a structure similar to the epidermal growth factor receptor (HER1/EGFR). It is a receptor tyrosine kinase associated with cell proliferation, HER2, which is overexpressed on the surface of cancer cells, such as those of breast cancer, gastric cancer, colorectal cancer, lung cancer, and bladder cancer, induces cancer cell proliferation by activating signal transmission. DS-8201 exerts its efficacy by binding to this HER2.

(2) DS-8201 overall development plan
The figure below shows the overall development plan for DS-8201 as of April 2019. We are currently discussing the future development plan with AstraZeneca.

DS-8201 development plan (as of April 2019)

<table>
<thead>
<tr>
<th>Project Target</th>
<th>Prescribed indications</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS-8201 (HER2)</td>
<td>Breast cancer / Gastric cancer / Colorectal cancer / Non-small cell lung cancer</td>
<td>Start clinical study in FY2019</td>
</tr>
<tr>
<td>U3-1402 (HER2)</td>
<td>Breast cancer / Non-small cell lung cancer</td>
<td>Start clinical study in FY2019</td>
</tr>
<tr>
<td>DS-1062 (TP53)</td>
<td>Non-small cell lung cancer</td>
<td>Start clinical study in FY2019</td>
</tr>
<tr>
<td>DS-7300 (B7-H3)</td>
<td>Gastrointestinal stromal tumor (GIST)</td>
<td>Start clinical study in FY2019</td>
</tr>
<tr>
<td>DS-6157 (GPR20)</td>
<td>Kidney cancer / Ovarian cancer</td>
<td>Start clinical study in FY2019</td>
</tr>
<tr>
<td>DS-6000 (undisclosed)</td>
<td>Solid tumors</td>
<td></td>
</tr>
</tbody>
</table>

2 Phase 1 study breast cancer, comparison to similar drugs

Breast

<table>
<thead>
<tr>
<th>Perjeta + trastuzumab (1L)</th>
<th>T-DM1 (1L, failed study)</th>
<th>T-DM1 (3L)</th>
<th>T-DM1 (3L, failed study)</th>
<th>DS-8201*</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS 18.5m 14.1m</td>
<td>9.6m 6.3m</td>
<td>22.1m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DoR 20.2m 20.7m</td>
<td>12.6m 9.7m</td>
<td>20.7m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OS 56.5m 53.7m</td>
<td>30.9m 22.7m</td>
<td>NR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORR 80% 60%</td>
<td>43.6% 31%</td>
<td>59.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median prior Rx for adv. disease</td>
<td>0 0 1 4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3 Phase 1 study gastric cancer, comparison to similar drugs

Gastric

<table>
<thead>
<tr>
<th>Trastuzumab + Chemotherapy (1L)</th>
<th>Ramucirumab + Chemotherapy (2L)</th>
<th>T-DM1 (failed study: 3L)</th>
<th>DS-8201*</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS 6.7m 4.4m</td>
<td>2.7m 5.6m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DoR 6.9m 4.4m</td>
<td>4.3m 7.0m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OS 13.8m 9.6m</td>
<td>7.9m 12.8m</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORR 47% 28%</td>
<td>21% 43.2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median prior LoT</td>
<td>0 1 1 3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Regarding breast cancer, overall response rate (ORR) was 59.5%, duration of response (DOR) was 20.7 month and overall survival (OS) was not reached in patients who were treated by DS-8201 after progression with T-DM1, standard therapy for first line treatment.

Regarding gastric cancer, ORR was 43.2%, DOR was 7.0 months and OS was 12.8 months in patients who were treated by DS-8201 after progression with trastuzumab, standard therapy for first line treatment. This trial is fully enrolled, and final results will be presented at a future international medical conference.

