

Passion for Innovation.  
Compassion for Patients.™



# **Deliver ADC Assets**

## **to as Many Patients as Possible as Fast as We Can**

**DAIICHI SANKYO CO., LTD.**

**Sunao Manabe**  
President and CEO

January 13, 2020

# Forward-Looking Statements

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**① Overview of Daiichi Sankyo**

**② R&D Focus**

**③ Upcoming Events and News**

**④ Key Takeaways**



# ① Overview of Daiichi Sankyo

## ② R&D Focus

## ③ Upcoming Events and News

## ④ Key Takeaways



# Financial Summary

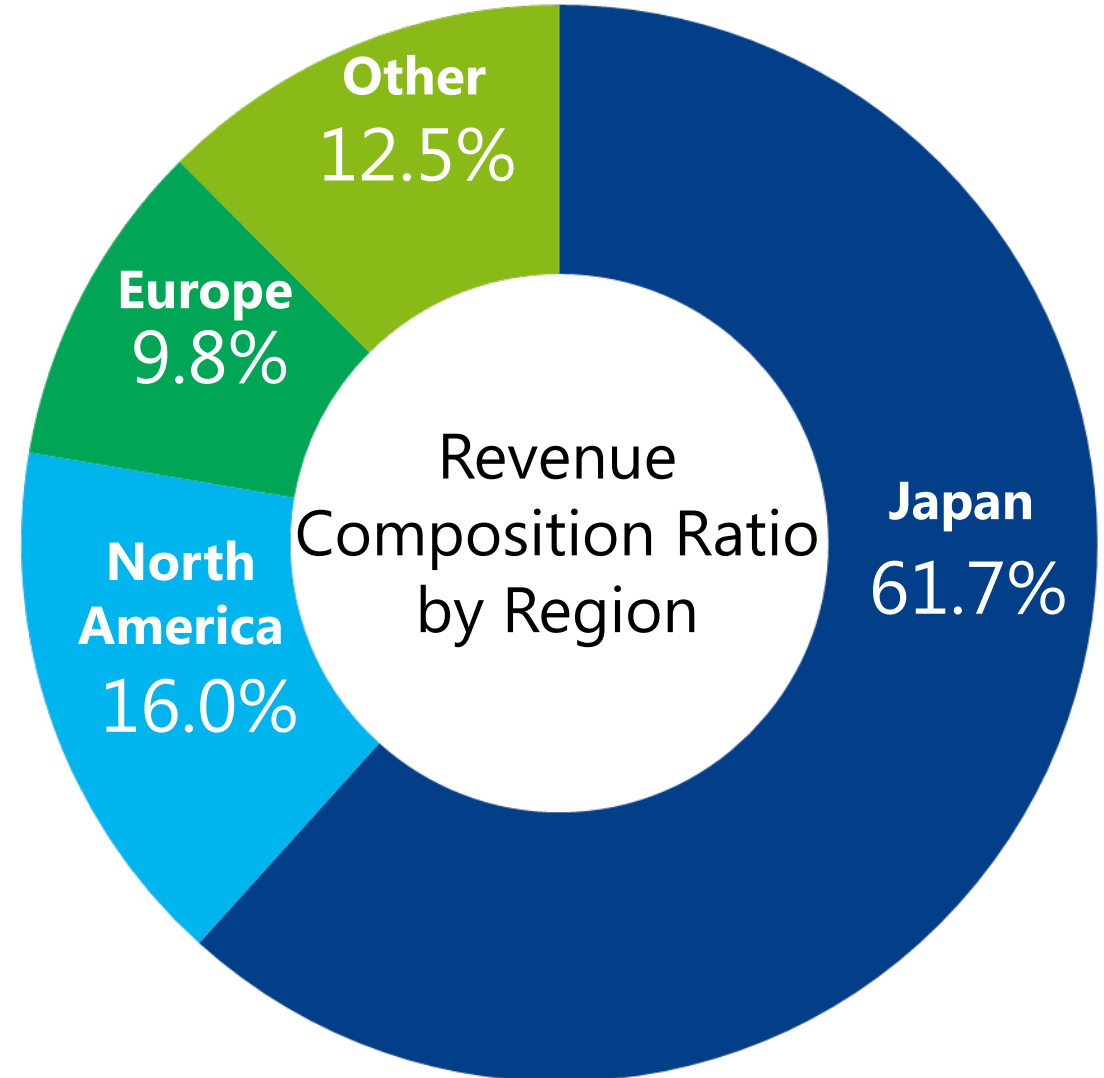
## FY2019 Forecast

Bn JPY

Ratio to revenue

<b>Revenue</b>	<b>955.0</b>	<b>100%</b>
<b>Cost of sales</b>	<b>330.0</b>	<b>34.6%</b>
<b>SG&amp;A expenses</b>	<b>290.0</b>	<b>30.4%</b>
<b>R&amp;D expenses</b>	<b>210.0</b>	<b>22.0%</b>
<b>Operating profit</b>	<b>125.0</b>	<b>13.1%</b>
<b>Profit attributable to owners of the Company</b>	<b>90.0</b>	<b>9.4%</b>

## FY2019 Forecast



# Major Products in Japan

Anticoagulant

★ **LIXIANA**



64.9 Bn JPY

Antihypertensive agent

**Olmotec**



14.9 Bn JPY

Antiplatelet agent

**Efient**



13.9 Bn JPY

Ulcer treatment

★ **NEXIUM**



78.3 Bn JPY

Alzheimer's disease treatment

★ **Memary**



50.2 Bn JPY

Type 2 diabetes mellitus treatment

**TENELIA**



25.3 Bn JPY

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

★ **PRALIA**



27.4 Bn JPY

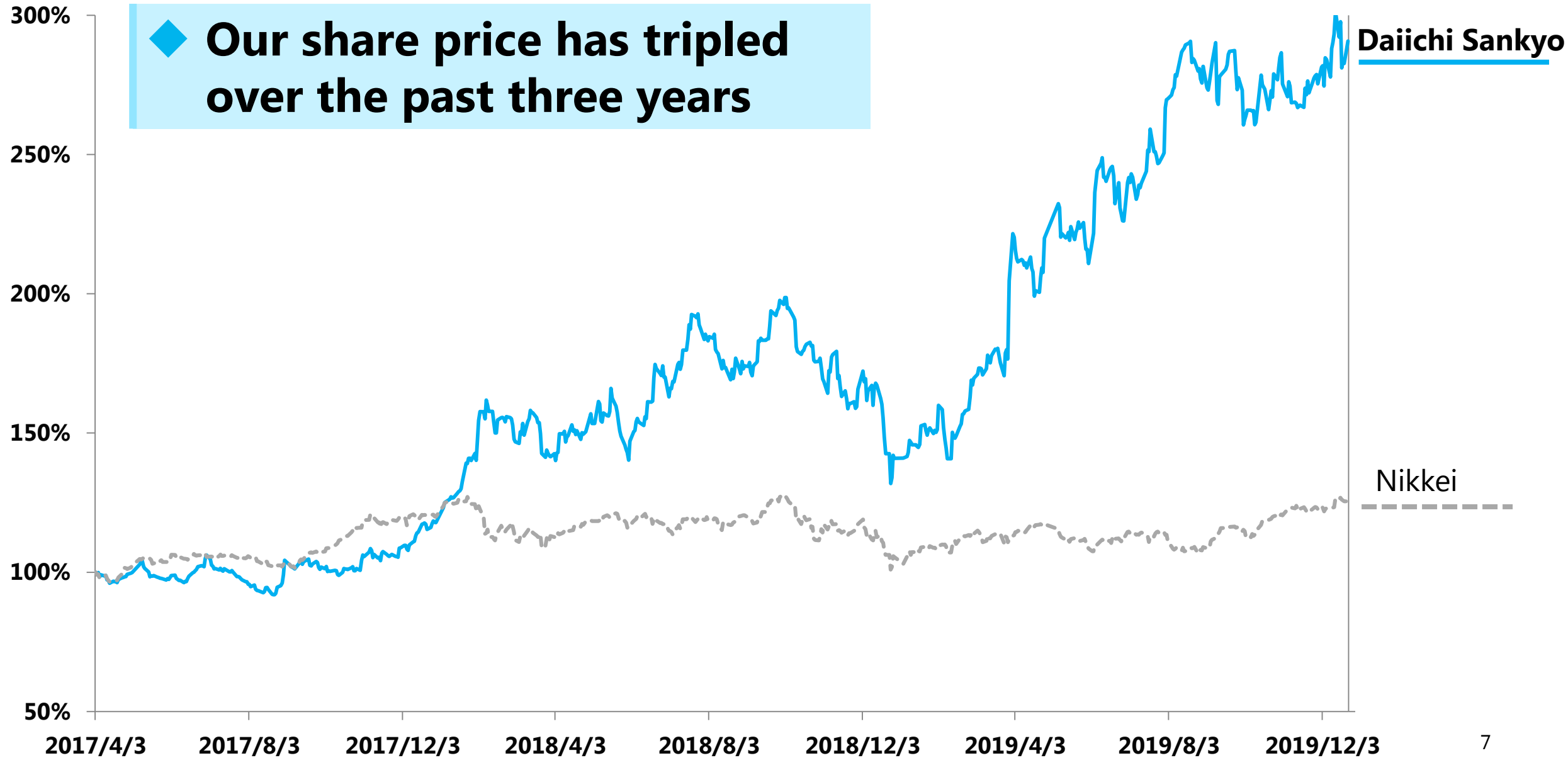
Treatment for bone complications  
caused by bone metastases from tumors

