Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

# Daiichi Sankyo IR Material

May 2025

# Forward-Looking Statements

Management strategies and plans, financial forecasts, future projections and policies, and R&D information that Daiichi Sankyo discloses in this material are all classified as Daiichi Sankyo's future prospects. These forward looking statements were determined by Daiichi Sankyo based on information obtained as of today with certain assumptions, premises and future forecasts, and thus, there are various inherent risks as well as uncertainties involved. As such, please note that actual results of Daiichi Sankyo may diverge materially from Daiichi Sankyo's outlook or the content of this material. Furthermore, there is no assurance that any forward-looking statements in this material will be realized. Regardless of the actual results or facts, Daiichi Sankyo is not obliged and does not have in its policy the duty to update the content of this material from the date of this material onward.

Some of the compounds under discussion are investigational agents and are not approved by the FDA or any other regulatory agency worldwide as a treatment for indications under investigation. Efficacy and safety have not been established in areas under investigation. There are no guarantee that these compounds will become commercially available in indications under investigation.

Daiichi Sankyo takes reasonable care to ensure the accuracy of the content of this material, but shall not be obliged to guarantee the absolute accuracy, appropriateness, completeness and feasibility, etc. of the information described in this material. Furthermore, any information regarding companies, organizations or any other matters outside the Daiichi Sankyo Group that is described within this material has been compiled or cited using publicly available information or other information, and Daiichi Sankyo has not performed in-house inspection of the accuracy, appropriateness, completeness and feasibility, etc. of such information, and does not guarantee the accuracy thereof.

The information described in this material may be changed hereafter without notice. Accordingly, this material or the information described herein should be used at your own judgment, together with any other information you may otherwise obtain.

This material does not constitute a solicitation of application to acquire or an offer to sell any security in the United States, Japan or elsewhere.

This material disclosed here is for reference purposes only. Final investment decisions should be made at your own discretion.

Daiichi Sankyo assumes no responsibility for any damages resulting from the use of this material or its content, including without limitation damages related to the use of erroneous information.

# Table of Contents

Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

# FY2024
# Financial Results Presentation


## DAIICHI SANKYO CO., LTD.

**Hiroyuki Okuzawa**

**President and CEO**


**April 25, 2025**

# Agenda

1. **FY2024 Financial Results**
2. Business Update
3. R&D Update
4. 5-Year Business Plan Update
5. FY2025 Forecast
6. Appendix

# Overview of FY2024 Results

(Bn JPY)

| | FY2023 Results | FY2024 Results | YoY | |
|---|---|---|---|---|
| **Revenue** | **1,601.7** | **1,886.3** | **+17.8%** | **284.6** |
| Cost of sales*1 | 414.8 | 415.7 | | 1.0 |
| SG&A expenses*1 | 627.3 | 724.8 | | 97.5 |
| DXd ADC profit share *2 | 170.6 | 226.2 | | 55.6 |
| Other SG&A expenses | 456.8 | 498.6 | | 41.9 |
| R&D expenses*1 | 364.3 | 432.9 | | 68.5 |
| **Core operating profit*1** | **195.3** | **312.8** | **+60.2%** | **117.6** |
| Temporary income*1 | 27.3 | 22.2 | | -5.1 |
| Temporary expenses*1 | 10.9 | 3.1 | | -7.9 |
| **Operating profit** | **211.6** | **331.9** | **+56.9%** | **120.3** |
| **Profit before tax** | **237.2** | **355.6** | | **118.4** |
| **Profit attributable to owners of the Company** | **200.7** | **295.8** | **+47.3%** | **95.0** |

| | | | | |
|---|---|---|---|---|
| Currency Exchange Rate | USD/JPY | 144.62 | 152.57 | +7.95 |
| | EUR/JPY | 156.79 | 163.74 | +6.95 |