<table>
<thead>
<tr>
<th>Listing of abbreviations</th>
<th>English</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>Complete response</td>
<td>Complete response (complete resolution of cancer)</td>
</tr>
<tr>
<td>DCR</td>
<td>Disease control rate</td>
<td>Disease control rate (percentage of patients with controlled disease status)</td>
</tr>
<tr>
<td>DOR</td>
<td>Duration of response</td>
<td>Duration of response (duration of response)</td>
</tr>
<tr>
<td>DLT</td>
<td>Dose limiting toxicity</td>
<td>Dose limiting toxicity (toxicities that may explain the inability to escalate dose)</td>
</tr>
<tr>
<td>MTD</td>
<td>Maximum tolerated dose</td>
<td>Maximum tolerated dose (maximum dose that can be administered without causing unacceptable side effects)</td>
</tr>
<tr>
<td>ORR</td>
<td>Overall response rate</td>
<td>Overall response rate (proportion of patients who responded to treatment and the sum of CR and PR)</td>
</tr>
<tr>
<td>OS</td>
<td>Overall survival</td>
<td>Overall survival (time from start of treatment to death)</td>
</tr>
<tr>
<td>PO</td>
<td>Progression disease</td>
<td>Progression disease (deterioration due to disease)</td>
</tr>
<tr>
<td>PFS</td>
<td>Progression-free survival</td>
<td>Progression-free survival (without cancer progression)</td>
</tr>
<tr>
<td>PR</td>
<td>Partial response</td>
<td>Partial response (reduction in the size of the cancer by 25% or more but that lasts for 4 weeks)</td>
</tr>
<tr>
<td>SD</td>
<td>Stable disease</td>
<td>Stable disease (the size of the cancer is almost unchanged before and after treatment)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abbreviations</th>
<th>English</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR</td>
<td>Complete response</td>
<td>Complete response (complete resolution of cancer)</td>
</tr>
<tr>
<td>DCR</td>
<td>Disease control rate</td>
<td>Disease control rate (percentage of patients with controlled disease status)</td>
</tr>
<tr>
<td>DOR</td>
<td>Duration of response</td>
<td>Duration of response (duration of response)</td>
</tr>
<tr>
<td>DLT</td>
<td>Dose limiting toxicity</td>
<td>Dose limiting toxicity (toxicities that may explain the inability to escalate dose)</td>
</tr>
<tr>
<td>MTD</td>
<td>Maximum tolerated dose</td>
<td>Maximum tolerated dose (maximum dose that can be administered without causing unacceptable side effects)</td>
</tr>
<tr>
<td>ORR</td>
<td>Overall response rate</td>
<td>Overall response rate (proportion of patients who responded to treatment and the sum of CR and PR)</td>
</tr>
<tr>
<td>OS</td>
<td>Overall survival</td>
<td>Overall survival (time from start of treatment to death)</td>
</tr>
<tr>
<td>PO</td>
<td>Progression disease</td>
<td>Progression disease (deterioration due to disease)</td>
</tr>
<tr>
<td>PFS</td>
<td>Progression-free survival</td>
<td>Progression-free survival (without cancer progression)</td>
</tr>
<tr>
<td>PR</td>
<td>Partial response</td>
<td>Partial response (reduction in the size of the cancer by 25% or more but that lasts for 4 weeks)</td>
</tr>
<tr>
<td>SD</td>
<td>Stable disease</td>
<td>Stable disease (the size of the cancer is almost unchanged before and after treatment)</td>
</tr>
</tbody>
</table>
(4) Interstitial lung disease

Interstitial lung disease is a group of disorders that damage the walls of the alveoli in the lungs and the spaces around the blood vessels and small airways. It is usually diagnosed by chest X-ray or chest CT. Over 380 drugs are known to induce ILD and other respiratory diseases, with significant issues being that the majority of ILD emerges from unpredictable, or idiopathic circumstances. Drug-related ILD is diagnosed by distinguishing signs and symptoms (such as fever, cough, and shortness of breath) from other disorders.

ILD has been recognized as a critical adverse event for DS-8201 from the earliest stage of the program. And a decision was taken to evaluate all suspected ILD cases via interarm data on suspected ILDs was presented for the 665 cases treated with DS-8201. Of the 665 cases, 66 cases (9.9%) were reported by the investigator to be potential ILD cases. Of these, a lower occurrence of 15 out of 269 cases (5.6%) was found in breast cancer patients treated with the low dose of 5.4 mg/kg. As a result, the dosage to be used in 3 breast cancer phase 3 trials was set to 5.4 mg/kg.

As early detection and early treatment is considered important in stopping ILDs from worsening, all study protocols were revised spring 2019. Prior to participating in the study, patients receive an explanation on the risks of ILDs when obtaining informed consent. They are then asked to immediately contact the physician in charge of their treatment should any symptoms or signs indicating the possibility of ILD appear. We also provide information to healthcare professionals about monitoring, evaluating, and treatment information of potential ILD symptoms. These changes of protocol are made to all our ADC projects. We continue to recognize ILD as critical adverse events and continue monitoring safety. At the same time, we are actively organizing a broad campaign to further drive awareness of safety use.

Current results indicate; disabling; limiting self care ADL (Grade 5) Interstitial lung disease

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Life-threatening consequences; urgent intervention indicated</td>
</tr>
<tr>
<td>Grade 5</td>
<td>Death related to adverse event</td>
</tr>
</tbody>
</table>

Number of ILDs by severity in all patients

<table>
<thead>
<tr>
<th>Population</th>
<th>Adjudication status</th>
<th>Grade</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects</td>
<td>Investigator reported, n (%)</td>
<td>30 (4.5)</td>
<td>23 (3.5)</td>
<td>6 (0.9)</td>
<td>2 (0.3)</td>
<td>5 (0.8)</td>
<td>66 (9.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cases adjudicated, n</td>
<td>16</td>
<td>13</td>
<td>4</td>
<td>0</td>
<td>5</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adjudicated as drug-related ILD, n</td>
<td>11</td>
<td>12</td>
<td>3</td>
<td>0</td>
<td>4</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