★ **RANMARK**



16.4 Bn JPY

# Share Price



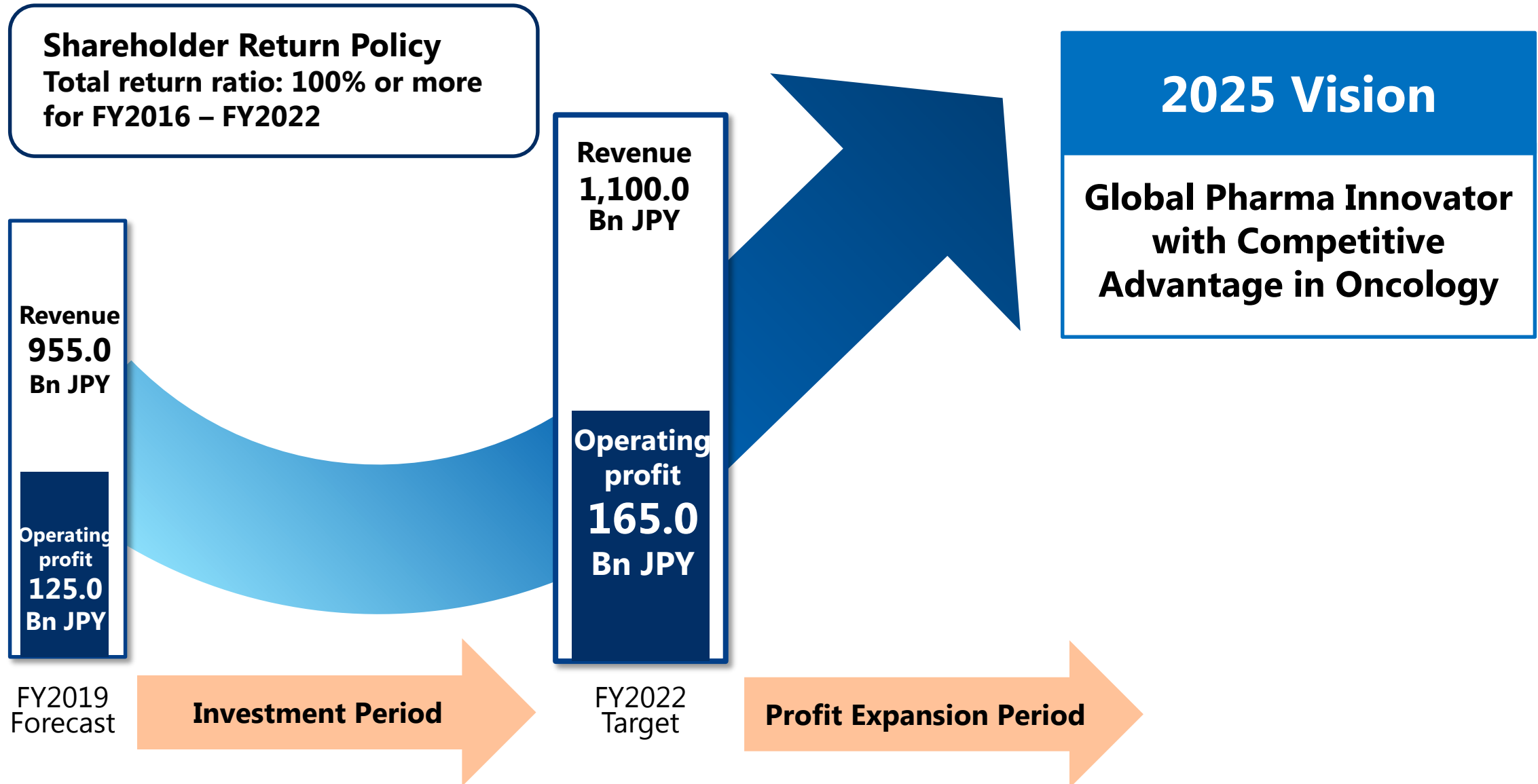
## Global Pharma Innovator with Competitive Advantage in Oncology

- *Build a specialty area\* centered on oncology as the core business*
- *Enrich regional value aligned with market needs*
- *Create innovative products*
  - *change SOC (Standard of Care)*
- *Realize shareholder value through highly efficient management*

\*specialty area: Drugs mainly prescribed at hospital and/or by specialty practitioners



# Five-Year Business Plan Targets



# ① Overview of Daiichi Sankyo

**Key Products**

**Edoxaban**

**TURALIO**

# ② R&D Focus

# ③ Upcoming Events and News

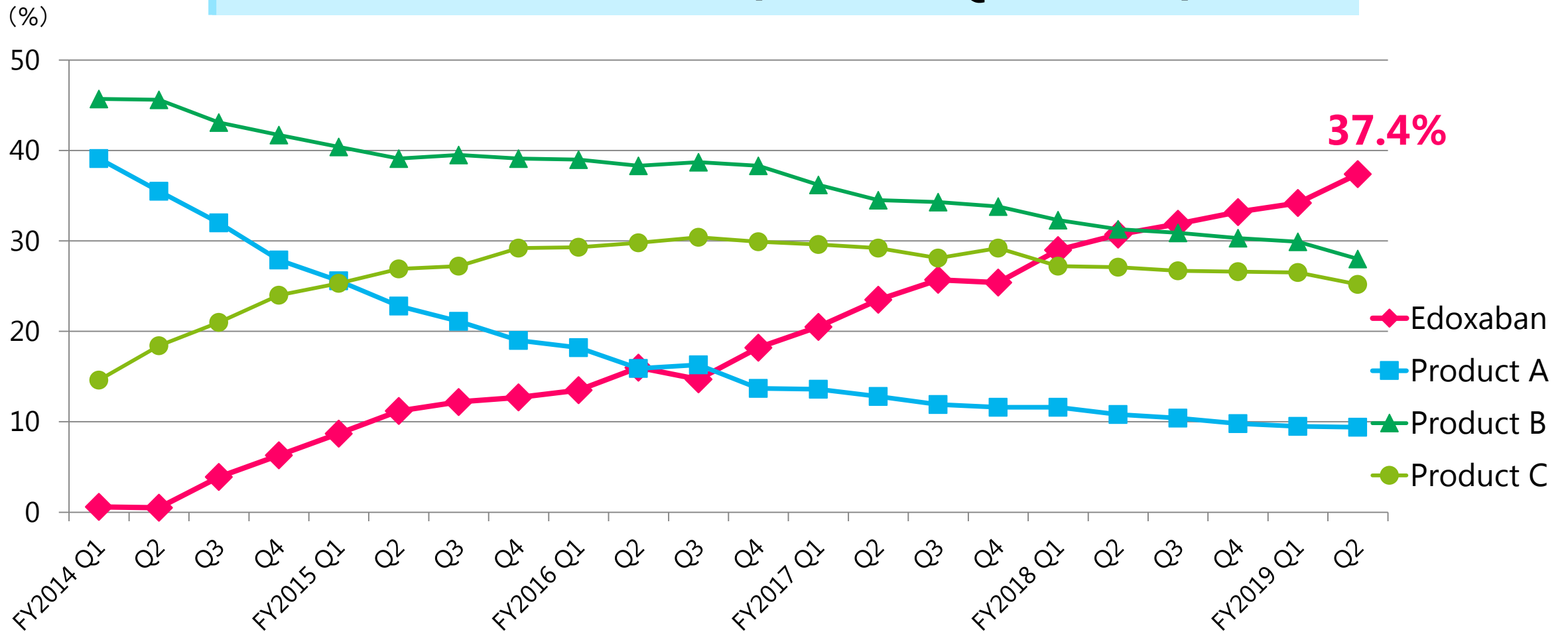
# ④ Key Takeaways



# Edoxaban: Growth in Japan



◆ No. 1 market share (FY2019 Q2: 37.4%)