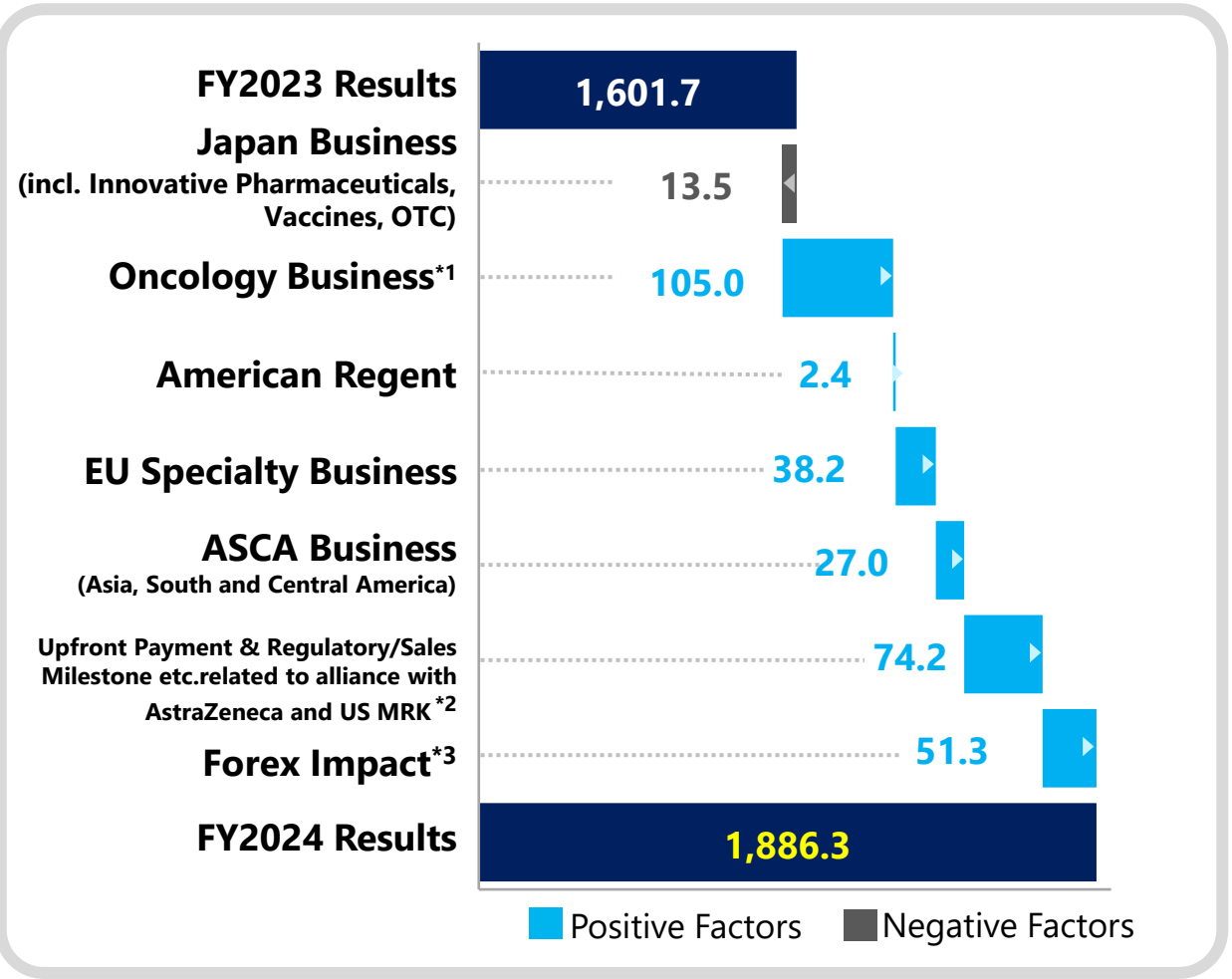
*1 As an indicator of ordinary profitability, "core operating profit" which excludes temporary income and expenses from operating income is disclosed. Income and expenses related to: sale of fixed assets, restructuring (excluding the sales of pipeline and launched products), impairment, loss compensation, reconciliation, and other non-temporary and material gains and losses are included in the "temporary income and expenses". Temporary income and expenses are excluded from results and forecast for cost of sales, SG&A expenses and R&D expenses shown in the list above. The adjustment table from operating profit to core operating profit is stated in the reference data.

*2 DS pays alliance partners 50% of gross profit for the product sales in countries/regions where DS book revenue (excluding Japan) to share profit with the partners.

# Revenue

## Increased by 284.6 Bn JPY (Increased by 233.3 Bn JPY excl. forex impact)

(Bn JPY)

