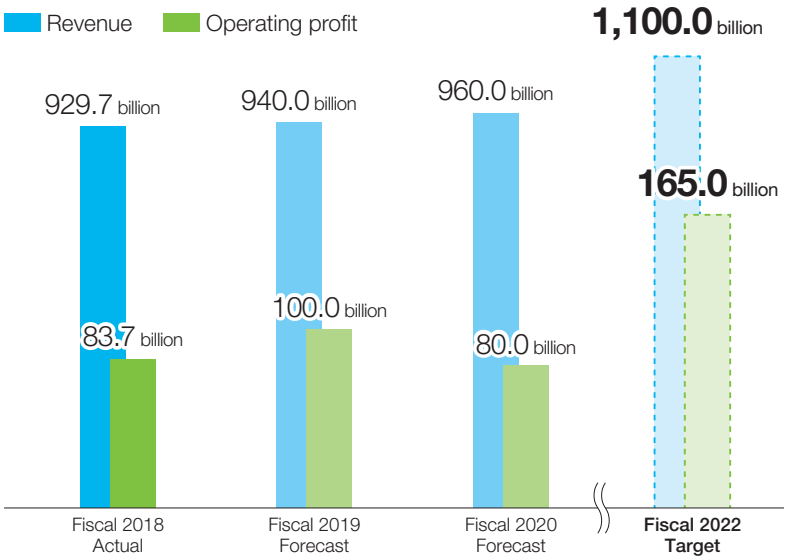
5-Year Business Plan Overview and Progress

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.

For details, refer to page 33.



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*

Achievements and Progress

- 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

Achievements and Progress

- 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*)

Expand U.S. Businesses

Achievements and Progress

- 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.

Establish Oncology Business

Achievements and Progress

- Accumulated promising clinical data on *DS-8201* and working ahead of schedule for the target date to submit an application for approval
- Presented 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)

Achievements and Progress

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

Enhance Profit Generation Capabilities

Achievements and Progress

- 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 manufuturing structure (two locations closed and decided to sell one location)

Growth Investments and Shareholder Returns

Prioritize growth investments while also enhancing shareholder returns

Achievements and Progress

- Reduced cross-shareholding shares (33 different stocks for a total amount of ¥46.0 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)

Message from the CFO

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.

Toshiaki Sai
Representative Director, Member of the Board, Executive Vice President and 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.

Establish Foundation for Sustainable Growth (Six Strategic Targets)

- Grow *Edoxaban*
- Grow as No. 1 Company in Japan
- Expand U.S. Business
- Establish Oncology Business
- Continuously Generate Innovative Medicine Changing Standard of Care (SOC)*
- Enhance Profit Generation Capabilities

* Broadly applied best treatment practice in today's medical science

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.

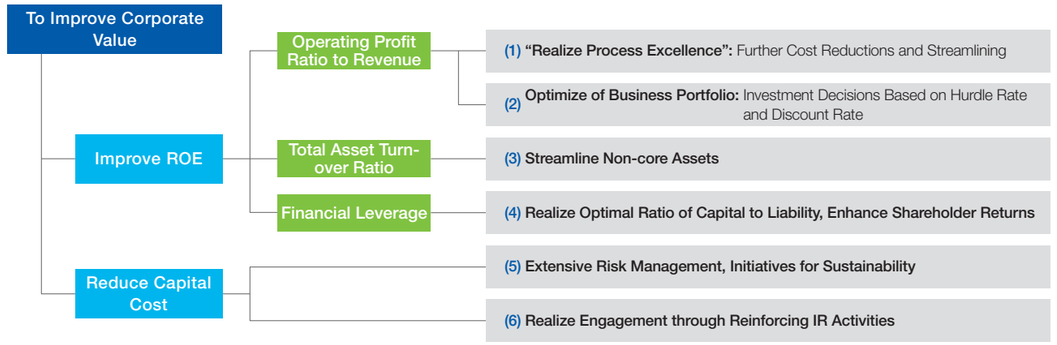
As for our oncology business, we decided to set a revenue target of ¥500 billion in fiscal 2025, exceeding the initial target of ¥300 billion by increasing and focusing our investment in the oncology business.

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 discussion 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.

(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.

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.

(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 ¥46.0 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 sell 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.

(Billions of yen)

		FY2016 Results	FY2017 Results	FY2018 Results	Total
Sale of properties	Sales proceeds	**3.2**	**10.7**	**11.0**	**25.0**
	Gain on sales	0.8	7.6	9.0	17.5
Reduce cross-shareholding shares	Number of stock brands	**14** brands	**9** brands	**10** brands	Aggregated total of 33 **33** brands
	Sales proceeds	**17.3**	**14.4**	**14.3**	**46.0**
	Gain on sales*	9.3	9.8	10.6	29.7
Gain on sales of business transfer	Gain on sales	-	-	(transferring long-listed products) **6.3**	**6.3**

* Booked in other comprehensive income
Gain on sales of Takatsuki Plant transfer (¥19.0 billion) and Nihonbashi building (¥10.6 billion) will be booked in FY2019

(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.

For details, refer to page 73.

With regard to sustainability, Daiichi Sankyo Group also works to address many issues relative to CSR in addition to mid-to-long-term initiatives and challenges. We also engage in proactive disclosure of ESG information to reduce the risk from the viewpoint of investors. We have been selected for various ESG indices including the "DJSI World Index," in which, we have been selected in the pharmaceutical sector for the first time as a Japanese company and also for two consecutive years.

For details, refer to page 96.

(6) Realize Engagement through Reinforcing IR Activities

Engagement means having conversation with purpose, and we will foster mutual understanding and increase transparency, and thus further improve corporate value through healthy discussions between investors and our management team. In the distribution of IR information, we disclose information in a timely manner while giving consideration to transparency and fairness, and we endeavor to undertake IR activities to narrow the gap between the corporate value envisioned by people inside and outside of the Company. Following the recent enhancement of our pipelines in particular, we have set up meetings and conference calls aimed at investors after presentations at major scientific conferences in the U.S. and Europe for better and deeper understanding among investors. In addition, we conduct more than 350 interviews with investors annually, including ten international road shows a year (interviews with international investors). As CFO, I myself engage by proactively holding conversations with investors and analysts, to realize engagement.

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 indevelopment.

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.)

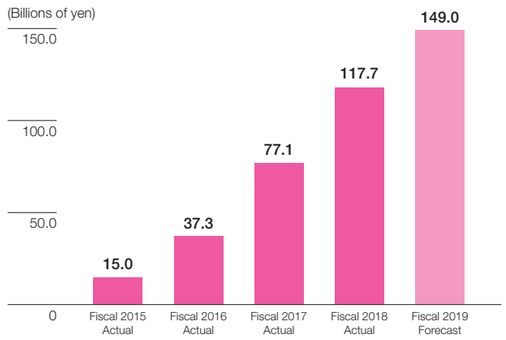
Edoxaban, direct oral anticoagulant (DOAC) is a mainstay product in place of *olmesartan*, a treatment for hypertension that has expired exclusivity. Since it's marketed, the Company has steadily expanded its market share, particularly in Japan, Europe, and Asia. Going forward, we will strengthen our 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.

Results to date



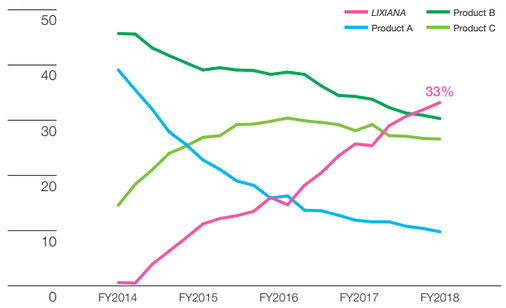
2 Progress to date

(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*.