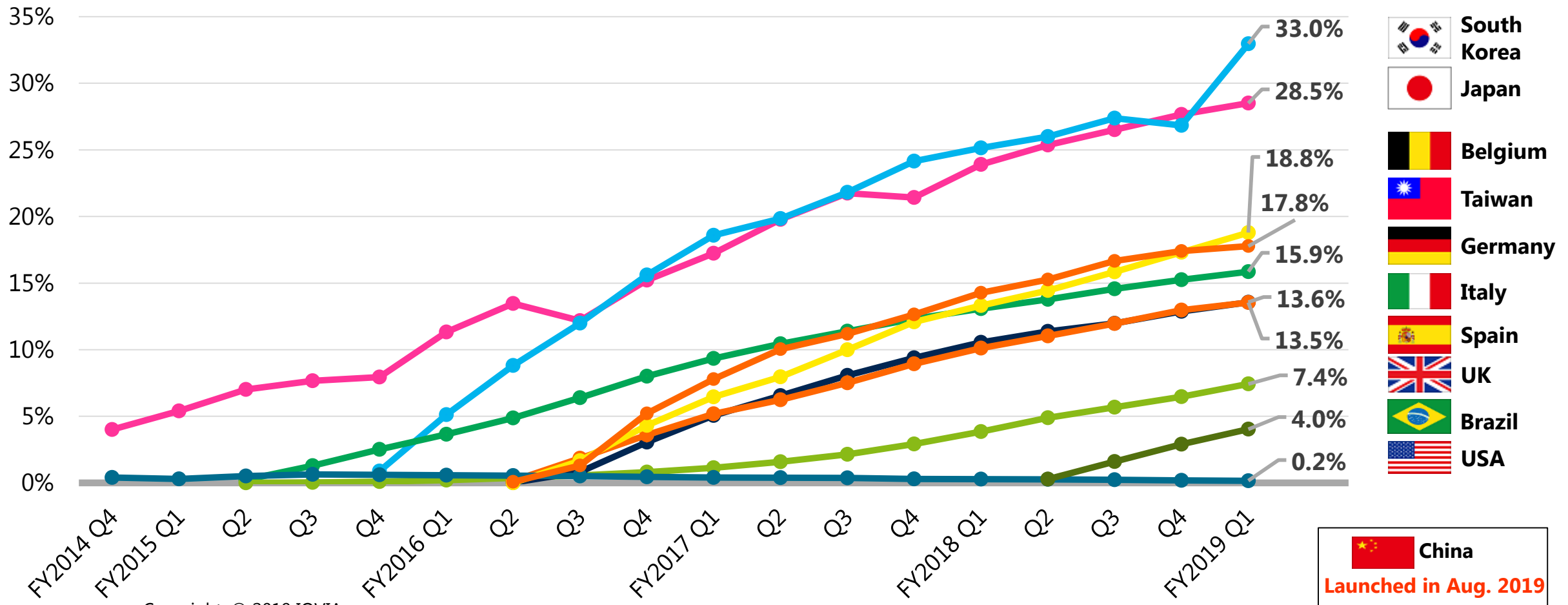
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# Edoxaban: Global Expansion

Volume



## ◆ Steady growth across markets



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## ◆ First and only FDA approved therapy for tenosynovial giant cell tumors (TGCT), launched in August 2019

- Indicated for adult patients with symptomatic TGCT associated with severe morbidity or functional limitations and not amenable to improvement with surgery



Localized TGCT	Diffuse TGCT
~80-90% of TGCT cases	~10-20% of TGCT cases
U.S. incidence (2019) ~15,000	U.S. incidence (2019) ~1,500

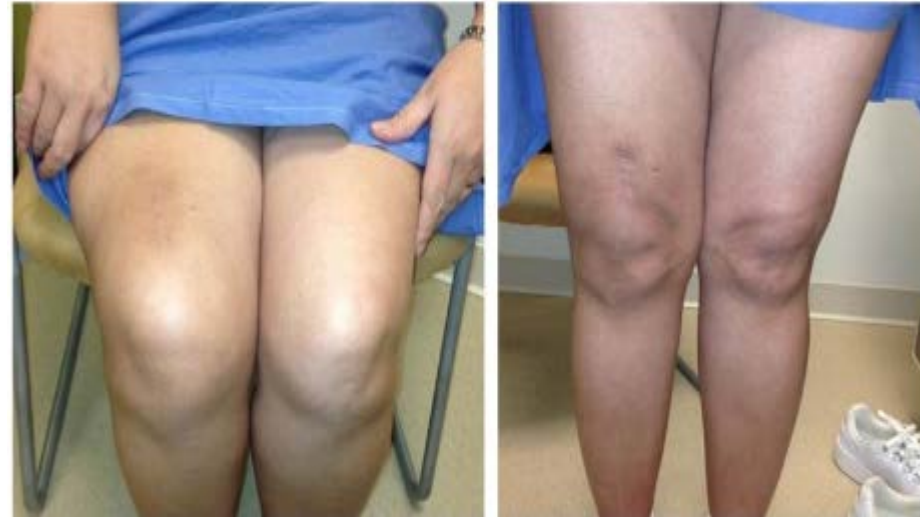
Hepatotoxicity with ductopenia and cholestasis has occurred in patients treated with TURALIO. Across 768 patients who received TURALIO in clinical trials, there were two irreversible cases of cholestatic liver injury. One patient died with advanced cancer and ongoing liver toxicity and one patient required a liver transplant. The mechanism of cholestatic hepatotoxicity is unknown and its occurrence cannot be predicted. It is unknown whether liver injury occurs in the absence of increased transaminases.

## ◆ Example of effective treatment

Before Treatment



After Treatment



- 56 years old female
- Diagnosed TGCT in 1988, followed by multiple surgeries
- Started Pexidartinib in Sep 2016 and still on-going

**1 Overview of Daiichi Sankyo**

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**4 Key Takeaways**



## **1. Realize 2025 Vision**

Deliver ADC assets to as many patients as possible as fast as we can

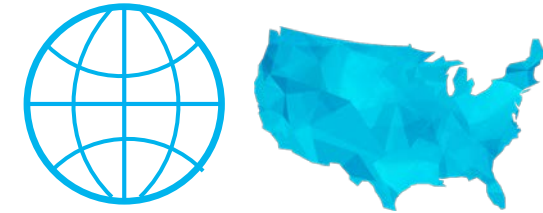
## **2. Strive for Sustainable Growth**

Creating assets beyond current ADCs



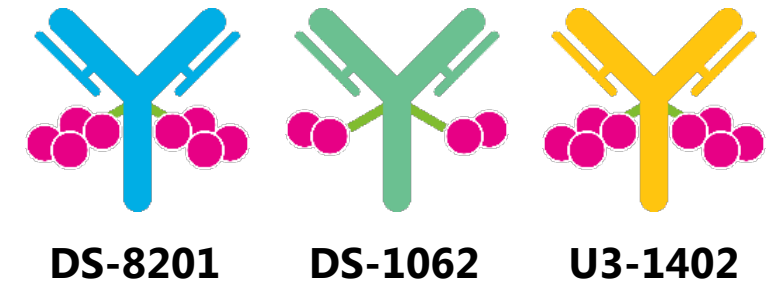
## ◆ Become world's No. 1 ADC company

### ◆ Enhance global development and commercial capabilities



### ◆ Expand investments

- Focusing R&D investments primary on 3 ADCs
- Invest more than 100.0 Bn JPY in CMC and manufacturing



**Realize 2025 Vision**

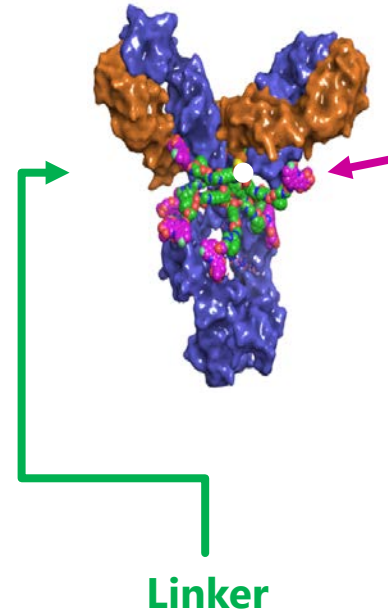
**“Global Pharma Innovator with Competitive Advantage in Oncology”**

# Seven ADC Assets and Major Innovations

## Seven ADC Assets

Project (Target)	Potential indications	Clinical Stage			
		Discovery	Pre-clinical	Phase 1	Pivotal/ approved
<b>DS-8201 (HER2)</b>	Breast, Gastric, NSCLC, CRC	[Progress bar: Discovery to Pivotal/ approved]			
<b>U3-1402 (HER3)</b>	Breast, NSCLC	[Progress bar: Discovery to Phase 1]			
<b>DS-1062 (TROP2)</b>	NSCLC	[Progress bar: Discovery to Phase 1]			
<b>DS-7300 (B7-H3)</b>	Solid tumors	[Progress bar: Discovery to Phase 1]			
<b>DS-6157 (GPR20)</b>	GIST	[Progress bar: Discovery to Pre-clinical]			
<b>DS-6000 (undisclosed)</b>	Renal, Ovarian	[Progress bar: Discovery to Pre-clinical]			
<b>DS-3939 (TA-MUC1)</b>	Solid tumor	[Progress bar: Discovery to Pre-clinical]			