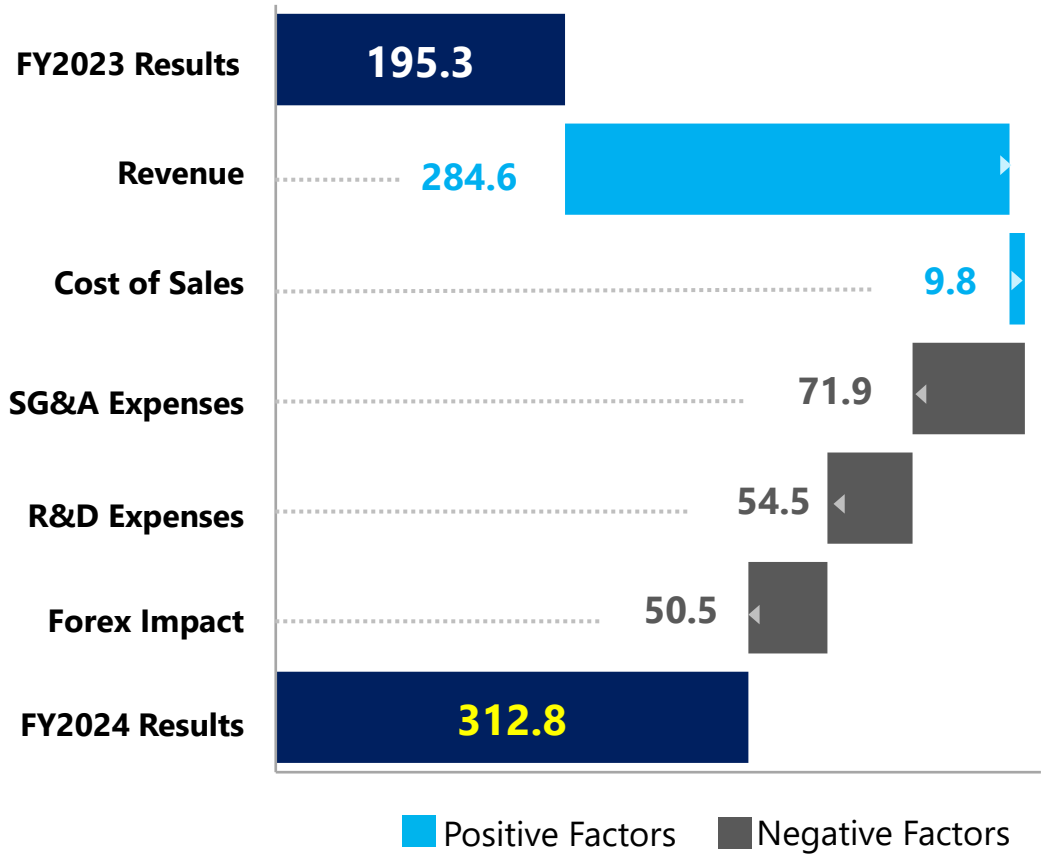



| Positive Factors | | Negative Factors | |
|---|---|---|---|
| **Japan Business Unit** | | | |
| Lixiana | +17.5 | Vaccine business | -19.5 |
| Tarlige | +10.0 | Daiichi Sankyo Espha | -83.0 |
| Enhertu | +7.1 | | |
| Daiichi Sankyo Healthcare | +10.7 | | |
| Realized gains of unrealized gains of inventory for Daiichi Sankyo Espha | +9.4 | | |
| **Oncology Business Unit*1** | | | |
| Enhertu | +100.6 | | |
| **American Regent Unit** | | | |
| GE injectables | +3.4 | Venofer | -2.2 |
| **EU Specialty Business Unit** | | | |
| Lixiana | +25.2 | olmesartan | -2.1 |
| Nilemdo/Nustendi | +16.9 | | |
| **ASCA (Asia, South and Central America) Business Unit** | | | |
| Enhertu | +26.9 | | |
| **Upfront Payment & Regulatory/Sales Milestone etc. related to alliance with AstraZeneca and US MRK *2** | | | |
| AstraZeneca | +45.3 | | |
| MRK | +28.9 | | |

*1 Revenue for Daiichi Sankyo, Inc. and Daiichi Sankyo Europe's oncology products
*2 Merck & Co., Inc., Rahway, NJ, USA
*3 Forex impact USD: +35.1, EUR : +16.0, ASCA: +0.2

# Core Operating Profit

**Increased by 117.6 Bn JPY** (Increased by 116.8 Bn JPY excl. forex impact)




(Bn JPY)

**Revenue** +284.6
incl. forex impact of +51.3

**Cost of Sales** -9.8
Improvement in cost of sales ratio by change in product mix

**SG&A Expenses** +71.9
Increase in expenses related to Enhertu
due to an increase in profit share of gross profit with AstraZeneca