Number of ILDs by severity in breast cancer patients treated with 5.4 mg/kg

<table>
<thead>
<tr>
<th>Population</th>
<th>Adjudication status</th>
<th>ILD Severity Grade</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer 5.4 mg/kg N = 269</td>
<td>Investigator reported, n (%)</td>
<td>8 (3.0)</td>
<td>4 (1.5)</td>
<td>2 (0.7)</td>
<td>0</td>
<td>1 (0.4)</td>
<td>15 (5.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cases adjudicated, n</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adjudicated as drug-related ILD, n</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

Number of ILDs by severity in all patients

<table>
<thead>
<tr>
<th>Population</th>
<th>Adjudication status</th>
<th>Grade</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects</td>
<td>Investigator reported, n (%)</td>
<td>30 (4.5)</td>
<td>23 (3.5)</td>
<td>6 (0.9)</td>
<td>2 (0.3)</td>
<td>5 (0.8)</td>
<td>66 (9.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cases adjudicated, n</td>
<td>16</td>
<td>13</td>
<td>4</td>
<td>0</td>
<td>5</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adjudicated as drug-related ILD, n</td>
<td>11</td>
<td>12</td>
<td>3</td>
<td>0</td>
<td>4</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

Number of ILDs by severity in breast cancer patients treated with 5.4 mg/kg

<table>
<thead>
<tr>
<th>Population</th>
<th>Adjudication status</th>
<th>ILD Severity Grade</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer 5.4 mg/kg N = 269</td>
<td>Investigator reported, n (%)</td>
<td>8 (3.0)</td>
<td>4 (1.5)</td>
<td>2 (0.7)</td>
<td>0</td>
<td>1 (0.4)</td>
<td>15 (5.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cases adjudicated, n</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Adjudicated as drug-related ILD, n</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

How to Read Graphs

Waterfall Chart

Maximum tumor shrinkage from baseline tumor status prior to drug administration. Each bar represents the outcome of each patient, from right to left, with a high rate of cancer shrinkage.

Spider Plot

Relationship between percent change in tumor size and duration of treatment. Each line represents the outcome of each patient.

(5) Progress of HER2 positive breast cancer clinical studies

HER2 positive breast cancer treatment has significantly improved compared to previous treatments with the emergence of trastuzumab, pertuzumab, T-DM1, which are HER2 targeted drugs. Even so, we believe that there still remains many challenges to be dealt with, such as patients refractory to treatment with existing drugs and attenuation of drug efficacy due to acquired drug resistance.

The graph below is a waterfall chart representing efficacy in HER 2 positive metastatic breast cancer patients. Favorable effects are suggested, despite the condition of some patients worsening post-treatment with trastuzumab and T-DM1 (some with pertuzumab).

HER2 positive breast cancer (SABCS 2018)

Topline results for the DESTINY-Breast01 study were obtained in April 2019, achieving the initial goals set out for the study. In response, we will submit applications in the United States during the first half of fiscal 2019, in Japan during the second half of fiscal 2019, and in Europe during the first half of fiscal 2020.

The US FDA has granted a Breakthrough Therapy Designation for the treatment of metastatic breast cancer beyond third line treatment. As a result, a faster review period compared to regular reviews is expected.

HER2 positive metastatic breast cancer 3rd line submission plan

<table>
<thead>
<tr>
<th>Country</th>
<th>Phase</th>
<th>Title</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>1st-line treatment</td>
<td>T-DM1</td>
<td>June 2019</td>
</tr>
<tr>
<td>Japan</td>
<td>2nd-line treatment</td>
<td>T-DM1</td>
<td>January 2020</td>
</tr>
<tr>
<td>EU</td>
<td>3rd-line treatment</td>
<td>T-DM1</td>
<td>June 2020</td>
</tr>
</tbody>
</table>

How to Read Graphs

Waterfall Chart

Maximum tumor shrinkage from baseline tumor status prior to drug administration. Each bar represents the outcome of each patient, from right to left, with a high rate of cancer shrinkage.

Spider Plot

Relationship between percent change in tumor size and duration of treatment. Each line represents the outcome of each patient.

COLUMNS

Grades of adverse events

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Life-threatening consequences; urgent intervention indicated</td>
</tr>
<tr>
<td>Grade 5</td>
<td>Death related to adverse event</td>
</tr>
</tbody>
</table>
Overview and progress of 5-Year Business Plan: Establish Oncology Business

(6) Progress of HER2 low expression breast cancer clinical study
To date, breast cancers HER2 status has been classified into two types by immunostaining that detects expression: HER2-positive and HER2-negative. However, it has been revealed that HER2 is expressed (IHC 2+/ISH-, IHC 1+) in some types of breast cancers classified as HER2-negative. For the purposes of our clinical development program, we are now calling these patients “HER2 low”. It is said that HER2 low accounts for approximately 44% of breast cancer patients. To date, there are no approved HER2 targeted agents that have shown clinical benefit for patients with HER2-low tumors.