## Seven Major Innovations



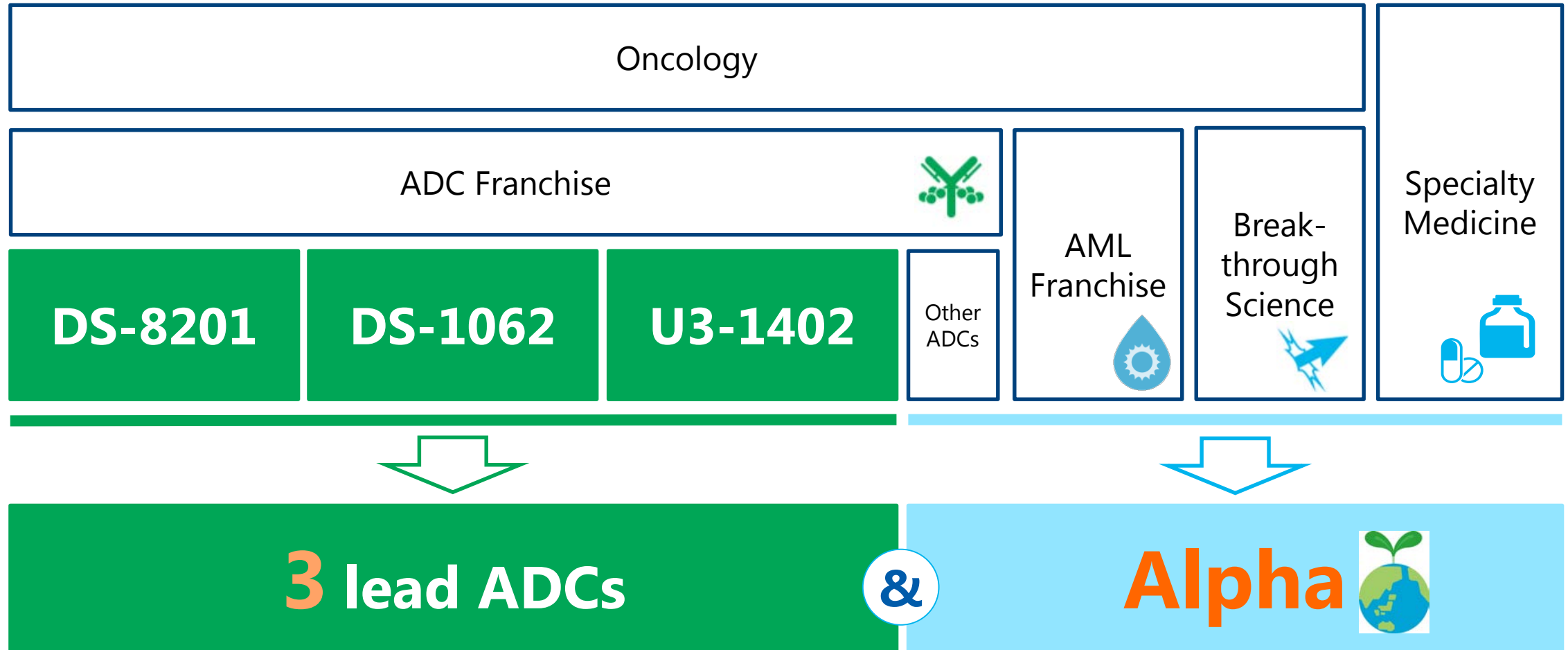
### Payload

- Novel cytotoxic MOA
- 10X more potent vs SN38
- High cell membrane cross-penetration for bystander effect, killing neighboring tumor cells
- Short systemic half-life

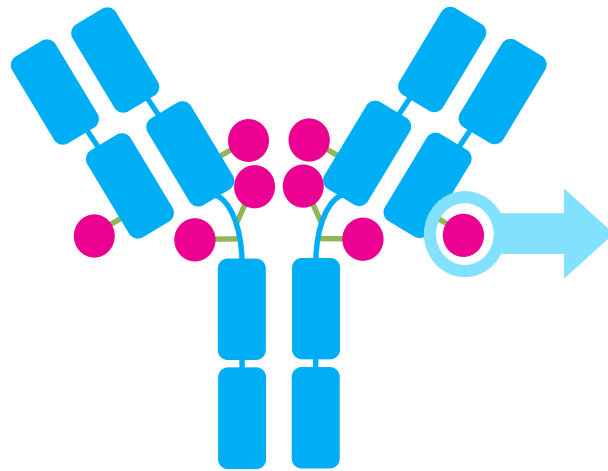
### Linker

- High stability, sparing non-cancerous tissue from toxicity
- Selectively cleaved by lysosomal enzymes that are upregulated in tumor cells
- Capability to accommodate a High number of payloads per antibody (DAR, drug antibody ratio)

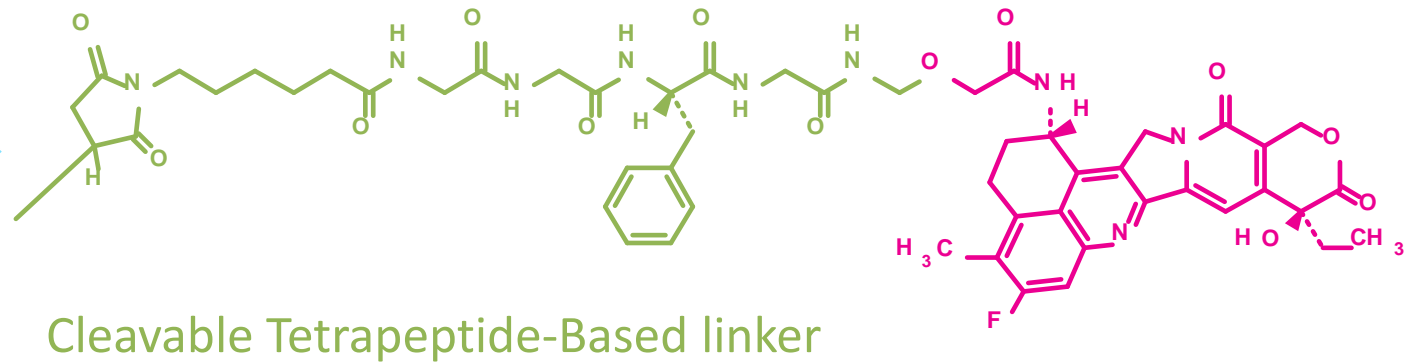
# New R&D Focus: 3 and Alpha



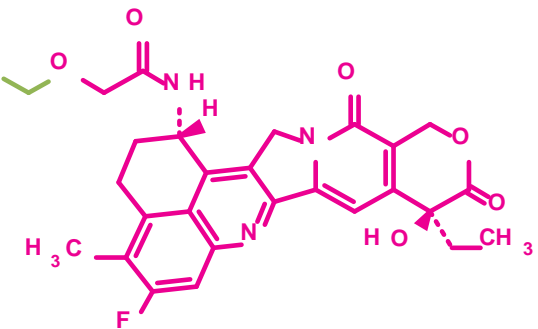
Humanized anti-HER2  
IgG1 mAb



DAR  $\approx$  8



Topoisomerase I Inhibitor payload  
(DXd)



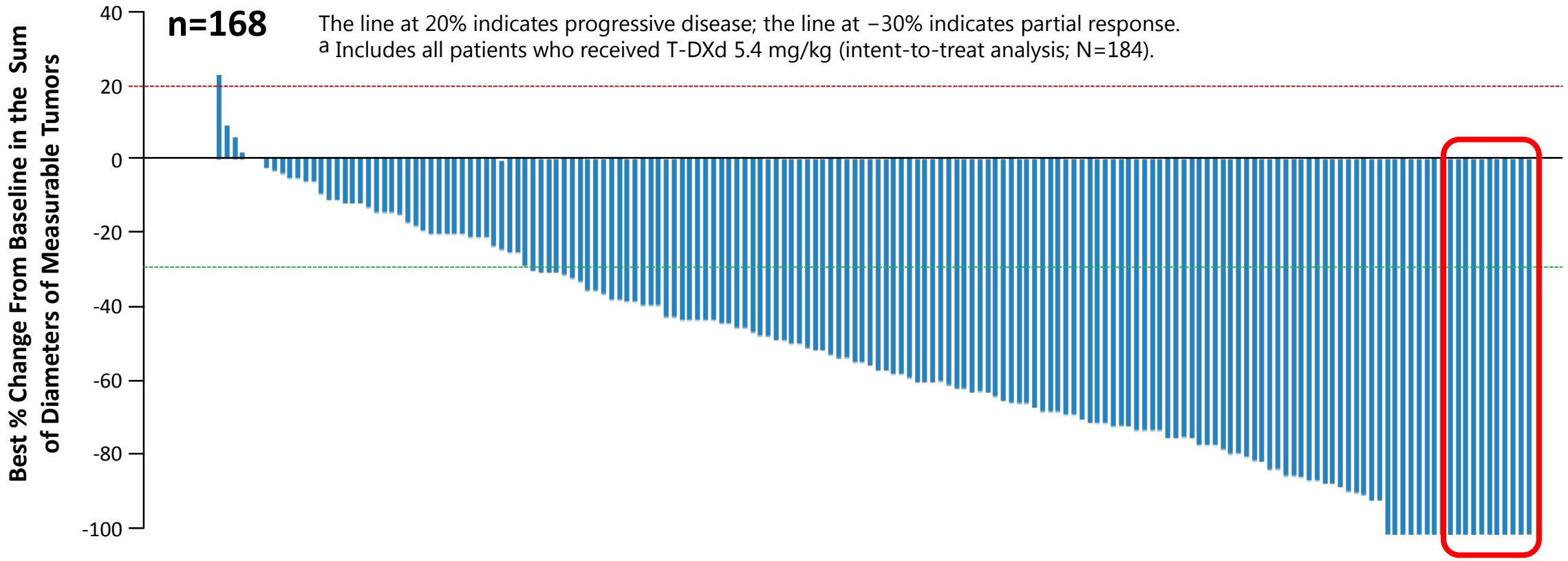
# ENHERTU®: Now Launched in U.S.