**R&D Expenses** +54.5
Increase in 5DXd ADCs* R&D investments

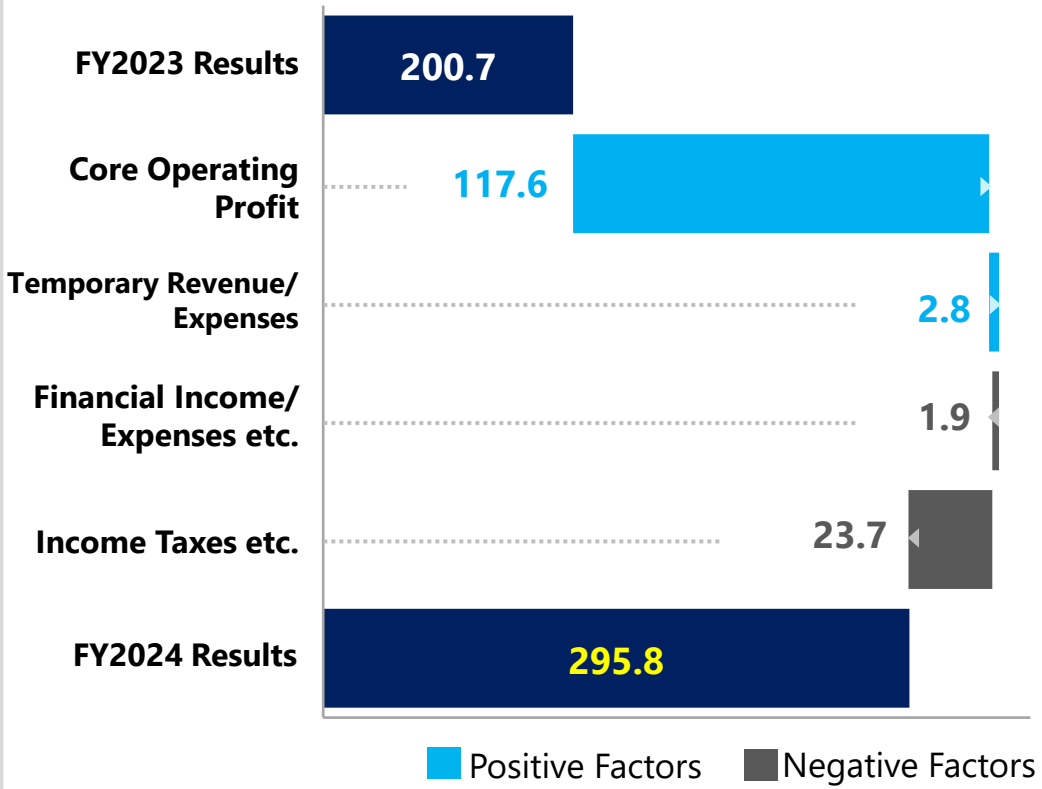
**Forex Impact** +50.5 (Profit Decreased)
Cost of Sales +10.8
SG&A Expenses +25.6
R&D Expenses +14.1

***ENHERTU®**: trastuzumab deruxtecan (International Nonproprietary Name: INN), T-DXd, DS-8201 (HER2-directed ADC), **DATROWAY®**: datopotamab deruxtecan (INN), Dato-DXd, DS-1062 (TROP2-directed ADC), **HER3-DXd**: patritumab deruxtecan (INN), U3-1402 (HER3-directed ADC), **I-DXd**: ifinatamab deruxtecan (INN), DS-7300 (B7-H3-directed ADC), **R-DXd**: raludotatug deruxtecan (INN), DS-6000 (CDH6-directed ADC)

# Profit Attributable to Owners of the Company

## Increased by 95.0 Bn JPY

(Bn JPY)




**Temporary Income/Expenses** ····· **+2.8 (Profit Increased)**

| | FY2023 Results | FY2024 Results | YoY |
|---|---|---|---|
| Temporary Income | 27.3*1 | 22.2*2 | -5.1 |
| Temporary Expenses | 10.9*3 | 3.1 | -7.9 |

*1 Lump sum payment received from Novartis following the settlement of Plexxikon's patent infringement lawsuit (26.4)
*2 Gains on stock transfer of Daiichi Sankyo Espha (16.3)
*3 Environmental expenditures related to former Yasugawa plant (4.1)

**Financial Income/Expenses etc.** ····· **-1.9 (Profit Decreased)**

- Deterioration in forex gains/losses ····· -4.5
- Increase in interest income ····· +3.3

**Income Taxes etc.** ····· **+23.7 (Profit Decreased)**

| | FY2023 Results | FY2024 Results | YoY |
|---|---|---|---|
| Profit before Tax | 237.2 | 355.6 | +118.4 |
| Income Taxes etc. | 36.2 | 59.9 | +23.7 |
| Tax rate | 15.3% | 16.8% | |

# Agenda

1. FY2024 Financial Results
2. **Business Update**
3. R&D Update
4. 5-Year Business Plan Update
5. FY2025 Forecast
6. Appendix

**Progress towards “Maximize 3ADCs”**

Progress towards “Profit growth for current business and products”

Progress towards “Identify and build pillars for further growth”

Progress towards “Create shared value with stakeholders”