Trends in sales share of DOACs in Japan



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COLUMN

Solubility of tablet

Slow  Rapid

Conventional tablet	OD tablet
taken by water	dissolved rapidly by oral saliva

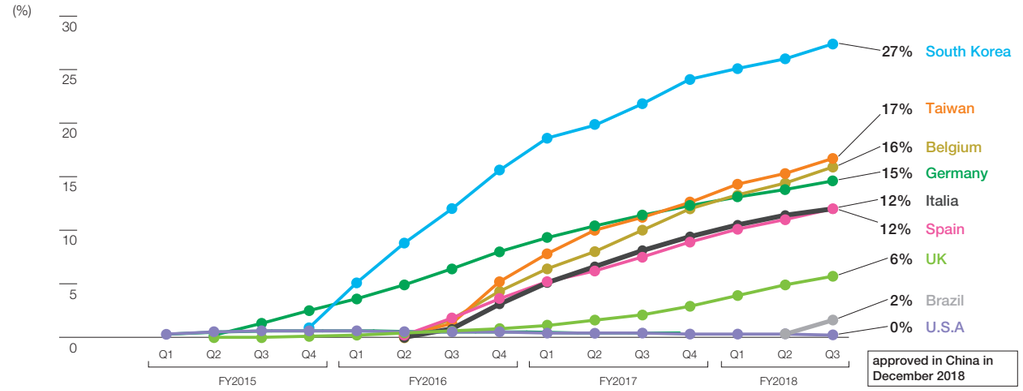
Process of dissolving

Sett 1 tablet on the mesh to evaluate disintegratability, using an injection barrel, drip refined water of 37 ± 2°C on the upper side of the tablet and measure the dissolving time

(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.

Growth of *edoxaban* by each country (volume share)



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(3) Life-cycle management initiatives

Currently, we are engaged in many clinical studies and lifecycle management activities, collectively referred to as EDOSURE*1 that create data on how *edoxaban* is used in clinical settings.

The efficacy and safety data for patients undergoing catheter ablation*2 was presented in a Late Breaking Session of the European Heart Rhythm Association (EHRA) in March 2019.

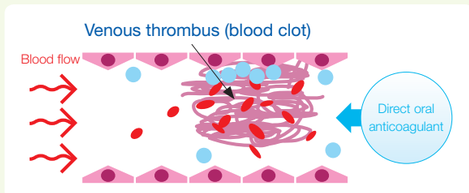
*1 Derived from two words, *edoxaban* and Assurance. It signifies our hope that doctors and patients will feel more reassured by anticoagulant therapy with *edoxaban*.
*2 A procedure used to ablate abnormal electrical pathways in the heart tissue by inserting a thin tube (catheter) through the blood vessels to the heart in order to restore normal rhythm of the heart of patients with AF.

COLUMN

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.



5-Year Business Plan Overview and Progress: Grow as the No.1 Company in Japan

Strategic Target

Grow as the No.1 Company in Japan

Japan is an important market for the Daiichi Sankyo Group in terms of its revenue generated on a regional basis. We aim to grow as the No.1 company in Japan in name and substance alike. To such ends, we will leverage the strengths of our innovative pharmaceuticals* business, while precisely addressing various social and medical needs such as prevention, self-medication and medical treatment, with the innovative business as well as our vaccines, generics and OTC drug businesses.

* Pharmaceuticals still protected by the exclusivity period granted by patents

1 5-Year business plan

In addition to *LIXIANA*, 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-o-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.

Ulcer treatment
NEXIUM

Alzheimer's disease treatment
Memary

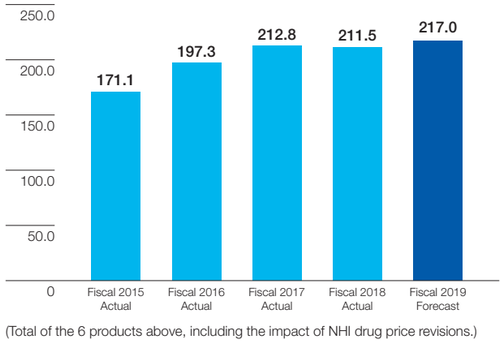
Treatment for osteoporosis / Inhibitor of the progression of bone erosion associated with rheumatoid arthritis
PRALIA

Treatment for bone complications caused by bone metastases from tumors
RANMARK

Antiplatelet agent
Efient

Type 2 diabetes mellitus treatment
TENELIA

Results to date



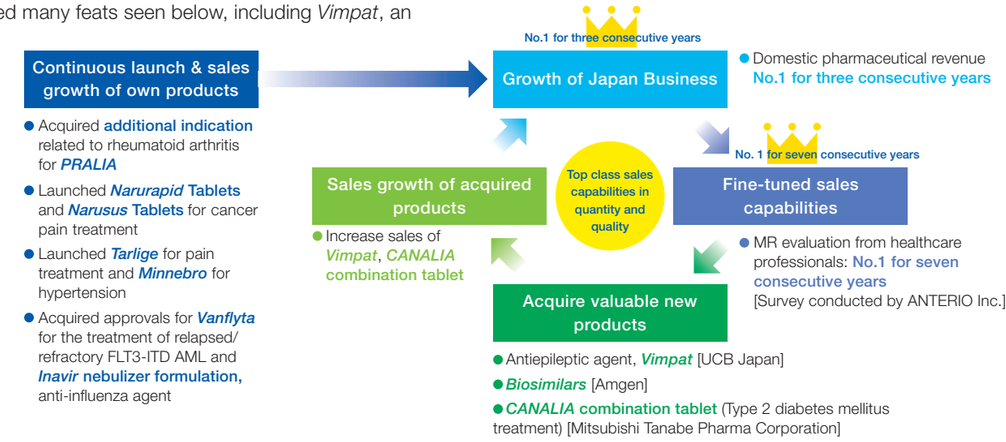
(Total of the 6 products above, including the impact of NHI drug price revisions.)

2 Progress to date

By continually launching and expanding sales of proprietarily developed products, we grew the innovative pharmaceuticals business. At the same time, we utilize the Company's superb 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.

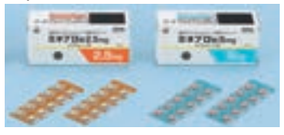


In fiscal 2019, we will add to our product portfolio our in-house developed drugs, *Tarlige* for pain treatment and *Minnebro* for hypertension, and *Vanfrita*, a promising new cancer product. We will aim to quickly nurture these new products.

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

***Tarlige* for pain treatment,** Launched in Apr. 2019

***Minnebro* for hypertension,** Launched in May 2019



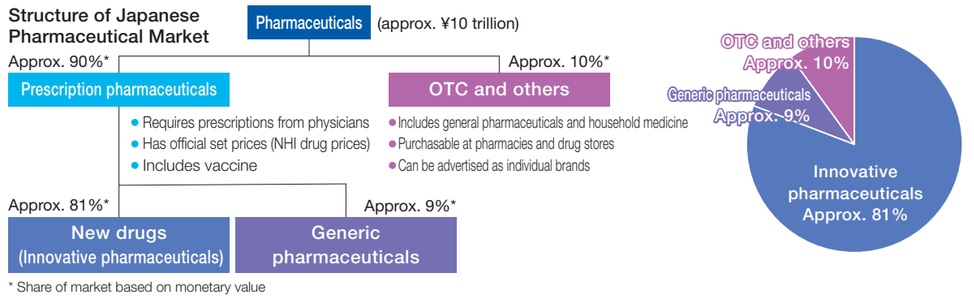
***Vanflyta* for the treatment of relapsed/refractory FLT3-ITD AML,** Approved in Jun. 2019

COLUMN

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 other 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)



* Share of market based on monetary value

Strategic Target

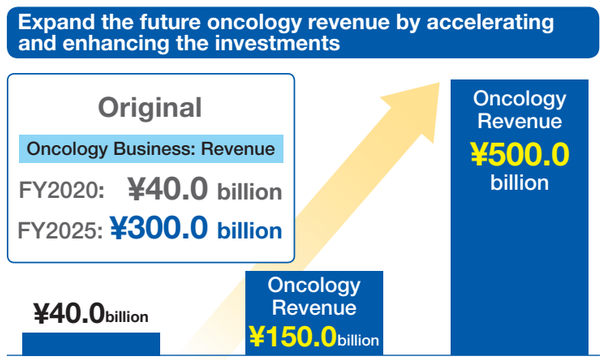
Establish Oncology Business

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.