The graph below is a waterfall chart representing efficacy in HER 2 low metastatic breast cancer patients. Even though some patients were heavily pre-treated, favorable effects, ORR 44%, are suggested.

Based on this result, a phase 3 study (DESTINY-Breast04 study) is currently underway for patients with HER2 low expressing metastatic breast cancer.

HER2 low expressing breast cancer (SABCS 2018)

(7) Progress of gastric cancer clinical study
About 10% to 25% of gastric cancer patients overexpress HER2. However, while trastuzumab has been approved for first line treatment, no other HER2-targeting drug has been approved following progression after trastuzumab.

The graph below is a waterfall chart representing efficacy in HER2 positive metastatic gastric cancer patients. As this interim data shows, DS-8201 exhibits high antitumor activity even for HER2 positive metastatic gastric cancer.

HER2 positive gastric cancer (ASCO 2018)

Based on this result, a phase 2 study (DESTINY-Gastric01 study) is currently underway in Japan and in Asia for patients with HER2 positive metastatic gastric cancer post trastuzumab. The study is proceeding with the goal to submit an application for approval by the first half of fiscal 2020.

The Ministry of Health, Labour and Welfare of Japan has granted a SAKGAKA4 Designation for this indication, resulting in a potentially faster review period.

In addition to the study in Japan and the Asia, a phase 2 study for patients in the US and Europe is planned to start in fiscal 2019.

(8) Progress of colorectal cancer clinical study
About 1% to 2% of colorectal cancer patients express HER2. However, no HER2-targeting drug has been approved following progression after trastuzumab.

The results of pre-clinical studies show that the efficacy of DS-8201 can be increased by combining with immune checkpoint inhibitors such as nivolumab without compromising safety.

Furthermore, preparations are being made for phase 1 studies in combination with pembrolizumab or avelumab.

Combination benefit of DS-8201a and an anti-PD-1 antibody in vivo

(9) Progress of lung cancer clinical study
According to the WHO worldwide cancer statistics (estimate), lung cancer was the most common cancer in terms of number of patients affected and number of deaths. Of the various lung cancers, it has been reported that 4% to 35% of non-small-cell lung cancer (NSCLC) patients are HER2-expressing, but similar to colorectal cancer, no HER2-targeting drug has been approved.

Although the number of cases are low at this point, a remarkable antitumor effect (see graph below) has been achieved in the treatment of HER2-mutated lung cancer in a phase 1 study. A global phase 2 study is currently underway for HER2-expressing and HER2-mutated lung cancer patients.

HER2-expressing non-small-cell lung cancer (WCLC 2018)

1. How to measure HER2
Since the expression level of HER2 varies depending on the cancer type and patient, patient selection in DS-8201 studies measure HER2 using the immunostaining method IHC/ISH.

Staining methods used in pathology
- Measure proteins and nucleic acids that you want to detect in tissues and cells
- A technique that enables microscopic observation through staining using pigments and enzymes
- IHC: abbreviation of immunohistochemistry
- Observes protein expression levels including HER2 (surface of cancer cell)
- ISH: abbreviation of in situ Hybridization
- Observes amplification levels of HER2 genes (DNA), etc (nucleus of cancer cell)
- FISH: Fluorescence in situ hybridization

2. Commonly used
<table>
<thead>
<tr>
<th>HER2 positive or HER2 overexpressing</th>
<th>HER2 positive</th>
<th>HER2 overexpressing</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2 positive IHC 2+/ISH-</td>
<td>2.0-2+</td>
<td></td>
</tr>
<tr>
<td>HER2 IHC 3+</td>
<td>3.0</td>
<td></td>
</tr>
</tbody>
</table>

3. Conclusion

In summary, we have achieved remarkable antitumor activity even for HER2 expressing gastric and colorectal cancer patients.

* Endpoint was set as >3000mm3 of tumor volume or any other efficacious measures.
Concerning the safety, U3-1402 was tolerated over the 7.6-month median exposure period. The dose was also increased to 8 mg/kg, but the maximum tolerated dose was not reached.

Currently, recommended dose for expansion was selected and the drug is undergoing the dose expansion part of the phase 1 study.

(3) Progress of EGFR-mutated non-small-cell lung cancer clinical study
A phase 1 study in patients with advanced EGFR-mutated non-small-cell lung cancer was started in January 2018, for which we presented interim efficacy and safety data from dose escalation part at the American Society of Clinical Oncology (ASCO) in 2019.

The graph below is a waterfall chart representing efficacy. Regarding the efficacy of the 16 evaluable cases, a shrinkage in tumor size was seen in all patients even though patients were enrolled without prior HER3 selection. Although there are a limited number of cases, some exhibited antitumor activity against tyrosine kinase inhibitors such as osimertinib. We will evaluate further.