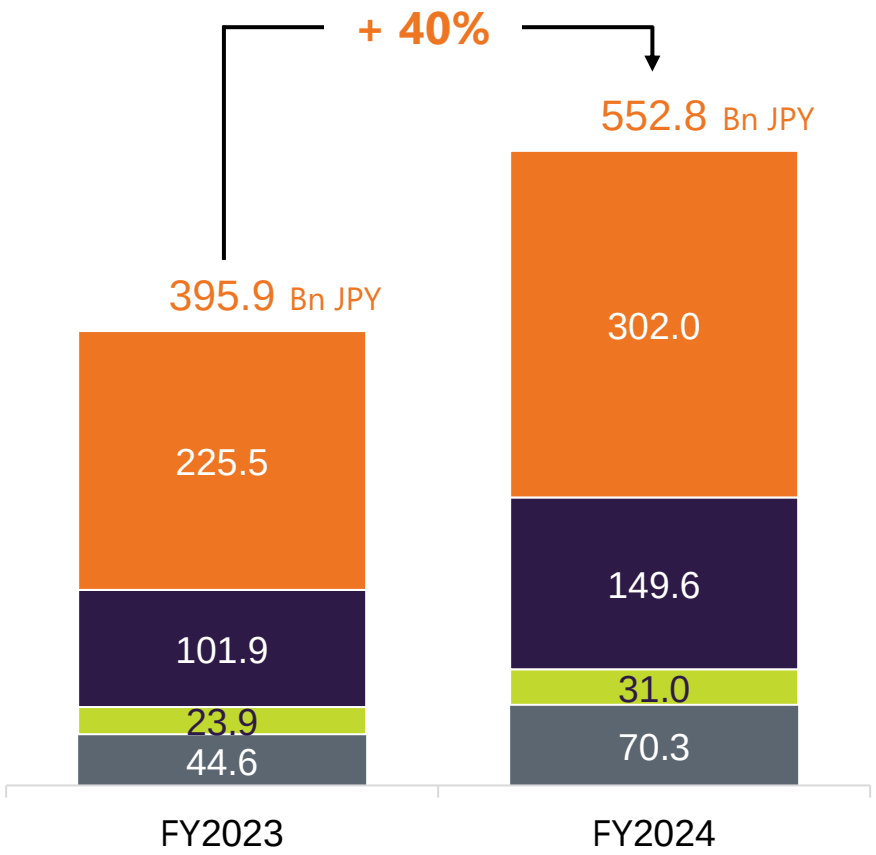
# ENHERTU® Performance

ENHERTU trastuzumab deruxtecan

Daiichi-Sankyo

## Global Product Sales

FY2024 Product Sales Result **552.8 Bn JPY** (YoY **+156.9 Bn JPY**) FY2025 Forecast **662.1 Bn JPY** (YoY **+109.3 Bn JPY**)




**Global Product Sales**

### ◆ Key Growth Factors (YoY YTD Results) and Key Updates

Achieved double-digit growth rate in all regions leading by HER2+ BC 2L and HER2 low BC (post-chemo)

| | |
|---|---|
| **US** (+34%) | Maintained No.1 new patient share in BC, GC, NSCLC indications; Expanded new patient uses in various tumor types in HER2+ solid tumors<br>➢ HR+, HER2 low* or HER2 ultralow** BC (chemo naïve) approved in Jan |
| **EU** (+47%) | Expanded sales leading by DE, FR, IT, ES; Achieved high new patient share in BC indications while maintaining No.1 position<br>➢ Spain: Began to be reimbursed for HER2 low BC (post-chemo) in Nov<br>➢ HR+, HER2 low* or HER2 ultralow** BC (chemo naïve) approved in Mar |
| **Japan** (+30%) | Maintained No.1 new patient share in all indications including early market adoption of HER2 low BC (post-chemo) |
| **ASCA** (+58%) | Expanded sales mainly in Brazil and China; Achieved and maintained No.1 new patient share in HER2+ BC 2L in Brazil<br>➢ China: HER2+ GC approved in Aug, HER2m NSCLC approved in Oct, NRDL listed for HER2+ BC and HER2 low BC (post-chemo) in Jan<br>➢ Brazil: HER2+solid tumors approved in Nov |

### ◆ NCCN Guideline Updates

Biliary Tract Cancers, NSCLC, Occult Primary, Pancreatic Adenocarcinoma, Colon Cancer, Rectal Cancer, Small Bowel Adenocarcinoma (April); Head and Neck Cancers, Vulvar Cancer, Bladder Cancer (May); Ampullary Adenocarcinoma (Dec)

* IHC 1+ or IHC 2+/ISH-, **IHC 0 with membrane staining

BC: breast cancer, DE: Germany, ES: Spain, FR: France, GC: gastric cancer, HR: hormone receptor, IT: Italy, NCCN: National Comprehensive Cancer Network, NSCLC: non-small cell lung cancer, NRDL: National Reimbursement Drug List

DATROWAY®
(Dato-DXd)

# Approved and Started Promotion

DATROWAY
datopotamab deruxtecan

Daiichi-Sankyo

## DATROWAY® (anti-TROP2 ADC) approved in Japan, the US and EU

### - Second product approved on our DXd ADC platform after ENHERTU®

- **Approval acquisition date**
  - Japan: December 2024
  - US: January 2025
  - EU: April 2025

- **Indication**
  Unresectable or metastatic, hormone receptor (HR) positive, HER2 negative (IHC 0, IHC 1+, or IHC 2+/ISH−) breast cancer with prior endocrine-based therapy and chemotherapy

- **Dosage and Administration**
  6 mg/kg per dose intravenously at 3-weeks intervals

- **Product sales results for FY2024 (Japan, US)**
  - 1.4 Bn JPY
  - Steady revenue uptake

- Included in NCCN guidelines (Jan)