Oncology business: Revenue target



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)

Worldwide	Japan	U.S.	Europe
9,555	409	617	1,943

Source: GLOBOCAN 2018, FACT SHEET

▶ **Number of new patients, number of patients with recurrent disease, 5-year survival (2018)**

		Japan	U.S.	5 European countries
Breast cancer	Newly diagnosed cancer (n)	92,000	327,000	262,000
	Recurrent cancer (n)	11,000	35,000	37,000
	5-year survival (%)	90%	85%	–
Gastric cancer	Newly diagnosed cancer (n)	130,000	26,000	56,000
	Recurrent cancer (n)	23,000	11,000	25,000
	5-year survival (%)	61%	24%	–
Non-small-cell lung cancer	Newly diagnosed cancer (n)	114,000	189,000	196,000
	Recurrent cancer (n)	40,000	65,000	72,000
	5-year survival (%)	38%	18%	–
Colorectal cancer	Newly diagnosed cancer (n)	144,000	157,000	239,000
	Recurrent cancer (n)	18,000	34,000	54,000
	5-year survival (%)	64%	56%	–

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

4 Cancer Treatment

(1) Cancer treatment

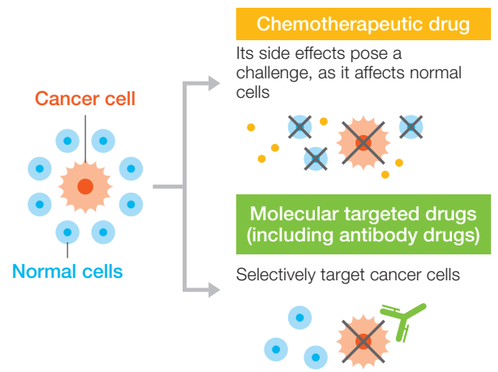
Cancer treatments are divided into two categories: systemic therapy and local therapy. Local therapy consists of surgery and radiotherapy.

	Type	Methodology	Characteristics
Systemic therapy	Drug therapy	Attacks cancer cells with drugs	• A mainstay of treatment if local therapy is inappropriate such as hematological cancer or metastatic 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 (chemotherapeutic drugs and molecular targeted drugs)

Previously, chemotherapeutic 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.

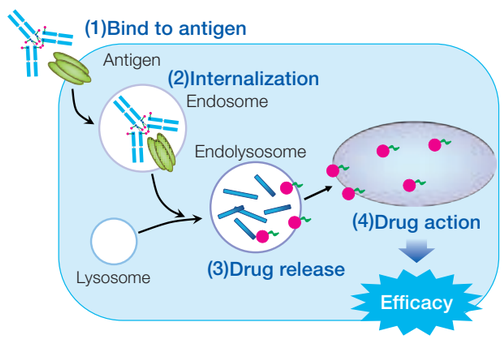
Antibody drug	Chemotherapeutic drug
● High target selectivity ● Fewer side effects, relative to chemo ● Sometimes insufficient efficacy	● Low target selectivity ● Many potential side effects ● Potent anti-tumor effects (cytocidal activity)

ADC
- High target selectivity
- Potent anti-tumor effects (cytocidal activity)
- Fewer side effects, relative to chemo

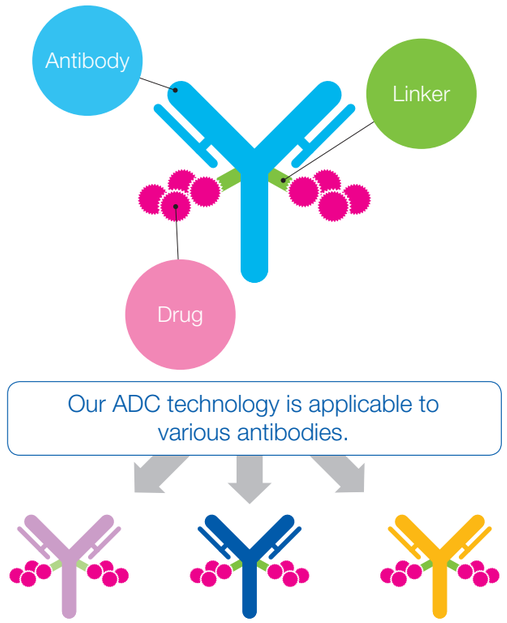
2 Mechanism of Action with ADC

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



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 *DS-8201* and other ADC products. The main characteristics of this technology are summarized in the figure below.

Each characteristic is described in detail on the following page.

Characteristic 1	New payload	Characteristics of Payload
Characteristic 2	High potency of payload	
Characteristic 3	Bystander effect	
Characteristic 4	Payload with a short systemic half-life	
Characteristic 5	Stable linker	Characteristics of Linker
Characteristic 6	Tumor selective cleavable linker	
Characteristic 7	High drug-antibody ratio	

Characteristic 1 New payload

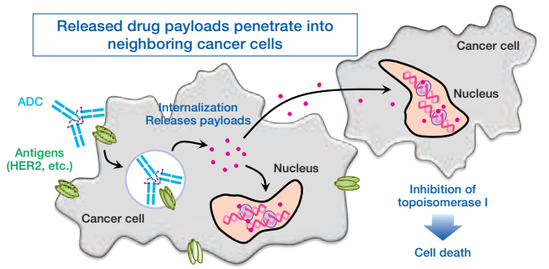
The payload of Daiichi Sankyo's ADCs currently in the research and development stage is *DXd*, a new derivative of the DNA topoisomerase I inhibitor *DX-8951* created by former Daiichi Pharmaceutical. As a cytotoxic in early development of *DX-8951* had promising potency, but with an unacceptable risk-benefit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

Characteristic 2 High potency of payload

DXd is approximately 10 times as potent as *SN-38* (the active metabolite of irinotecan featuring the same mechanism of action). Providing further rationale was the pre-clinical pharmacology finding that demonstrated that *DXd* is effective in cancer cells that are less sensitive or resistant to the payload of *T-DM1*, the standard of care for certain type of HER2 positive breast cancer.

Characteristic 3 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.



Characteristic 4 Payload with a short half-life in the blood

After intravenous administration, an increased blood concentration of drug payloads released from an ADC has the potential to cause side effects. Daiichi Sankyo's drug payload is less likely to be released while in the blood because of its stable linker, and the drug payload is designed to be eliminated quickly from the blood (a short half-life) following release.

Payloads	Half-life in rats (hours)
DXd *1 (payload of Daiichi Sankyo's ADC)	0.9
*DM1**2 (payload of *T-DM1*)	3.3-10

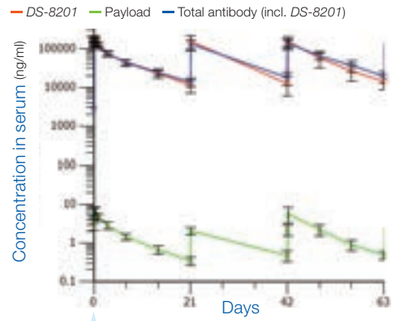
Source: *1 In-house report *2 *KADCYLA* BLA

Characteristic 5 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.

The graph below demonstrates that the linker is stable by showing that the blue line representing the blood concentration of antibodies (antibodies present as ADC and the antibody following ADC degradation) high overlap with the red line representing the blood concentration of *DS-8201*.

Pharmacokinetics profile of *DS-8201* Phase 1 6.4mg/kg



This logarithmic scale starts at 1 and goes up and down in powers of ten, unlike a linear scale where each mark on the axis indicates an equal interval.

Source: Tamura-K *et al* ., Abstract #4585 (LBA17), ESMO 2016

Characteristic 6 Selectively cleaved linker in cancer cells

The linker must be stable in the blood and yet readily release its payload once internalized into the cancer cell following binding to the cancer-cell antigen. The linker of Daiichi Sankyo's ADC is cleaved by enzymes including cathepsins, which are highly expressed in cancer cells, causing payload release. Therefore, the possibility of the linker being cleaved in parts other than cancer cells is minimized. In addition, the cleavage site is situated at an appropriate location for efficiently releasing the payload inside cancer cells.