(2) Progress of HER3-positive breast cancer clinical study
A phase 1 study in patients with HER3-positive refractory/metastatic breast cancer was started in December 2016, for which we presented interim efficacy and safety data from the dose escalation part of the study at the San Antonio Breast Cancer Symposium (SABCS) in 2018.

The graph below is a waterfall chart representing efficacy. Favorable antitumor effects are suggested with ORR 42.9%, despite the condition that most patients progressed after multiple available drugs.

Concerning safety, most of the adverse events were of grade 1 or 2, and while there is dose-limiting toxicity, the maximum tolerated dose had not yet been reached.

The drug will undergo the dose expansion part of the phase 1 study in the second half of fiscal 2019.

In addition, HER3 is highly expressed in cancers such as colorectal cancer and prostate cancer, so expansion into other types of cancer is being considered.

(3) Progress of non-small-cell lung cancer clinical study
A phase 1 study in patients with non-small-cell lung cancer (NSCLC) was initiated in February 2018, for which we presented interim efficacy and safety data from dose escalation part at the American Society of Clinical Oncology (ASCO) in 2019.

With respect to efficacy, 10 of the 19 evaluable patients showed partial responses (responses in 7 of these patients require further confirmation). As shown in below waterfall chart, partial responses are seen in cohort above the 2.0 mg/kg. Also shown in spider plot, partial responses are dose dependent.

This study was conducted in NSCLC patients who were unresponsive to standard treatments, experienced recurrence with standard treatments, or where a standard treatment does not exist. In addition, as TROP2 is highly expressed in non-small-cell lung cancer, and as such, presence or absence of TROP2 expression was not measured prospectively. Regardless of this condition, this study is notable that it displays dose-dependent antitumor effect.
Overview and progress of 5-Year Business Plan: Establish Oncology Business

Breast Cancer

The current status of breast cancer and the existing standard of care

Breast cancer is the most common cancer in women, and the numbers of new and recurrent breast cancer cases in Japan, U.S. and Europe in 2017 are provided in the figure to the right.

Data published by the Ministry of Health, Labour and Welfare shows that the number of patients who died of breast cancer in Japan continues to rise and reached approximately 14,000 in 2016, more than three times higher than 35 years ago, with breast cancer ranked first as the cause of death in women aged 30 to 64 years.

Breast cancer generally classified into the stages below, and surgery is the standard of care. Pre-operative or post-operative drug therapy is given to some patients to prevent cancer recurrence. In addition, in patients in whom surgical procedures are inappropriate because of metastases and other conditions, drug therapy is principally used.

In drug therapy for breast cancer, tests are performed to look at receptors on cancer cells first, and select anticancer drugs which are appropriate for the receptor status.

Breast cancer subtype classification and our pipeline

Pre-clinical research is currently underway for DS-6000 (target undisclosed), which targets renal cancer and ovarian cancer, as well as ADC of anti-TA-MUC1 antibody from Glycotope.

The drug linker of these compounds are the same as the DS-8201, U3-1402 and DS-1062. Since Daiichi Sankyo’s ADC technologies are applicable to a wide variety of antibodies, we are always examining possibilities for collaboration with other companies to increase the range of antibodies we can apply our ADC technologies to.

We are also focusing on developing different drugs and linkers and research on antibody-modifying technologies, assuming that DS-8201 and other ADCs are ineffective or become resistant during treatment in some cases.

ADC pipeline

<table>
<thead>
<tr>
<th>Project code</th>
<th>Project target</th>
<th>Prescribed indications</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS-8201 (HER2)</td>
<td>Breast cancer</td>
<td>Start clinical study in FY2019</td>
<td></td>
</tr>
<tr>
<td>U3-1402 (ER/PR)</td>
<td>Breast cancer</td>
<td>Start clinical study in FY2019</td>
<td></td>
</tr>
<tr>
<td>DS-7300 (HER2)</td>
<td>Non-invasive lung cancer</td>
<td>Start clinical study in FY2019</td>
<td></td>
</tr>
<tr>
<td>DS-6157 (GPR20)</td>
<td>Gastrointestinal stromal tumor (GIST)</td>
<td>Start clinical study in FY2019</td>
<td></td>
</tr>
<tr>
<td>DS-6300 (GPR20)</td>
<td>Kidney cancer</td>
<td>Ovarian cancer</td>
<td>Solid tumors</td>
</tr>
</tbody>
</table>

Strategic Target

54

Daiichi Sankyo Group Value Report 2019

Source: created based on the National Cancer Center’s Cancer Information Service

Breast Cancer patients by stage (new, recurrence) 2017

<table>
<thead>
<tr>
<th>Stage</th>
<th>Japan</th>
<th>U.S.</th>
<th>Europe</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>12</td>
<td>0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>II</td>
<td>45</td>
<td>2.3</td>
<td>1.2</td>
</tr>
<tr>
<td>III</td>
<td>95</td>
<td>4.0</td>
<td>4.3</td>
</tr>
<tr>
<td>IV</td>
<td>99</td>
<td>6.3</td>
<td>5.6</td>
</tr>
</tbody>
</table>

Source: CancerMPact®, Kantar Health/Synix inc. (Strict diversion of confidential information)

Gastrointestinal stromal tumors (GIST).