# Co-development and Co-commercialization for MK-6070

**Added MK-6070*, which is being developed by Merck & Co., Inc., Rahway, NJ, USA (MRK), to the existing global co-development and co-commercialization agreement for 3 DXd ADC products (HER3-DXd, I-DXd, R-DXd)**

## Development

- **Co-develop MK-6070 worldwide** (excluding Japan)
- Plan to evaluate MK-6070 in **combination with I-DXd** in certain patients with **SCLC**** as well as other potential products
- The companies will share **R&D expenses equally**
  But **R&D expenses related to MK-6070 in combination with 3 DXd ADC products** will be shared in a manner consistent with the original agreement (MRK will be responsible for 75% of the first 2 Bn USD of R&D expenses for each product, and the companies will share R&D expenses equally thereafter)

## Commercialization

- **Global (excluding Japan):**
  - The companies will **co-promote** and **share gross profit** and **promotional expenses etc.**
- MRK will book product sales worldwide
- **Japan:** MRK will solely commercialize (DS will **receive royalty** from MRK)

## Manufacturing

- MRK will **manufacture** and **supply** MK-6070

## Financial Terms

- Consideration for collaboration：**320Mn USD**
  - DS's contingent quid rights*** from the original agreement (equivalent to 150Mn USD) is applied to the collaboration for MK-6070. In addition, 170Mn USD is paid in cash as an upfront payment
- Accounting treatment
  - Consideration of 320Mn USD (46.5Bn JPY) will be recorded as an expense over the expected loss of exclusivity (LOE) period starting from the regulatory approval of MK-6070
  - 150Mn USD (21.8Bn JPY) related to DS's contingent quid rights will be recorded as revenue over the expected LOE period of 3 DXd ADC products in collaboration with MRK under the original agreement

* DLL3 directed tri-specific T-cell engager (Formerly: HPN328, generic name: gocatamig) ** small cell lung cancer

***Rights to develop and/or commercialize MRK's developed products or products solely by DS or jointly with MRK. If the rights are not exercised within a certain period, DS receives 150Mn USD from MRK.

Progress towards “Maximize 3ADCs”

**Progress towards “Profit growth for current business and products”**

Progress towards “Identify and build pillars for further growth”

Progress towards “Create shared value with stakeholders”

# Other Regional Initiatives

## Japan

- **EZHARMIA® Anti-Cancer Agent / EZH1 and EZH2 Inhibitor**
  - Jun. 2024 Approved for the treatment of adult patients with relapsed or refractory peripheral T-cell lymphoma (PTCL)
- **Belsomra® Anti-Insomnia Treatment / Dual Orexin Receptor Antagonist**
  - Jul. 2024 Decision made to transfer of distribution rights from MSD to Daiichi Sankyo
    - Started sale and promotional activities from October 1, 2024 onwards
- **DAICHIRONA®INTRAMUSCULAR INJECTION COVID-19 Vaccine**
  - Sep. 2024 Launched Omicron JN.1-adapted mRNA vaccine
- **FLUMIST®INTRANASAL SPRAY Influenza Vaccine**
  - Oct. 2024 Launched Intranasal live attenuated influenza vaccine
- **LIXIANA® Anticoagulant / FXa inhibitor**
  - Feb. 2025 Approved for the prevention of thromboembolism in patients with chronic thromboembolic pulmonary hypertension

## EU

- **Nilemdo®/Nustendi® Cholesterol-lowering agent**
  - May 2024 Approved for treatments to reduce the risk of adverse cardiovascular event
    - The first and only non-statin LDL-C-lowering treatments indicated for primary and secondary prevention of cardiovascular events

Progress towards “Maximize 3ADCs”

Progress towards “Profit growth for current business and products”

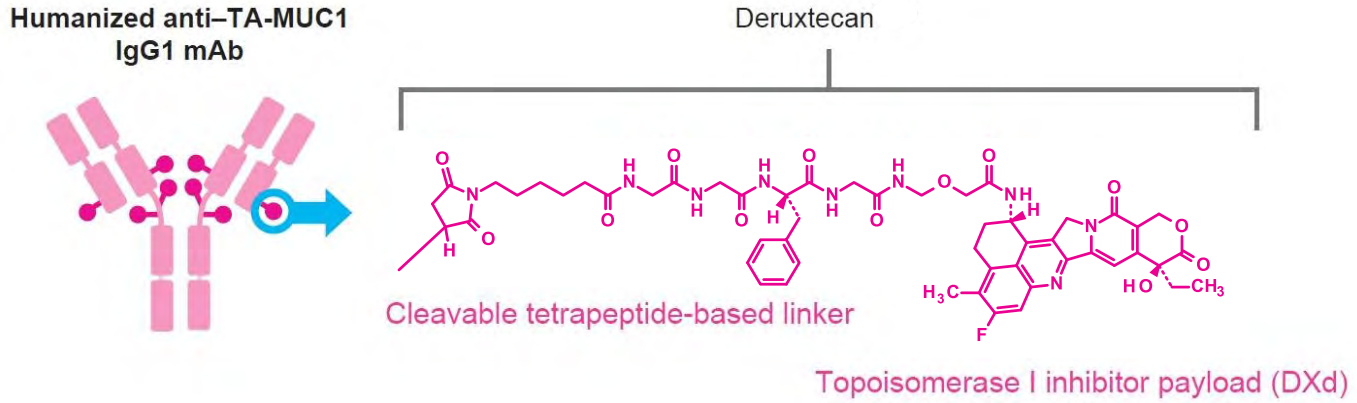
**Progress towards “Identify and build pillars for further growth”**