## ◆ DS-8201: Remarkable speed to approval



ENHERTU® (fam-trastuzumab deruxtecan-nxki), a HER2 directed antibody drug conjugate (ADC), is indicated for the treatment of adult patients with unresectable or metastatic HER2 positive breast cancer who have received two or more prior anti-HER2-based regimens in the metastatic setting. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. ENHERTU is approved with a Boxed WARNING for Interstitial Lung Disease (ILD)/pneumonitis and Embryo-Fetal Toxicity.

◆ **Confirmed ORR: 60.9%<sup>a</sup>** (95% CI, 53.4%–68.0%)  
◆ **11 CRs**



ENHERTU is approved with a Boxed WARNING for Interstitial Lung Disease (ILD)/pneumonitis and Embryo-Fetal Toxicity. The data on this slide was presented at San Antonio Breast Cancer Symposium®, December 10-14, 2019. This presentation is the intellectual property of the author/presenter; it is being used with permission from the author.

# DS-8201: How Does it Compare?

These are not head to head comparison data

	Pertuzumab + trastuzumab + docetaxel (1L) <sup>1</sup>	T-DM1 (1L, failed study) <sup>2</sup>	T-DM1 (2L) <sup>3</sup>	T-DM1 (3L+) <sup>4</sup>	DS-8201 <sup>5</sup>
mPFS	18.5m	14.1m	9.6m	6.2m	<b>16.4m</b>
DoR	20.2m	20.7m	12.6m	9.7m	<b>14.8m</b>
OS	56.5m	53.7m	30.9m	22.7m	<b>NE</b>
ORR	80%	60%	43.6%	31%	<b>60.9%</b>
Median prior Rx for adv. disease	0	0	1	4	<b>6</b> 100% prior T-DM1 66% prior pertuzumab

<sup>1</sup>CLEOPATRA (NEJM 2012), <sup>2</sup>MARIANNE (J Clin Oncol 2017), <sup>3</sup>EMILIA (NEJM 2012), <sup>4</sup>TH3RESA (Lancet Oncol 2017),

<sup>5</sup>Lancet Oncology, April 29, 2019, m: Month, NR:Not Reached

# DS-8201: Strategic Collaboration with AstraZeneca

◆ Financial Consideration: **Up to \$6.9 billion** in total\*

*Unique  
Science*



*Extensive expertise  
in oncology*



Opportunity for strategic collaboration with excellent partner with a rich heritage in breast cancer



Accelerate building in-house oncology business infrastructure, while optimizing resources



Maximize product value oncology products

- Earlier penetration in global market
- Expand to new indications

\* Incl. upfront payment, regulatory and other contingencies (max) and sales-related milestones (max)

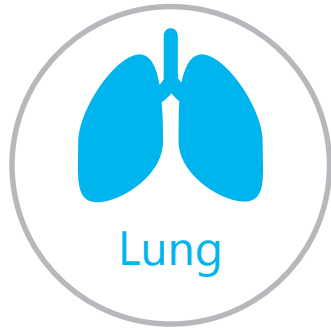


# DS-8201: Directional View of CDP



Breast

**4**  
studies



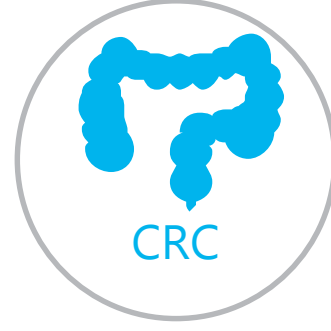
Lung

**1**  
study



Gastric

**2**  
studies



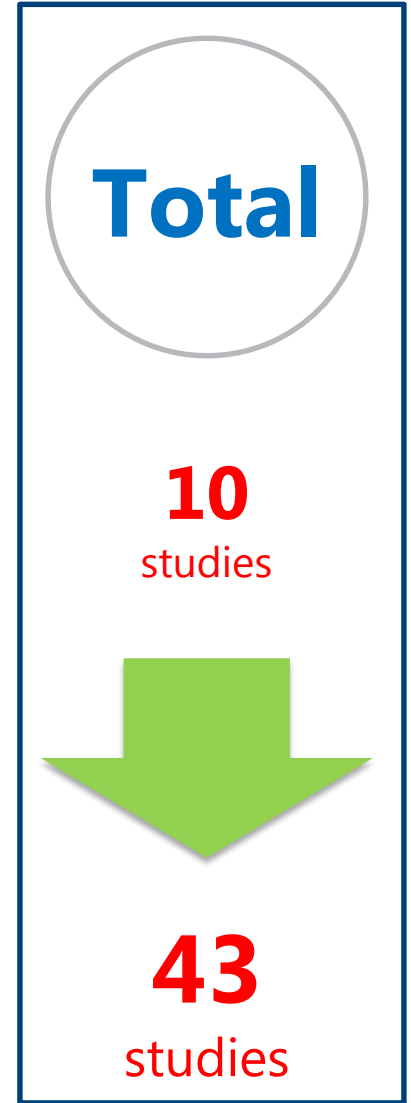
CRC

**1**  
study




Tumor Agnostic,  
I/O Combination,  
Multiple tumors,  
Others

**2**  
studies



**Total**

**10**  
studies



**43**  
studies

**16**  
studies

**7**  
studies

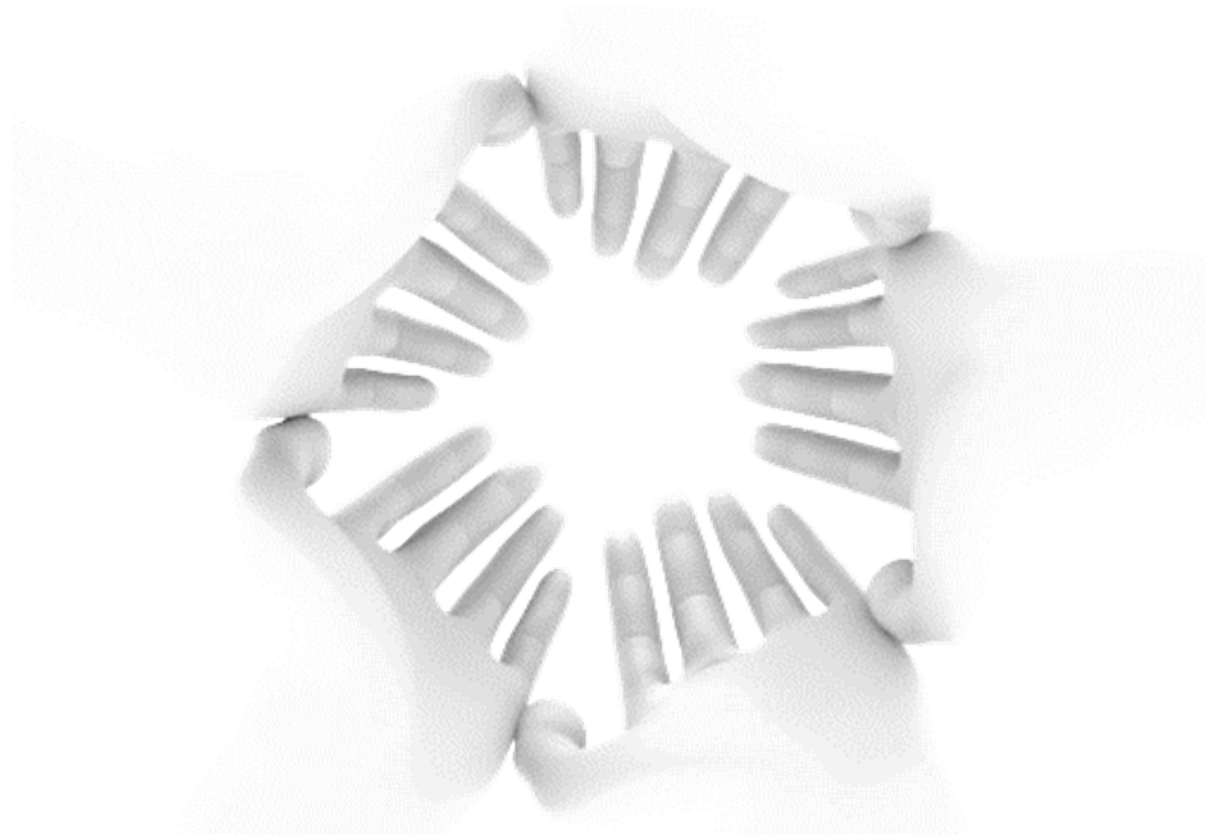
**5**  
studies

**6**  
studies

**9**  
studies

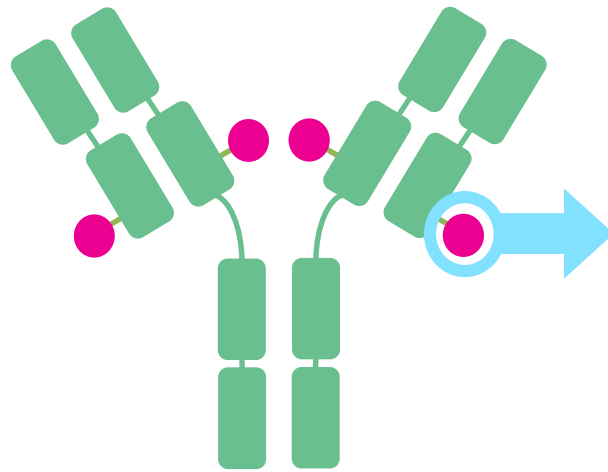
## Transform treatment for **HER2 Tumors**