GPR20 is an orphan G protein-coupled receptor (GPCR).

GIST (gastrointestinal stromal tumors).

Stage IV

The lump has spread to other organs (lung, bone, liver, brain, etc.)

Stage III

The lump has spread to several lymph nodes

Stage II

The lump has spread to several lymph nodes

Stage I

The lump has spread to lymph nodes

Early stage cancer

Pre-operative drug therapy

Operation

Drug therapy suppresses a growth factor

Postoperative adjuvant therapy

Radium therapy

Strategic Target

54

Daiichi Sankyo Group Value Report 2019

Source: created based on the National Cancer Center’s Cancer Information Service

Breast Cancer subtype classification and our pipeline

<table>
<thead>
<tr>
<th>HER2+</th>
<th>HER2+</th>
<th>HER2+</th>
<th>HER2+</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS-8201</td>
<td>DS-8201</td>
<td>DS-8201</td>
<td>DS-8201</td>
</tr>
</tbody>
</table>

We are conducting clinical studies in DS-8201 for HER2 positive and HER2 low metastatic breast cancer and in U3-1402 for HER2 positive refractory/metastatic breast cancer.

Concerning safety, of the 39 non-small-cell lung cancer (NSCLC) patients, 16 (41.0%) experienced adverse events grade 3 or higher at least once. Although dose-limiting toxicity was observed as a grade 3 rash (in one patient), the maximum tolerated dose had not yet been reached (at the data cut-off date).

DS-1062 initiated the dose expansion part of phase 1 study from July 2019. Based on the interim data from this study, we are considering to expand development of DS-1062 into other cancer indications.

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

DS-7300 is an anti-B7-H3 ADC which our proprietary linker and payload are conjugated to an anti-B7-H3 antibody. The drug linker is the same as that of DS-8201 and U3-1402, but DS-7300 has a DAR of 4 like DS-1062.

1 What is B7-H3?

B7-H3 is a type 1 transmembrane protein belonging to the B7 family. B7-H3 is overexpressed in many types of solid tumors, and is suggested to be related to a poor prognosis in some solid-tumors such as NSCLC and prostate cancer.

DS-7300 exerts its efficacy by binding to this B7-H3.

2 Phase 1 study in patients with selected solid tumor

In fiscal 2019, initiation of phase 1 study of DS-7300 in patients with selected solid tumors is planned.

5 DS-6157 (anti-GPR20-ADC)

DS-6157 is an anti-GPR20 ADC which our proprietary linker and payload are conjugated to an anti-GPR20 antibody. The drug linker is the same as that of the DS-8201.

1 What is GPR20?

GPR20 is an orphan G protein-coupled receptor (GPCR). GPR20 is a seven-pass transmembrane protein and specifically expressed in GIST (gastrointestinal stromal tumors).

DS-6157 exerts its efficacy by binding to this GPR20.

2 What is GIST?

GIST is the most common mesenchymal tumors of the gastrointestinal tract. Currently, three tyrosine kinase inhibitors have been approved in its treatment, but there are still unmet medical needs in regard to relapse, refractory, and resistant patients.

In fiscal 2019, initiation of phase 1 study of DS-6157 in patients with GIST is planned.
Lung Cancer

The current status of lung cancer and the existing standard treatments

Lung cancer occurs when bronchial or lung cells become cancerous through a variety of factors, with smoking known to be the largest risk factor. Other risk factors include chronic obstructive pulmonary disease, the inhalation of asbestos, arsenic, chromium, or other carcinogens due to occupational exposure or air pollution, as well as aging.

According to statistics (estimates) provided by the WHO regarding cancer around the world in 2018, lung cancer has the highest number of incident cases and deaths worldwide, with 2.09 million patients and 1.76 million people dying from the disease.

Lung cancers are classified into two groups based on their histological characteristics: small-cell lung cancers and non-small-cell lung cancers, with the latter accounting for about 85% of all cases.

The following paragraphs describe treatments for non-small-cell lung cancers.

Lung cancer is categorized into stages I through IV based on a combination of the size and extension of infiltration of the tumor (T), the degree of metastases to nearby lymph nodes (N), and the presence of distant metastases (M). Treatments for non-small-cell lung cancers include surgery, radiotherapy, drug therapy, or combinations of these. The method of treatment is selected based on the stage of the cancer. If the tumor can be removed, treatment is carried out centered on surgery. However, if surgery is not a viable option due to the patient’s general state, age, or the presence of other complicating diseases, treatment is carried out with a focus on radiotherapy. Drug therapy is used if tumors progressed further.