Characteristic 7 High drug-antibody ratio

The drug-antibody ratios (the number of payloads held on a single antibody) for currently approved ADCs range unevenly between two and seven, whereas Daiichi Sankyo's ADC can load a maximum of eight payloads with high uniformity. Historically, ADCs bearing more payloads per antibody cause aggregation after being formulated. But Daiichi Sankyo's ADC construct and its formulation minimizes aggregation, even with the high DAR. For example, *DS-8201* and *U3-1402* have a DAR of eight, but they are highly uniformed. Furthermore, we possess technology to control the drug-antibody ratios according to antigen expression and internalization rates. For example, *DS-1062* is optimized as a DAR of four.

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*.

▶ADC franchise pipeline

Project (target)	Preceded indications	Discovery	Pre-clinical	Phase 1	Pivotal
DS-8201 (HER2)	Breast cancer Gastric cancer Colorectal cancer Non-small-cell lung cancer				
U3-1402 (HER3)	Breast cancer Non-small-cell lung cancer				
DS-1062 (TROP2)	Non-small-cell lung cancer				
DS-7300 (B7-H3)	Solid tumors			Start clinical study in FY2019	
DS-6157 (GPR20)	Gastrointestinal stromal tumor (GIST)			Start clinical study in FY2019	
DS-6000 (undisclosed)	Kidney cancer Ovarian cancer				
Project code pending (TA-MUC1)	Solid tumors				

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?

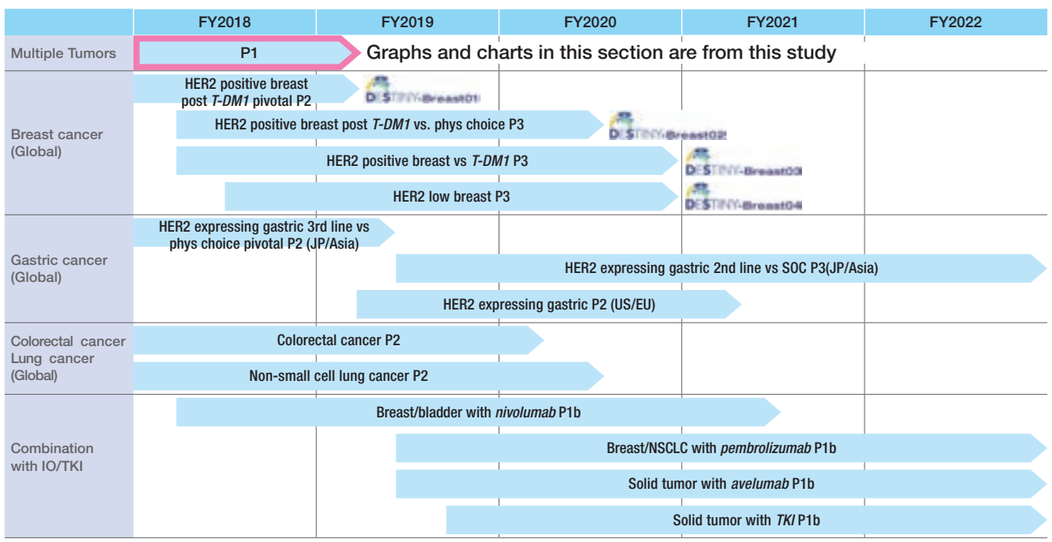
HER2 is an antigen found on the cell surface. It has a structure similar to the epidermal growth factor receptor (HER1/EGFR). It is a receptor tyrosine kinase associated with cell proliferation. HER2, which is overexpressed on the surface of cancer cells, such as those of breast cancer, gastric cancer, 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)



(3) Phase 1 study for multiple tumor targets

In the phase 1 study, which was started in September 2015, *DS-8201* was administered to approximately 300 patients with HER2-expressing breast cancer, gastric cancer, colorectal cancer, lung cancer, and other solid tumors. Although they were heavily pre-treated, many of them showed a siginificant response irrespective of cancer types.

Interim data from this study was presented at American Society of Clinlcal Oncology (ASCO), European Society for Medical Oncology (ESMO), World Conference on Lung Cancer, and San Antonio Breast Cancer Symposium (SABCS) in 2018.

In addition, papers on the breast cancer and gastric cancer from phase 1 study were accepted in April 2019 by the journal *The Lancet Oncology*. The major data compared to similar drugs are shown below.

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 second 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.

▶Phase 1 study breast cancer, comparison to similar drugs

Breast	*Pertuzumab + trastuzumab + docetaxel* (1L)†1	*T-DM1* (1L, failed study)†2	*T-DM1* (2L)†3	*T-DM1* (3L+)†4	*DS-8201*†5
mPFS	18.5m	14.1m	9.6m	6.2m	22.1m
DoR	20.2m	20.7m	12.6m	9.7m	20.7m
OS	56.5m	53.7m	30.9m	22.7m	NR
ORR	80%	60%	43.6%	31%	59.5%
Median prior Rx for adv. disease	0	0	1	4	7 100% prior *T-DM1* 88% prior *pertuzumab*

*1 CLEOPATRA (NEJM 2012), *2 MARIANNE (J Clin Oncol 2017), *3 EMILIA (NEJM 2012), *4 TH3RESA (*The Lancet Oncol* 2017) *5 *The Lancet Oncology*, 29 April 2019, m: Months, NR:Not Reached

▶Phase 1 study gastric cancer, comparison to similar drugs

Gastric	*Trastuzumab* + Chemo (1L)†1	*Ramucirumab* + Chemo (2L)†2	*T-DM1* (failed study; 2+L)†3	*DS-8201*†4
mPFS	6.7m	4.4m	2.7m	5.6m
DoR	6.9m	4.4m	4.3m	7.0m
OS	13.8m	9.6m	7.9m	12.8m
ORR	47%	28%	21%	43.2%
Median prior LoT	0	1	1	3

*1 ToGA (*The Lancet* 2010), *2 RAINBOW (*The Lancet Oncol*. 2014), *3 GATSBY (*The Lancet Oncol*. 2017), *4 *The Lancet Oncology*, published April 29, 2019, LoT: Line of Therapy, m: Month

COLUMN

Listing of abbreviations

Abbreviations	English	Implications
CR	Complete response	Complete response (complete resolution of cancer)
DCR	Disease control rate	Disease control rate (percentage of patients with controlled disease status)
DOR	Duration of response	Duration of response (duration of response)
DLT	Dose limiting toxicity	Dose-limiting toxicities (toxicities that may explain the inability to escalate doses)
MTD	Maximum tolerated dose	Maximum tolerated dose (Maximum dose of a drug that can be administered without causing unacceptable side effects)
ORR	Overall response rate	Overall response rate (expressed as the proportion of patients who responded to treatment and the sum of CR and PR)
OS	Overall survival	Overall survival (time from start of treatment to death)
PD	Progress disease	Disease progression (worsening disease despite treatment)
PFS	Progression-free survival	Progression-free survival (without cancer progression)
PR	Partial response	Partial response (a reduction in the size of the cancer by 30% or more that lasts for 4 weeks)
SD	Stable disease	The size of the cancer is almost unchanged before and after treatment

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

(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 idiosyncratic 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 an external and independent adjudication committee. At the December 2018 San Antonio Breast Cancer Symposium (SABCS), interm 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, interruption of *DS-8201* as needed and the 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.

▶ **Number of ILDs by severity in all patients**

Population	Adjudication status	Grade					Total
		1	2	3	4	5	
All subjects All doses, N = 665	Investigator reported, n (%)	30 (4.5)	23 (3.5)	6 (0.9)	2 (0.3)	5 (0.8)	66 (9.9)
	Cases adjudicated, n	16	13	4	0	5	38
	Adjudicated as drug-related ILD, n	11	12	3	0	4	30

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

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

Source: Powell *et al.*, Abstract #P6-17-06, SABCS 2018

COLUMN

Grades of adverse events

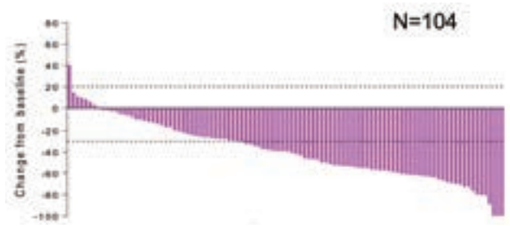
Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL
Grade 3	Severe or medically significant but not immediately life-threatening;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

(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*).