Progress towards “Create shared value with stakeholders”

# DS-3939 Acquisition of Intellectual Property Rights for Anti-TA-MUC1 Antibody

**In Dec. 2024, acquired the intellectual property rights for gatipotuzumab (anti-TA-MUC1 antibody) from Glycotope***

- **Anti-TA-MUC1** antibody**
  - Antibody of our sixth DXd ADC, DS-3939, currently under development by Daiichi Sankyo




- **Development status of DS-3939**
  - Being evaluated in a phase 1/2 clinical trial in patients with several types of solid tumors including non-small cell lung, breast, urothelial, ovarian, biliary tract and pancreatic ductal adenocarcinoma, etc.

- **Background and overview of the acquisition of intellectual property rights**
  - In 2018, in-licensed exclusive rights to develop and commercialize gatipotuzumab (anti-TA-MUC1 antibody) as an ADC from Glycotope.
  - In Dec. 2024, acquired the intellectual property rights of gatipotuzumab considering the product potential of DS-3939.
  - Consideration：132.5 Mn USD（22.0 Bn JPY）
    - This consideration satisfies all potential milestone payments, as well as royalties as part of a 2018 licensing agreement.
    - After the sales approval of DS-3939, this consideration will be recorded as an expense over the anticipated exclusive sales period.

* Glycotope GmbH (Berlin, Germany)
**TA-MUC1：A transmembrane glycoprotein overexpressed in broad range of tumors including non-small cell lung, breast, urothelial, ovarian, biliary tract and pancreatic ductal adenocarcinoma

Progress towards “Maximize 3ADCs”

Progress towards “Profit growth for current business and products”

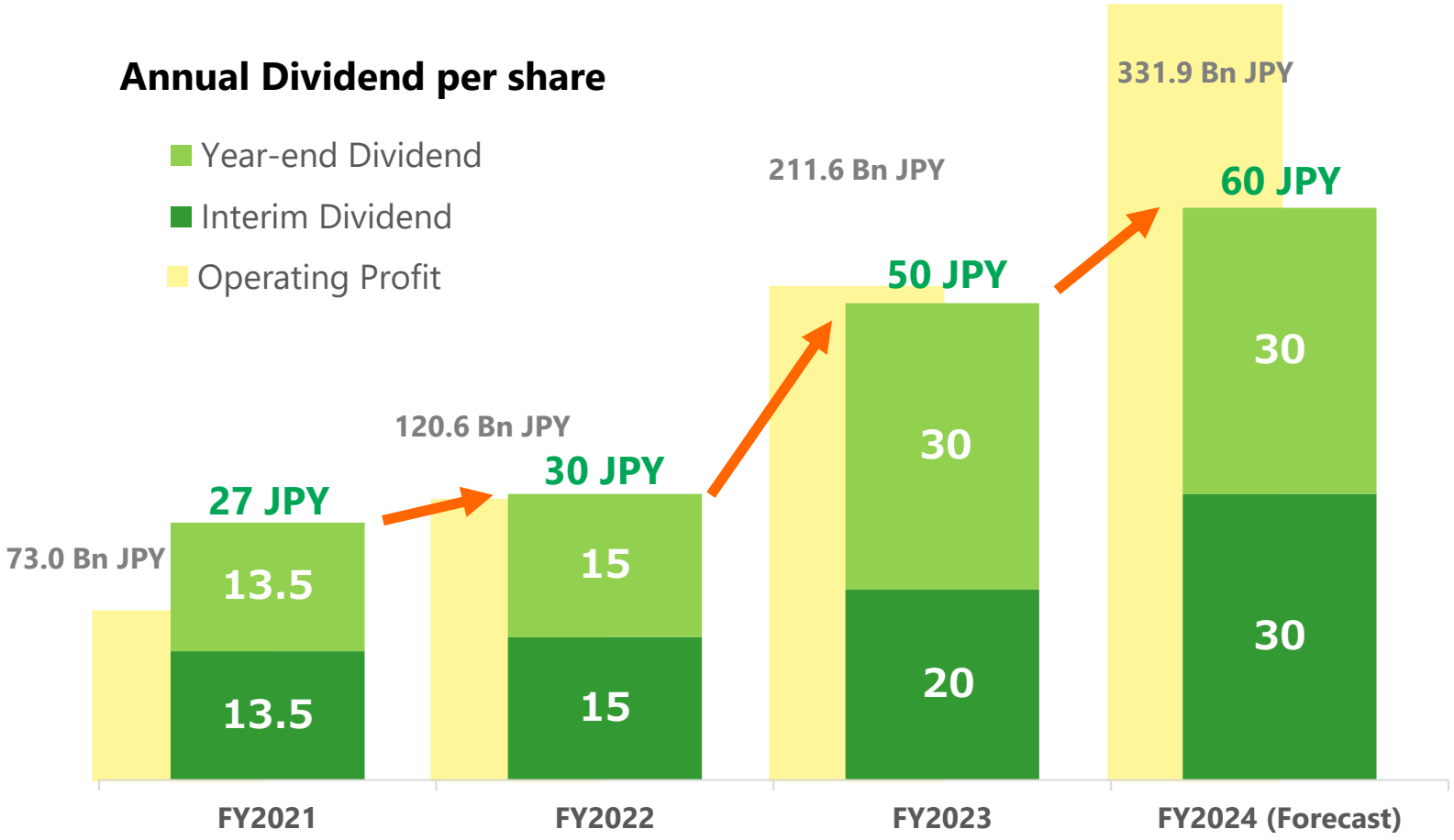
Progress towards “Identify and build pillars for further growth”