In drug therapy for non-small-cell lung cancers, different treatments are used depending on the stage. A platinum-based drug combination therapy was conventionally used for stages Ib to IV, but recent methods of treatment involve selecting drugs after investigating the genetic mutations in the tumors.

In Daiichi Sankyo, several clinical studies are underway for NSCLC; DS-8201 for HER2-expressing or HER2 mutated NSCLC, U3-1402 for EGFR-mutated NSCLC and DS-1962 for NSCLC patients who are unresponsive or progressed with standard therapy.

AML is a disease with high mortality rate. In particular, AML patients with mutated FLT3, which is a receptor tyrosine kinase involved in the proliferation of cancer cells, are known to have a particularly high degree of malignancy and extremely poor prognosis with a rate of recurrence two years after bone marrow transplants that is three times higher than that of other forms of AML. Quizartinib is a tyrosine kinase inhibitor that displays specific potent inhibitory activity against FLT3-ITD.

In 2018, we applied for approval in Japan, the United States, and Europe, based on the results of the QUANTUM-R study in patients with relapsed/refractory AML. In Japan, the Ministry of Health, Labour and Welfare approved quizartinib for the treatment of relapsed/refractory FLT3-ITD AML in June 2019. We will launch it under the brand name VANXELYA®. In the United States, we received a Complete Response Letter in June 2019. We plan to decide upon our next step in the United States after detailed review of the contents of the Complete Response Letter. In Europe, quizartinib is under review, with approval expected in the second half of fiscal 2019.

Enrollment of patient is proceeding smoothly in the QUANTUM-First study to evaluate the efficacy and safety of quizartinib in combination with the standard of care as first line treatment for AML as well as in continuation therapy.

1 Quizartinib (FLT3 inhibitor)

AML is a disease with high mortality rate. In particular, AML patients with mutated FLT3, which is a receptor tyrosine kinase involved in the proliferation of cancer cells, are known to have a particularly high degree of malignancy and extremely poor prognosis with a rate of recurrence two years after bone marrow transplants that is three times higher than that of other forms of AML. Quizartinib is a tyrosine kinase inhibitor that displays specific potent inhibitory activity against FLT3-ITD.

In 2018, we applied for approval in Japan, the United States, and Europe, based on the results of the QUANTUM-R study in patients with relapsed/refractory AML.

In Japan, the Ministry of Health, Labour and Welfare approved quizartinib for the treatment of relapsed/refractory FLT3-ITD AML in June 2019. We will launch it under the brand name VANXELYA®. In the United States, we received a Complete Response Letter in June 2019. We plan to decide upon our next step in the United States after detailed review of the contents of the Complete Response Letter. In Europe, quizartinib is under review, with approval expected in the second half of fiscal 2019.

Enrollment of patient is proceeding smoothly in the QUANTUM-First study to evaluate the efficacy and safety of quizartinib in combination with the standard of care as first line treatment for AML as well as in continuation therapy.

1 Quizartinib (FLT3 inhibitor)

AML is a disease with high mortality rate. In particular, AML patients with mutated FLT3, which is a receptor tyrosine kinase involved in the proliferation of cancer cells, are known to have a particularly high degree of malignancy and extremely poor prognosis with a rate of recurrence two years after bone marrow transplants that is three times higher than that of other forms of AML. Quizartinib is a tyrosine kinase inhibitor that displays specific potent inhibitory activity against FLT3-ITD.

In 2018, we applied for approval in Japan, the United States, and Europe, based on the results of the QUANTUM-R study in patients with relapsed/refractory AML.

In Japan, the Ministry of Health, Labour and Welfare approved quizartinib for the treatment of relapsed/refractory FLT3-ITD AML in June 2019. We will launch it under the brand name VANXELYA®. In the United States, we received a Complete Response Letter in June 2019. We plan to decide upon our next step in the United States after detailed review of the contents of the Complete Response Letter. In Europe, quizartinib is under review, with approval expected in the second half of fiscal 2019.

Enrollment of patient is proceeding smoothly in the QUANTUM-First study to evaluate the efficacy and safety of quizartinib in combination with the standard of care as first line treatment for AML as well as in continuation therapy.
Daiichi Sankyo’s Breakthrough Science

Breakthrough Science is the third pillar, with the goal of creating first-in-class or best-in-class compounds with breakthrough mechanism of action or modality.