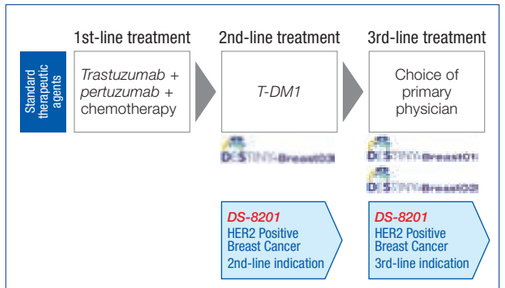
▶ **HER2 positive breast cancer (SABCS 2018)**



Source: Iwata-H *et al.*, Abstract #2501, ASCO 2018

Currently, 1) pivotal phase 2 study for third line treatment (post *T-DM1*) of HER2 positive metastatic breast cancer (DESTINY-Breast01 study), 2) phase 3 study for the same treatment (DESTINY-Breast02 study), and 3) phase 3 study for second line treatment (vs. *T-DM1*) of HER2 positive metastatic breast cancer (DESTINY-Breast03 study) are being conducted in Japan, the United States, Europe, and Asia.

▶ **HER2 positive breast cancer drug therapy**



In the drug therapy of cancer, the therapeutic drug is changed to the following drugs, when a drug becomes ineffective.

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**

US	Japan	EU
Submit application in the first half of fiscal 2019 Estimated evaluation time: 6 months after application is received by FDA **Fast Track Designation**[*1] **Breakthrough Therapy Designation** (Breakthrough Therapy)[*2]	Submit application in the second half of fiscal 2019 Estimated evaluation time: Up to 12 months after application	Submit application in the first half of fiscal 2020 Estimated evaluation time: 12 months after application

*1 A system in the U.S. aimed at expediting the development and review of drugs that can be expected to have a high therapeutic effect on severe unmet medical needs

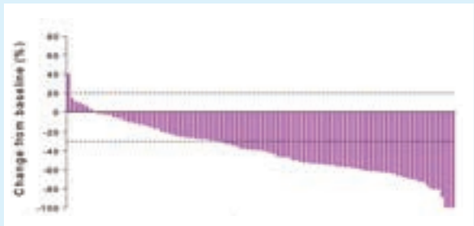
*2 A system that facilitates the development and review in the U.S. of drugs that may be more effective than existing drugs for serious diseases

COLUMN

How to Read Graphs

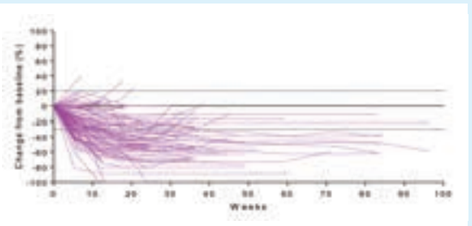
Waterfall Chart

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.



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

(6) Progress of HER2 low expression breast cancer clinical study

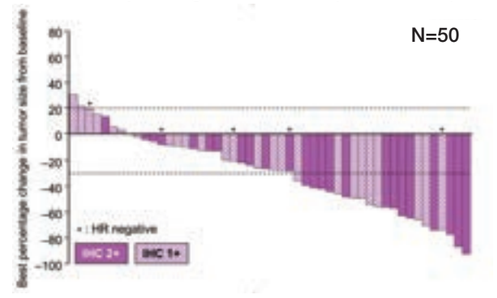
To date, breast cancers HER2 status has been classified into two types by immunostaining that detects expression: HER2-positive and HER2-negative. However, it has been revealed that HER2 is expressed (IHC2+/ISH-, IHC1+) in some types of breast cancers classified as HER2-negative. For the purposes of 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)**

N=50



	Confirmed ORR n/N (%)	Confirmed DCR n/N (%)	Duration of Response, median (range), mo	PFS median (95% CI), mo
All (N = 51)	**19/43 (44.2)**	**34/43 (79.1)**	**9.4 (1.5+, 23.6+)**	**7.6 (4.9, 13.7)**
Subgroups				
IHC 1+ (n=27)	7/21 (33.3)	14/21 (66.7)	7.9 (2.1+, 11.3)	5.7 (1.4, 7.9)
IHC 2+ (n=24)	12/22 (54.5)	20/22 (90.9)	11.0 (1.5+, 23.6+)	13.6 (NA)
HR+ (n=45)	18/38 (47.4)	31/38 (81.6)	11.0 (1.5+, 23.6+)	7.9 (4.4, 13.7)
Prior CDK4/6 inhibitor (n=15)	4/12 (33.3)	9/12 (75.0)	NR	7.1 (NA)

Source: Modi-S *et al*., Abstract #P6-17-02, SABCS 2018

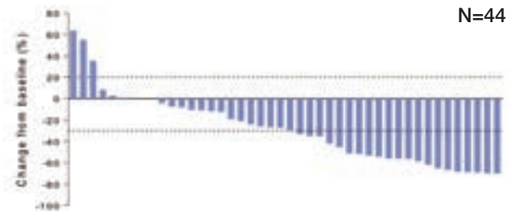
(7) Progress of gastric cancer clinical study

About 10% to 20% 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 HER 2 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)**

N=44



Source: Iwata-H *et al*., Abstract #2501, 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 SAKIGAKE 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.

COLUMN

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 gene (DNA), etc.(nuclear of cancer cell)
- Ex.) FISH (Fluorescence in situ hybridization)

Commonly Used	HER2 Status	DS terminology for Future Use	Percentage in Total Breast Cancer
HER2 positive or HER2 over-expressing	IHC 3+	HER2 positive (HER2 overexpressing)	20.3%
	IHC 2+/ISH+		
HER2 negative	IHC 2+/ISH-	HER2 low	43.9%
	IHC 1+/ISH-		
	IHC 0	HER2 negative	35.8%

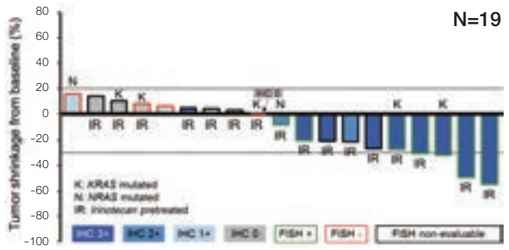
(8) Progress of colorectal cancer clinical study

About 1% to 2% of colorectal cancer patients express HER2. However, no HER2-targeting drug has been approved so far.

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

▶ **HER2-expressing Colorectal Cancer (ESMO 2018)**

N=19



	Confirmed ORR, % (n/N)	Confirmed DCR, % (n/N)	DOR, median (range), months	PFS, median (range), months	OS, median (range), months
CRC N=19	15.8% (3/19)	84.2% (16/19)	NR (0.0+, 5.5+)	3.9 (2.1,8.3)	NR (1.0+, 17.9+)

Source: Yoshino-T *et al*., Abstract #563P, ESMO 2018

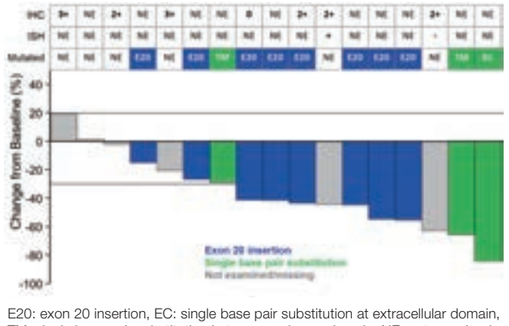
(9) Progress of lung cancer clinical study

According to the 2018 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)**

N=18



E20: exon 20 insertion, EC: single base pair substitution at extracellular domain, TM: single base pair substitution in transmembrane domain, NE: not examined.