**Our obligation to patients is beyond what one company can achieve alone.**

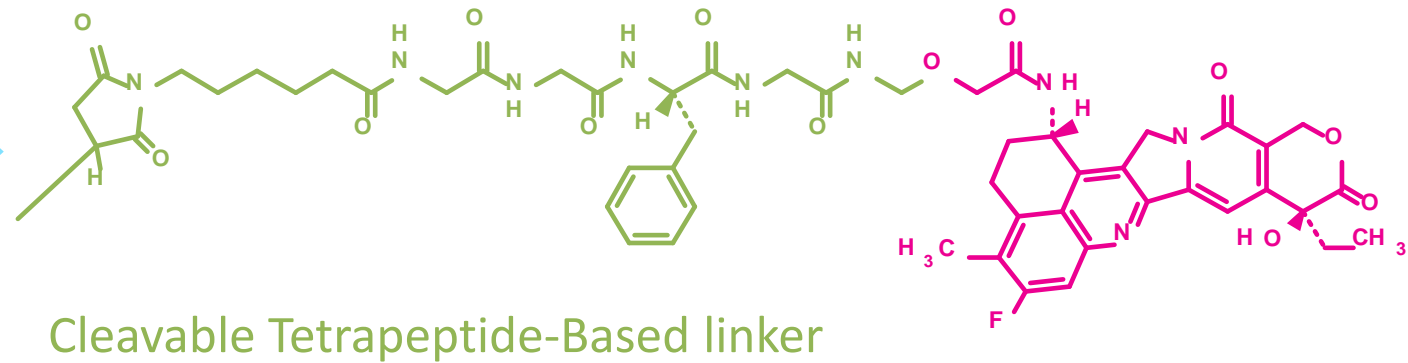


- ◆ **Launched in just 4 years** after initiating first in human trial in September 2015
- ◆ First and foremost, a significantly advanced **technological break through** product
  - It was designed to achieve best-in-class technology
  - It delivers unique practice-changing evidence
- ◆ We want to **maximize** the value of DS-8201 with **breadth & depth expansions**, and fully leverage the value of **our collaboration with AZ**
  - Accelerated and broadened geographical coverage
  - Expansion into multiple indications

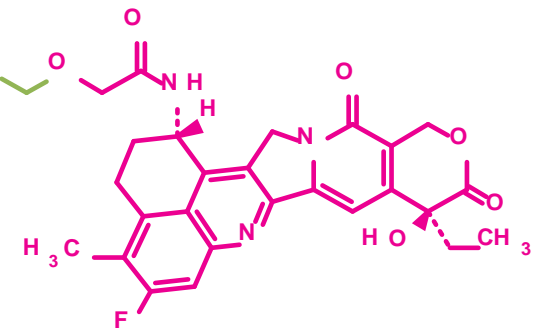
Humanized anti-TROP2  
IgG1 mAb



DAR  $\approx$  4



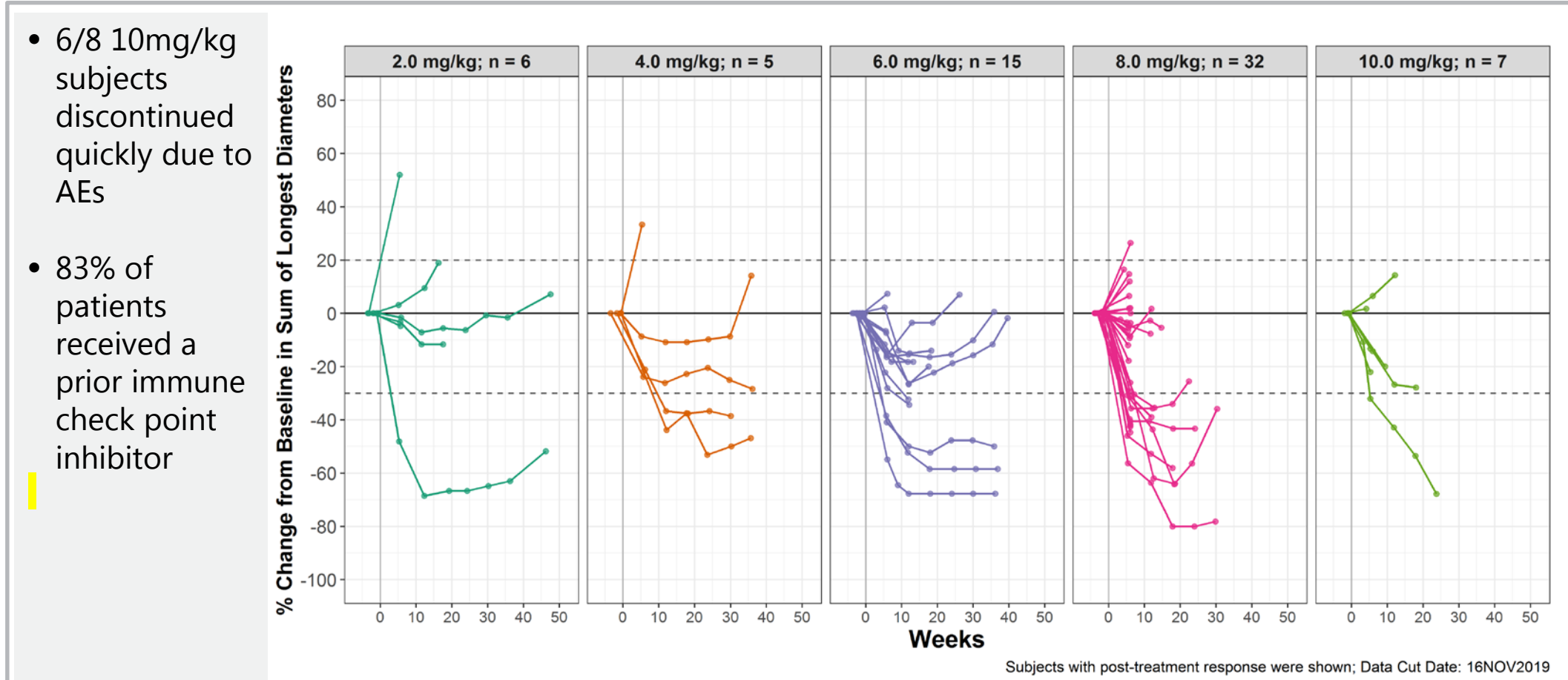
Topoisomerase I Inhibitor payload  
(DXd)



\*Drug positions are not limited, ADC is mixture of regioisomer.

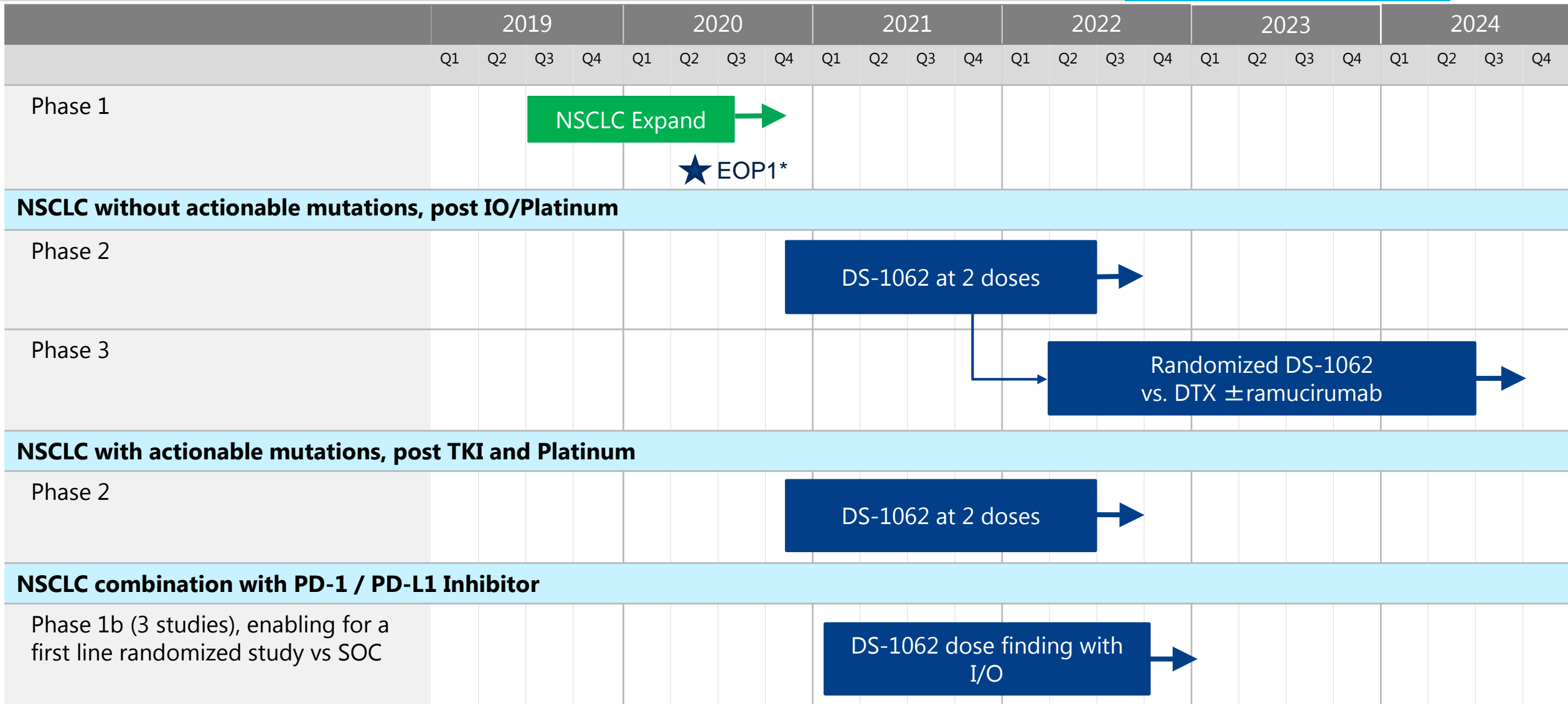
# DS-1062: Phase 1 Recent Update | Efficacy\* (as of Nov. 16 2019, preliminary data)