Breakthrough science pipeline

<table>
<thead>
<tr>
<th>Product (Target)</th>
<th>Inhibitor</th>
<th>Mechanism of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pexidartinib (CSF-1R/KIT/FLT3)</td>
<td>Sulforhab</td>
<td>Receptor tyrosine kinase inhibitor showing specific inhibitory activity against CSF-1R, KIT and FLT3-ITD</td>
</tr>
<tr>
<td>DS-1647 (G47Δ)</td>
<td>p2</td>
<td>In third generation of oncolytic herpes simplex virus 1 (HSV-1) created by using genetic modification technologies to modify HSV-1 so that it only multiplies in cancer cells</td>
</tr>
<tr>
<td>DS-1205 (AXL)</td>
<td>p1</td>
<td>AXL receptor tyrosine kinase inhibitor. High expression of AXL in patients is associated with resistance to EGFR tyrosine kinase inhibitors in patients with non-small cell lung cancer</td>
</tr>
<tr>
<td>DS-1001 (mutant IDH1)</td>
<td>p1</td>
<td>A selective inhibitor of mutant isocitrate dehydrogenase IDH. Inhibits mutant enzyme expressed by IDH1 gene mutation frequently seen in malignant brain tumors (glioma), acute myeloid leukemia, oligodendroglioma, cholangiocarcinoma</td>
</tr>
</tbody>
</table>

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

Pexidartinib is a receptor tyrosine kinase inhibitor showing specific inhibitory activity against CSF-1R/KIT and FLT3. We obtained approval in the United States in August 2019 based on the results of a placebo-controlled phase 3 study (ENLIVEN) in patients with tenosynovial giant cell tumor (TGCT) and launched under the brand name ENLIVEN) in patients with tenosynovial giant cell tumor (TGCT) and launched under the brand name ENLIVEN. We also applied for approval in Europe in March 2019. TGCT is a type of benign tumor occurring in joints. It is known that there is no treatment method other than surgery and it can cause extreme inconvenience in daily life. The recurrence rate for diffuse disease is also high, and in some cases, limb amputation may be unavoidable. Pexidartinib is the first drug to be indicated for TGCT.

2 DS-1647 (oncolytic virus G47Δ)

DS-1647 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. Clinical and pre-clinical studies are ongoing for glioblastoma and several other cancer types. Daiichi Sankyo is working with Professor Todo to develop G47Δ. Glioma is classified into four grades according to the grade of malignancy and glioblastoma is the most common and most malignant (grade 4). Even if radiation therapy is given after surgery, the 5-year survival rate is about 10%, making it extremely difficult to cure. In investigator initiated study in glioblastomas conducted by Professor Todo, interim analysis was conducted in July 2018, and the primary endpoint, 1-year survival rate, was 92.3%, confirming that the drug has high efficiency. Using this result, we plan to apply for approval in 2H of fiscal 2019. The Ministry of Health, Labour and Welfare granted a SAKIGAKE Designation, resulting in a potentially faster review period.

Oncolytic virus therapy

- Virus infection
- Virus proliferation and destruction of cancer cells
- Spread of viruses to the surrounding cells

3 DS-1001 (mutant IDH1 inhibitor)

It is known that mutations in the gene encoding isocitrate dehydrogenase 1 (IDH1) are frequently seen in a variety of tumors including glioma, acute myeloid leukemia, cholangiocarcinoma, and chondrosarcoma. DS-1001 is a selective inhibitor of mutant IDH1 and has characteristic of high penetration into the brain. We presented interim efficacy and safety data from the phase 1 study in patients with recurrent IDH mutated glioma that started in January 2017 at the American Society of Clinical Oncology (ASCO) in 2019. The graph below is a waterfall chart representing efficacy. Although this study had a small sample size, we observed a certain level of efficacy from DS-1001 in both enhancing and non-enhancing patients. Regarding safety, the maximum tolerated dose was not reached up to 1,400mg/kg twice daily, and preliminary safety data suggested that DS-1001 is well tolerated.

Glioma (ASCO 2019)

- Enhancing
- Non-enhancing

COLUMNS

Classification of gliomas

A glioma is a type of malignant brain tumor that begins in glial cells in the brain and spinal cord. Brain tumors are not staged the other cancer but are classified as grades I to IV.

- Grade I: Low-grade glioma
- Grade II: Anaplastic astrocytoma
- Grade III: Anaplastic oligodendroglioma
- Grade IV: Glioblastoma

- Enhancing Patients who have tumors with gadolinium enhancement on MRI images. It is common in high-grade gliomas like glioblastoma
- Non-enhancing Patients who have no gadolinium-enhanced tumor. Most common in low-grade gliomas

In glioma, IDH1 mutations are said to be present in around 80% of lower grade gliomas. Lower-grade gliomas often arise in the generation in their 30s and 40s, who are in the prime of their working life. Although they are generally growing slowly, most of them eventually transform into more aggressive tumors and result in death. Treatment options for lower grade gliomas and its recurrent disease are very limited. We will continue to move forward with development of DS-1001, to assess its efficacy and safety in glioma.