	Comfirmed ORR, % (n/N)	Comfirmed DCR, % (n/N)	DOR, median (range), months	PFS, median (range), months
HER2-expressing or HER2-mutated NSCLC N=18	58.8% (10/17)	88.2% (15/17)	9.9 (0.0+, 11.5)	14.1 (0.9, 14.1)
HER2-mutated NSCLC N=11	72.7% (8/11)	100% (11/11)	11.5 (0.03+, 11.5)	14.1 (4.0+, 14.1)

Source: Tsurutani-J *et al*., Abstract #13325, WCLC 2018

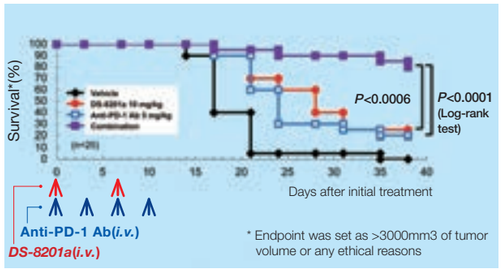
(10) Progress of studies on combinations with immune checkpoint inhibitors

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.

To identify the most effective combination, we are considering a combination study with three different immune checkpoint inhibitors. Currently, a phase 1 study in combination with *nivolumab* is underway for patients with breast cancer and bladder cancer.

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**



Source: Iwata-T *et al*., Abstract #1031, ASCO 2017

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

2 *U3-1402* (anti-HER3-ADC)

U3-1402 is an anti-HER3 ADC which our proprietary linker and payload are conjugated to *patritumab* (an anti-HER3 antibody). Several studies involving *patritumab* reached phase 2. However, limited efficacy was observed, while side effects were limited. Thus its development as an antibody drug was abandoned. It now finds new life as an ADC and is developing for potential first-in-class drug approval.

(1) What is HER3?

HER3 is found on the cell surface. It is receptor tyrosine kinase and has a structure similar to the epidermal growth factor receptor (HER1/EGFR). HER3 is over-expressed on the surface of cancer cells, such as those of breast cancer, lung cancer, colorectal cancer, and prostate cancer, and the expression of HER3 is induced by some antitumor drugs.

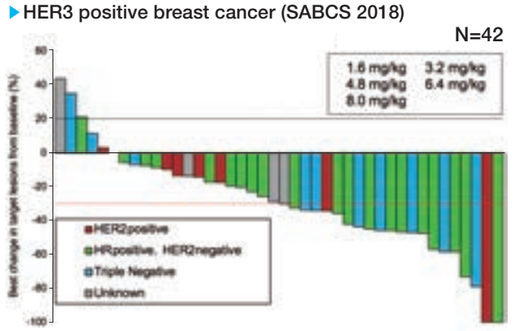
U3-1402 exerts its efficacy by binding to this HER3.

(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.

▶ HER3 positive breast cancer (SABCS 2018)



Source: Masuda-N *et al*., Abstract #PD1-03, SABCS 2018

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.

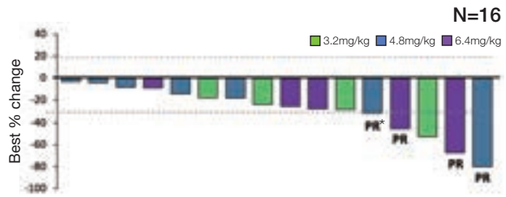
Currently, recommended dose for expansion was selected and the drug is undergoing the dose expansion part of the phase 1 study.

(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 were 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 mutated cancer cells that appear after treatment with tyrosine kinase inhibitors such as *osimertinib*. We will evaluate further.

▶ EGFRm NSCLC (ASCO 2019)



* PR: Confirmed partial response
Source: Janne-P *et al*., Abstract #9010, ASCO 2019

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 *DS-1062* (anti-TROP2-ADC)

DS-1062 is an anti-TROP2 ADC which our proprietary linker and payload are conjugated to an anti-TROP2 antibody.

(1) What is TROP2?

TROP2 is an antigen highly expressed on the membrane of cancer cells, and is known to be associated with cancer cell proliferation, metastasis, and drug resistance.

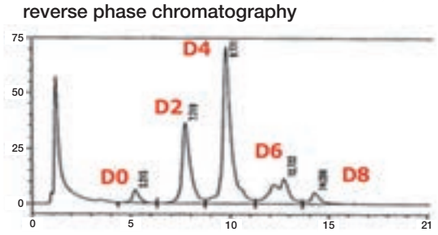
DS-1062 exerts its efficacy by binding to this TROP2.

(2) Why is the drug-antibody ratio (DAR) four?

The drug linker and payload of *DS-1062* is the same as *DS-8201* and *U3-1402*, but *DS-1062* has an average of 4 payloads per antibody compared to 8 of *DS-8201* and *U3-1402*.

Since it is known that TROP2 is expressed in normal cells, such as skin cells, the number of payloads is controlled at four in order to maintain a better safety margin.

▶ Distribution of the number of payloads by reverse phase chromatography



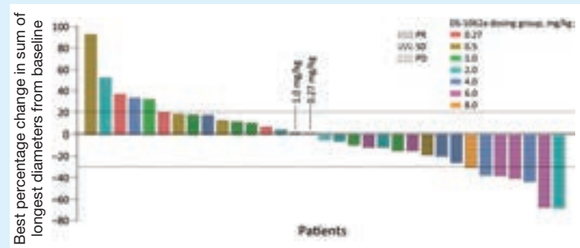
(3) Progress of non-small-cell lung cancer clinical study

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 for the first time.

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.

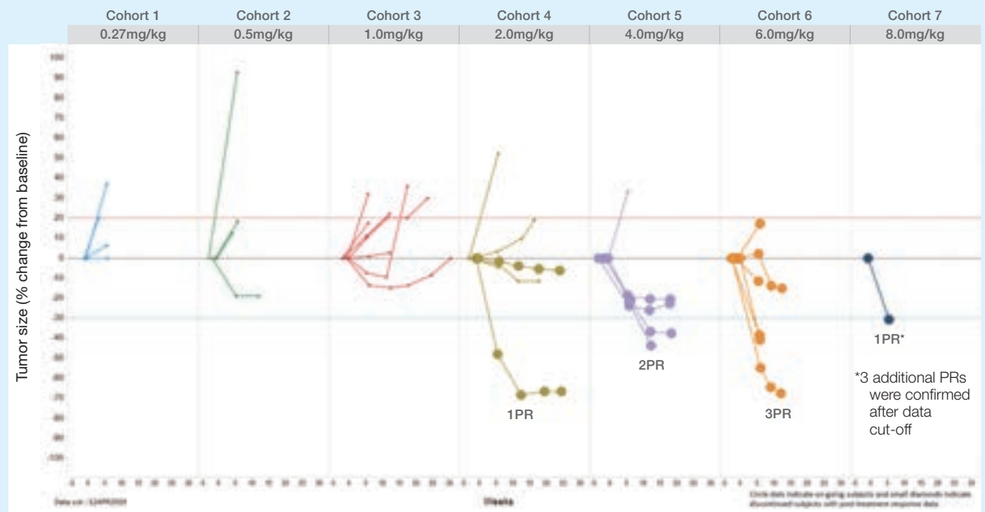
This study was conducted in NSCLC patients who were unresponsive to standard treatments, experienced recurrence with standard treatments, or where a standard treatment does not exist. In addition, as TROP2 is highly expressed in non-small-cell lung cancer, and as such, presence or absence of TROP2 expression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

▶ NSCLC (ASCO2019)



Source: Sands-J *et al*., Abstract #9051, ASCO 2019

▶ NSCLC (ASCO2019)



Source: Sands-J *et al*., Abstract #9051, ASCO 2019

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

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 I 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, initiaion 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 the *DS-8201* and *U3-1402*, with 8 payloads.

(1) What is GPR20?

GPR20 is an orphan G protein-coupled receptor (GPCR) whose ligand has not been identified. 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.