Dose dependent increase in tumor response in heavily pretreated, unselected NSCLC patients having progressed on standard of care, including immune checkpoint inhibitors, EGFR inhibitors, and ALK inhibitors



\*Source: Internal data on file at Daiichi Sankyo.

# DS-1062: NSCLC Development Plan



 Study Started
  Planned Study Start

All dates are approximates

\* End of phase 1 study

- ◆ **DS-1062** has “**drug-to-be**” characteristics

- Maintains clear efficacy, dose response, durability and tolerability

- ◆ We aim to **swiftly and independently develop DS-1062**

- Fast to market in late line NSCLC patient population

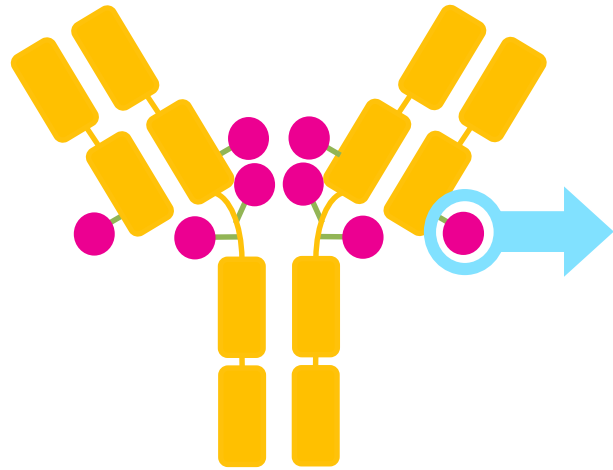
- ✓ Set up **pivotal monotherapy phase 2 study**

- as soon as feasible: about second half of 2020

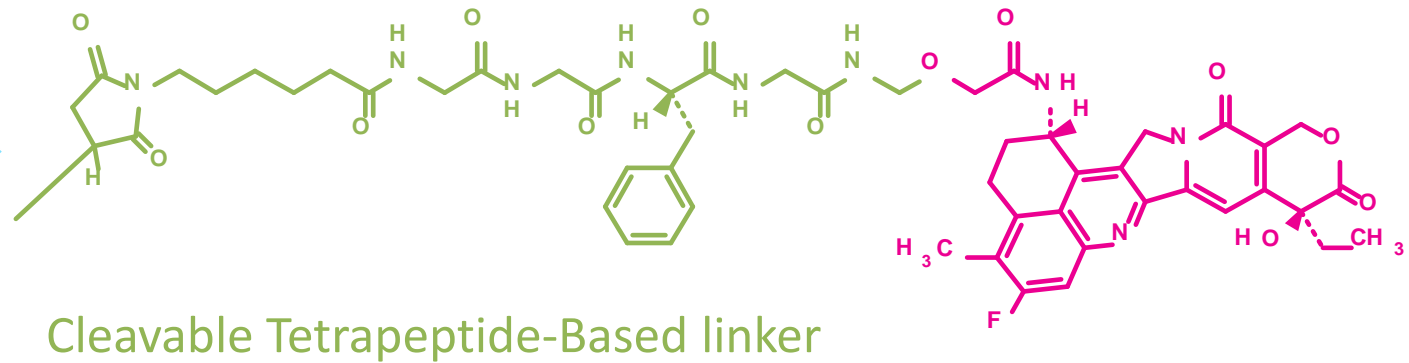
- **Potential expansion into first line NSCLC (I/O Combo)** and indications with high TROP-2 level



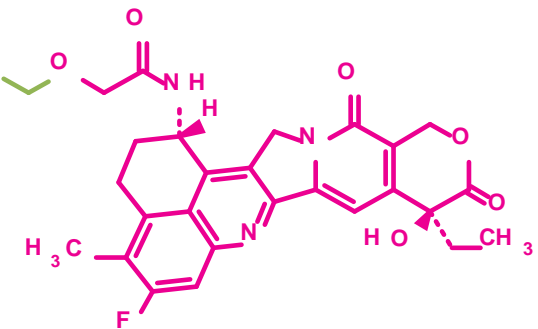
Human anti-HER3  
IgG1 mAb



DAR  $\approx$  8

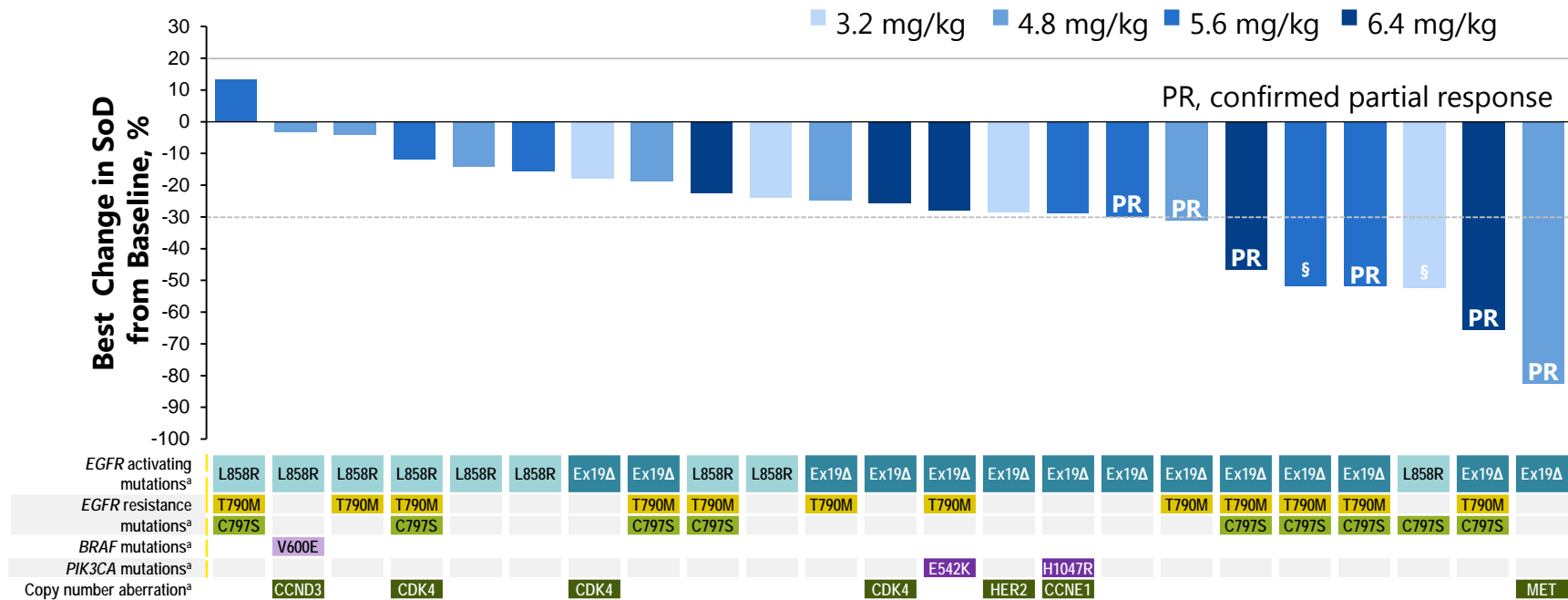


Topoisomerase I Inhibitor payload  
(DXd)