6 Other ADCs

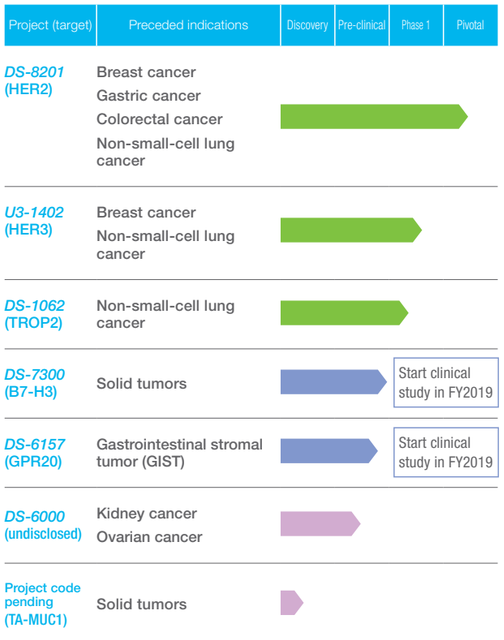
Pre-clinical research is currently underway for *DS-6000* (target undisclosed), which targets renal cancer and ovarian cancer, as well as ADC of anti-TA-MUC1 antibody from Glycotope.

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 franchise pipeline



COLUMN

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 patients by stage (new, recurrence) 2017

(thousand people)

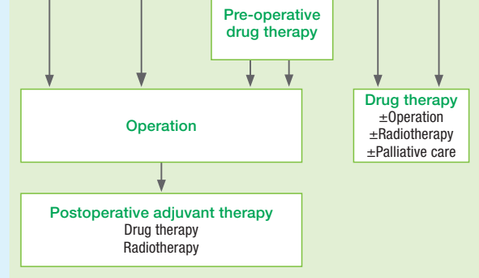
	Japan		U.S.		Europe	
	New	Recurrence	New	Recurrence	New	Recurrence
Stage 0	12	0.1	63	0.1	—	—
Stage I	40	0.1	133	2	121	1
Stage II	33	1	84	2	88	2
Stage III	7	1	26	3	35	4
Stage IV	2	9	16	27	16	30
Total	95	11	321	34	260	37

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

Breast cancer is 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.

Stage 0	Non-invasive cancer (including Paget's disease)
Stage I	The lump (tumor) in the breast is 20 mm or smaller and has not spread to the lymph nodes
Stage II	The lump is between 20 mm-50 mm and has not spread to the lymph nodes or the lump is 20 mm or smaller and has spread to the lymph nodes
Stage III	The lump has spread to several lymph nodes The lump is larger than 50 mm and has spread to the lymph nodes The lump has spread to skin and chest wall, inflammatory breast cancer
Stage IV	The lump has spread to other organs (lung, bone, liver, brain, etc.)

Source: created based on the Nyugan toriatsukai kiyaku [Breast cancer handling rules] 18th edition



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

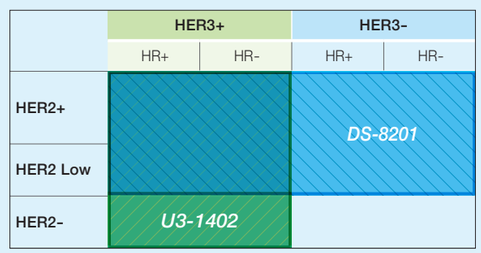
In drug therapy for breast cancer, tests are performed to look at receptors on cancer cells first, and select anticancer drugs which are appropriate for the receptor status.

Subtype	Treatment option (example)
HER2 positive	HER2 targeted drugs
HR* positive / HER2 negative	Hormone therapy
HR negative / HER2 negative (triple negative)	Chemotherapy

* hormone receptor

We are conducting clinical studies in *DS-8201* for HER2 positive and HER2 low metastatic breast cancer and in *U3-1402* for HER3 positive refractory/metastatic breast cancer.

▶ Breast cancer subtype classification and our pipeline



COLUMN

Lung Cancer

The current status of lung cancer and the existing standard treatments

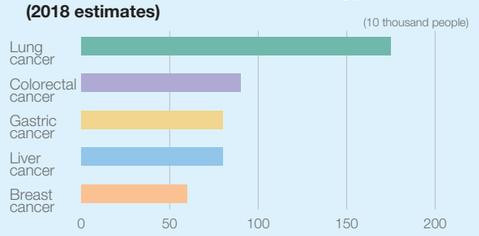
Lung cancer occurs when bronchi or lung cells become cancerous through a variety of factors, with smoking known to be the largest risk factor. Other risk factors include chronic obstructive pulmonary disease, the inhalation of asbestos, arsenic, chromium, or other carcinogens due to occupational exposure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

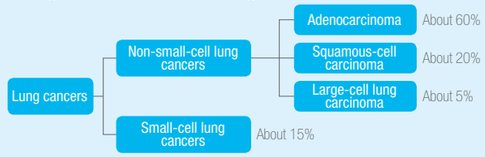
The following paragraphs describe treatments for non-small-cell lung cancers.

Number of deaths related to different types of cancers (2018 estimates)



Source: Based on WHO CANCER TODAY

Organizational chart of lung cancers



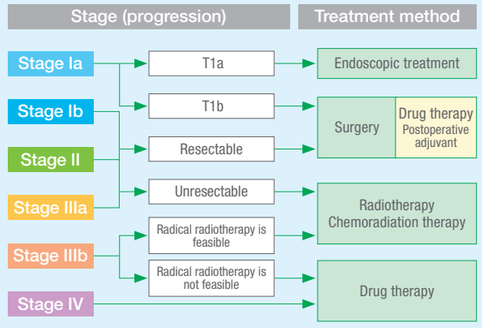
Source: Based on an illustrated reference guide, vol. 3

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 metastasis (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 IIIb to IV, but recent methods of treatment involve selecting drugs after investigating the genetic mutations in the cancers.

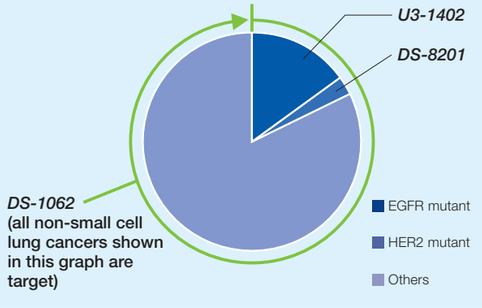
In Daiichi Sankyo several clinical studies are underway for NSCLC; *DS-8201* for HER2-expressing or HER2 mutated NSCLC, *U3-1402* for EGFR-mutated NSCLC and *DS-1062* for NSCLC patients who are unresponsive or progressed with standard of therapy.



Source: Based on an illustrated reference guide, vol. 3

Stage	Treatment option (example)
I	Postoperative adjuvant chemotherapy
II-IIIa	Postoperative adjuvant chemotherapy (cisplatin and vinorelbine in combination)
IIIb-IV	Selecting molecular targeted drugs to use based on the results of genetic and PD-L1 testing

Percentage of non-small cell lung cancer driver genes (US/EU) and our pipeline



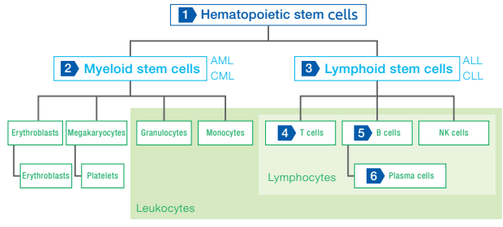
Daiichi Sankyo's AML Franchise

Leukemia is a disease in which hematopoietic stem cells in the bone marrow multiply at an abnormal rate and then become cancerous. Leukemia is classified into four types: acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphocytic leukemia (ALL) and chronic lymphocytic leukemia (CLL). Although there are cancer types such as CML for which remission can be expected with molecular targeted drugs, the five-year survival rate of AML is still about 26%, which is very low. Daiichi Sankyo is developing AML therapeutics with various targets, aiming to eliminate AML unmet medical needs.

AML franchise pipelines

Development status	Stage	Mechanism of action
Quizartinib (FLT3)	P3/LCM	FLT3 inhibitor. Displays a potent inhibitory activity against mutated gene called FLT3-ITD, which is present in around 30% of AML patients.
DS-3032 (MDM2)	P1	MDM2 inhibitor. Activates p53, a tumor suppressor gene, by inhibiting MDM2, which suppresses wild-type p53 activity.
DS-3201 (EZH1/2)	P1	EZH1/2 inhibitor. Both EZH1 and EZH2 are an enzyme to suppress gene expression. Inhibits both EZH1 and EZH2 which facilitating the inactivation of tumor suppressor genes.
PLX2853 (BET)	P1	BET inhibitor. Suppresses the expression of cancer related genes by inhibiting binding between BET and histone acetylated lysine.
Axi-Cel® (CD19 CAR-T)	P2	A cell therapy (chimeric antigen receptor T cell: CAR-T) targeting CD19 expressed on the surface of B cells.

Differentiation of hematopoietic stem cell



	Disease	Overview	Applicable Daiichi Sankyo Compounds
1	Myelodysplastic syndrome	● Disease resulted from abnormality in hematopoietic stem cells	*DS-3032*
2	Myeloid leukemia	● Disease in which myeloid stem cells become cancerous ● Acute (AML) and chronic (CML) variations	*Quizartinib* *DS-3201,* *DS-3032,* *PLX2853*
3	Lymphocytic leukemia	● Disease in which lymphoid cells become cancerous ● Acute (ALL) and chronic (CLL) variations	*DS-3201*
4	T-cell lymphoma	● Generic term for hematopoietic tumors derived from mature T cells. Peripheral T-cell lymphoma (PTCL), adult T-cell lymphoma (ATL), etc.	*DS-3201*
5	B-cell lymphoma	● non-Hodgkin's lymphoma in which B-cell become cancerous	*DS-3201* *Axi-Cel®*
6	Multiple myeloma	● Disease in which plasma cells in bone marrow become cancerous	

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.

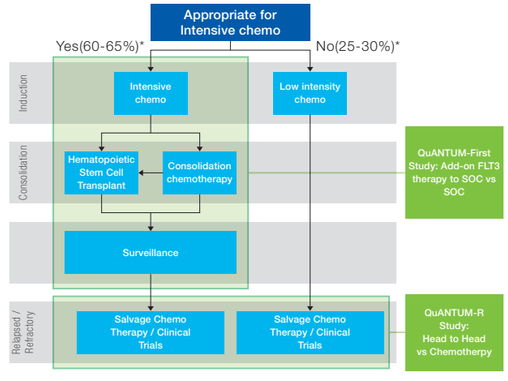
In Japan, the Ministry of Health, Labour and Welfare approved *quizartinib* for the treatment of relapsed/refractory FLT3-ITD AML in June 2019. We will launch it under the brand name *VANFLYTA*®.

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 a first line treatment for AML as well as in continuation therapy.

* A document issued by the FDA when the approval application has been reviewed and the current content does not result in approval



* Patients who cannot treated by intensive/low intensity chemo (5-10%)

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

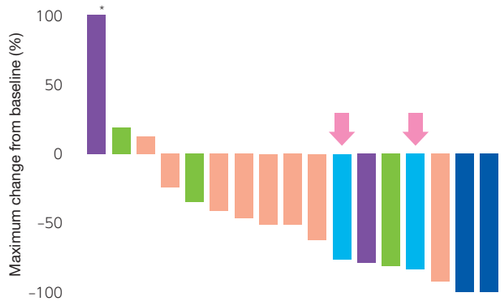
2 *DS-3201* (EZH1/2 inhibitor)

EZH1 and EZH2 are histone-methylating enzymes with similar functions, and some cancer cells shows dependent growth on them.

The phase 1 study of *DS-3201* is currently underway in patients with relapsed/refractory non-Hodgkin's lymphoma in Japan and the US. Based on the favorable interim data from this study, particularly in patients with relapsed or refractory peripheral T-cell lymphoma (PTCL), the Ministry of Health, Labour and Welfare has granted *DS-3201* SAKIGAKE Designation.

PTCL is a type of non-Hodgkin's lymphoma that occurs in T-cells, and is said to have a particularly poor prognosis if it recurs. There are few treatment options and a high degree of unmet medical need.

Non-Hodgkin's lymphoma (ASH 2017)



(N=2) Adult T-cell leukemia/lymphoma (ATL/L)
(N=2) Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS)
(N=2) Angioimmunoblastic T-cell lymphoma (AITL)
(N=3) Diffuse large B-cell lymphoma (DLBCL)
(N=8) Late-onset B-cell lymphoma

* Tumor size increase of 147% truncated at 100%

Source: Maruyama-D *et al.*, Abstract #4070, ASH 2017

The phase 1 study of *DS-3201* is ongoing in the U.S. in patients with relapsed/refractory acute myeloid leukemia and acute lymphatic leukemia. In addition, phase 1 study is ongoing in the U.S. in patients with small cell lung cancer.

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.*

* The foundation of drug development and therapeutic approaches such as protein drugs including low molecular compounds, peptide (medium sized molecule) drugs, and antibody drugs, nucleic acid drugs, cell therapy and regenerative medicine.

Breakthrough science pipeline

Products (Targets)	Indication	Mechanism of action
Pexidartinib (CSF-1R/KIT/FLT3)	Submitted	Receptor tyrosine kinase inhibitor showing specific inhibitory activity against CSF-1R, KIT and FLT3-ITD
DS-1647 (*G47Δ*) (oncolytic herpes virus)	P2	A third-generation strand 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
DS-1205 (AXL)	P1	AXL receptor tyrosine kinase inhibitor. High expression of AXL is said to be associated with resistance to EGFR tyrosine kinase inhibitors in EGFR-mutant non-small cell lung cancer
DS-1001 (mutant IDH1)	P1	A selective inhibitor of mutant isocitrate dehydrogenase IDH1. Inhibits mutant enzyme expressed by IDH1 gene mutation frequently seen in malignant brain tumors (glioma), acute myeloid leukemia, cholangiocarcinoma, chondrosarcoma

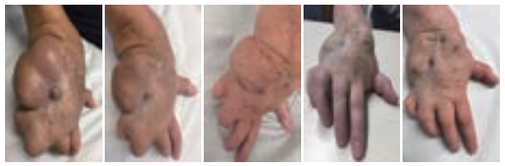
1 *Pexidartinib* (CSF-1R/KIT/FLT3 inhibitor)

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 *Turalio*™. 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.

Extreme example of effective treatment from phase 3 study (ENLIVEN Study)



October, 2016 November, 2016 September, 2017 June, 2017 May, 2018

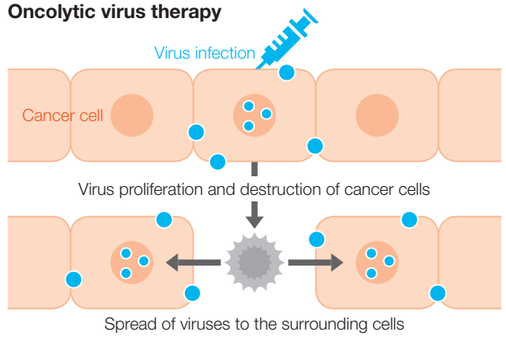
2 *DS-1647* (oncolytic virus *G47Δ*)

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 efficacy. 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



COLUMN

Classification of gliomas

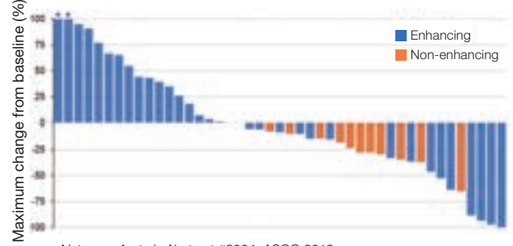
A glioma is a type of malignant brain tumor that begins in glial cells in the brain and spinal cord. Brain tumors are not staged like other cancer but are classified as grades I to IV.

Malignancy Grade	Major Types of Glioma	
	Diffuse stellate cell tumor	Oligodendrocyte tumor
Ⅱ	Diffuse astrocytoma	Oligodendroglioma
Ⅲ	Anaplastic astrocytoma	Anaplastic oligodendroglioma
Ⅳ	Glioblastoma	

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)



urce: Natsume-A *et al.*, Abstract #2004, ASCO 2019

Enhancing	Patients who have tumor(s) with gadolinium enhancement on MR 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.