# U3-1402: Antitumor Activity Across Diverse EGFR TKI Resistance Mechanisms



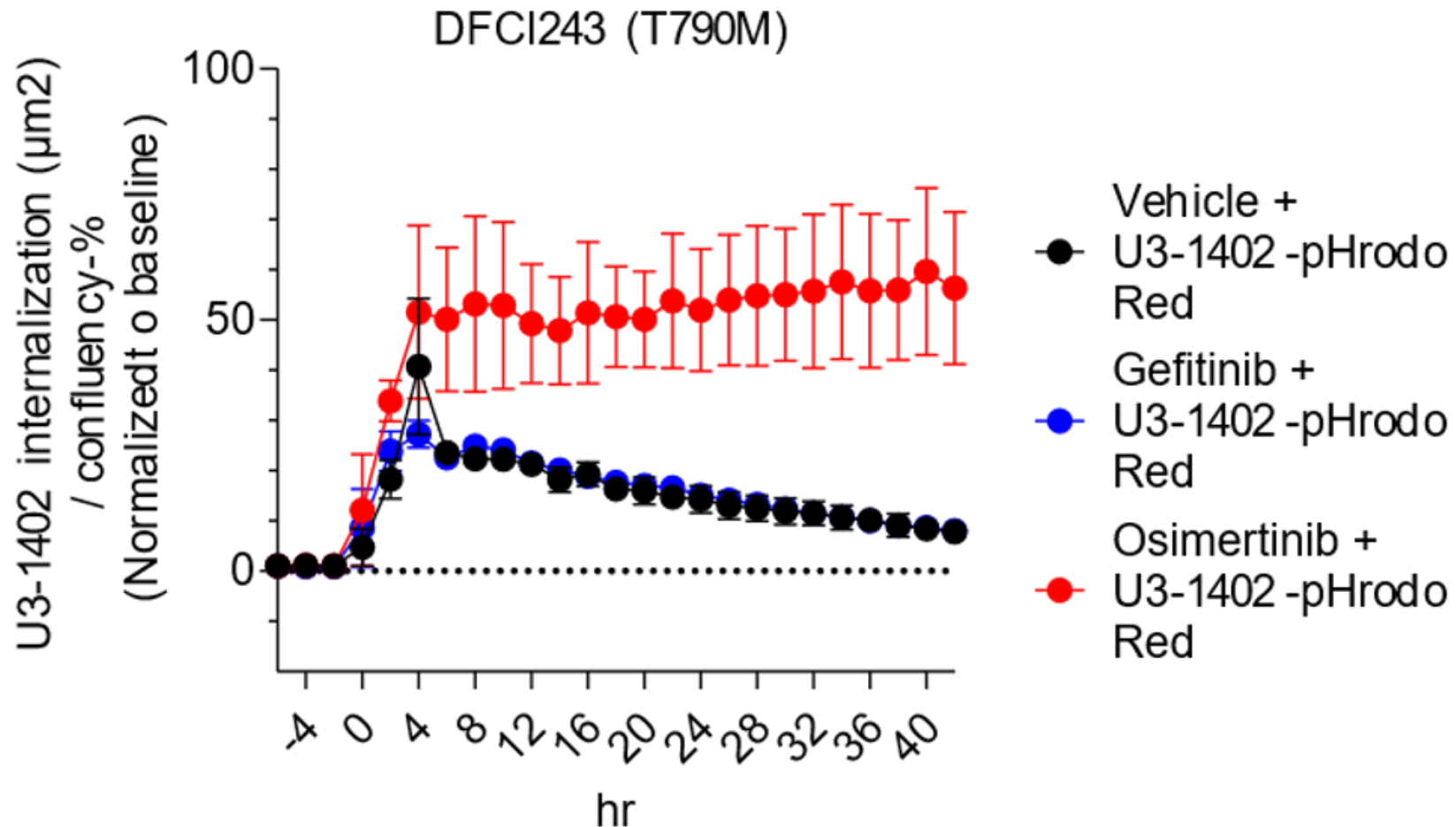
n = 23  
Median follow-up:  
4.5 months

A phase 1 study of U3-1402 in NSCLC (NCT03260491). <sup>§</sup>2 patients had  $\geq 30\%$  reduction in SoD, which were not considered confirmed PRs; 1 experienced transient tumor size reduction and 1 had not yet been confirmed at data cutoff. <sup>a</sup>Performed centrally using OncoPrint™ Comprehensive Assay v3 from formalin-fixed, paraffin-embedded tumor tissue. Results from local testing are included for patients where tissue was unavailable for central analysis. Additional mutations detected from cfDNA in blood collected prior to treatment with U3-1402 using GuardantOMNI assay are included. For cfDNA analysis, a minor allelic frequency of 1% was used as a threshold for detection of mutations. The copy number data from cfDNA are not shown. cfDNA, cell-free DNA; EGFR, epidermal growth factor receptor; HER3, human epidermal growth factor receptor 3; PR, partial response; SoD, sum of diameters; TKI, tyrosine kinase receptor.

# Sustained Internalization Rate of U3-1402 in EGFRm Lung Cancer\*

Monotherapy or in Combination with Osimertinib

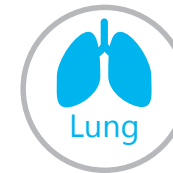
## Quantification of Internalization Over Time



\*Data are preliminary

Courtesy of Dr. Pasi Janne, Dana Farber Cancer Institute

- ◆ **U3-1402** appears **effective in NSCLC**, adding to breast cancer activity previously reported
  
- ◆ We aim to **swiftly and independently develop U3-1402**
  - **Lung cancer**: EGFRm presents a clear opportunity
    - ✓ HER3 consistently expressed and internalized post TKI
    - ✓ **Combination with osimertinib** will be pursued
  - **Colorectal** and **Prostate** cancers: Phase 2 studies planned



Patients who received 5.4 mg/kg of DS-8201 (N=184)

Preferred Term, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any Grade/ Total
Interstitial lung disease	5 (2.7)	15 (8.2)	1 (0.5)	0	4 (2.2)	<b>25 (13.6)</b>

Drug related; ILD was determined by the Independent ILD Adjudication Committee based on 44 preferred terms.

Among the 25 total events:

- Median time to investigator-reported onset was 193 days (range, 42-535 days)
- 13 of 20 patients with grade  $\geq 2$  ILD received corticosteroids
- 7 patients recovered, 2 were recovering, 12 were either outcome unknown or not followed until resolution, and 4 died
- Of the 4 fatal cases, onset was from 63-148 days, 3 received steroids as part of treatment, and death occurred 9-60 days after ILD diagnosis

Recommendations: Monitor for symptoms. Hold T-DXd and start steroids as soon as ILD is suspected

ILD, interstitial lung disease.

The data on this slide was presented at San Antonio Breast Cancer Symposium®, December 10-14, 2019  
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## Goal: Drive ILD awareness, detection, and management



- Comprehensive education of MSLS
- Develop tools for MSLS to use in proactive direct communication with treating physicians

***Develop internal understanding & external communication plans***



### HCPs

- Prioritize investigators with patients on treatment
- Ensure continuous education and 'top of mind' status, through numerous outlets (in-person, online)

***Give HCPs tools to reduce ILD severity and improve management***



### Resources for Patients

- Educate patients around risk of ILD and need to self-monitor for symptoms

***Drive awareness and give patients tools to support detection & management***

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# Upcoming Events

Jan. 2020

FY2019 Q3 financial results announcement

Apr. 2020

FY2019 Q4 financial results announcement

May 2020

ASCO 2020

Jul. 2020

FY2020 Q1 financial results announcement

Aug. 2020

WCLC 2020

## DS-8201

### **HER2 Positive mBC Pivotal Phase 2 Study – DESTINY-Breast01**

- Japan: NDA submitted and accepted on September 9, 2019
- EU: MAA submission planned for 1H FY2020



### **HER2 Positive mGC Pivotal Phase 2 Study – DESTINY-Gastric01**

- Japan and South Korea: TLR anticipated for 4Q FY2019



### **ASCO 2020 Planned Presentations**

- DESTINY-Gastric01 Results
- Colorectal Phase 2
- NSCLC Phase 2
- Breast/Bladder – Nivolumab Combo – Phase 1



## DS-1062

### ASCO 2020 Planned Presentation

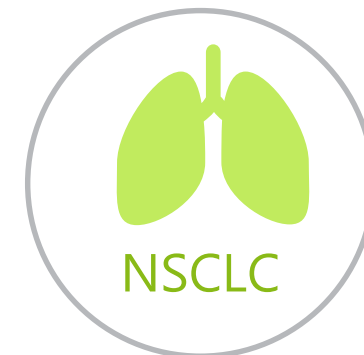
- NSCLC Phase 1 Expansion Update



## U3-1402

### WCLC 2020 Planned Presentation

- NSCLC Phase 1 Expansion Update



# Reestablish Mid-to-Long-Term Vision

- ◆ In parallel with the next five-year business plan development, reestablish mid-to-long-term vision beyond 2025



**① Overview of Daiichi Sankyo**

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**④ Key Takeaways**



- ◆ **Current business is solid**
- ◆ **ADC assets** empower us to **pursue further growth** in the near future
- ◆ Daiichi Sankyo will **deliver ADC assets to as many patients as possible as fast as we can**

## Contact address regarding this material

Daiichi Sankyo Co., Ltd.

**Corporate Communications Department**

**TEL: +81-3-6225-1126**

**Email: [DaiichiSankyoIR@daiichisankyo.co.jp](mailto:DaiichiSankyoIR@daiichisankyo.co.jp)**