**Progress towards “Create shared value with stakeholders”**

# FY2024 Annual Dividend Forecast

**Increase annual dividend forecast per share from 50 JPY (FY2023) to 60 JPY (FY2024)**

**due to strong performance of ENHERTU® and others**



# Flexible Acquisition of Own Shares (Results)

- **Acquired own shares to strengthen and enhance shareholder returns**
- **FY2025 DOE is expected to be over 8.5%**

| | |
|---|---|
| **Apr. 2024 Resolution** | ➢ Acquisition period: **Apr. 26, 2024 – Jan. 9, 2025**<br>➢ Aggregate amount of acquisition cost: **200 billion JPY (maximum)**<br>➢ Total number of shares to be acquired: **38.71 million stocks (maximum)**<br>➢ Completed the cancellation of all of acquired own shares |
| **Feb. 2025 Resolution** | ➢ Acquisition period: **Mar. 3, 2025 – Apr. 8, 2025**<br>➢ Aggregate amount of acquisition cost: **50 billion JPY (maximum)**<br>➢ Total number of shares to be acquired: **13.97 million stocks (maximum)**<br>➢ Scheduled to cancel all of acquired own shares on May 30, 2025. |

# Agenda

1. FY2024 Financial Results
2. Business Update
3. **R&D Update**
4. 5-Year Business Plan Update
5. FY2025 Forecast
6. Appendix

**Progress towards “Maximize 3ADCs”**

Progress towards “Profit growth for current business and products”

ASCO 2025

News Flow

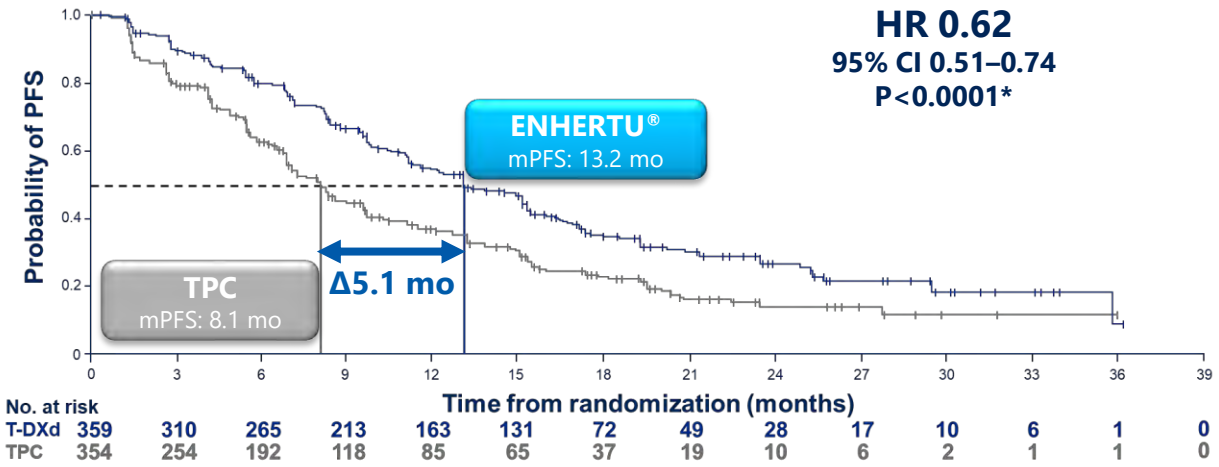
ENHERTU®

# Achievements in FY2024: Pioneered New Classifications of HER2

DESTINY-Breast06 Ph3

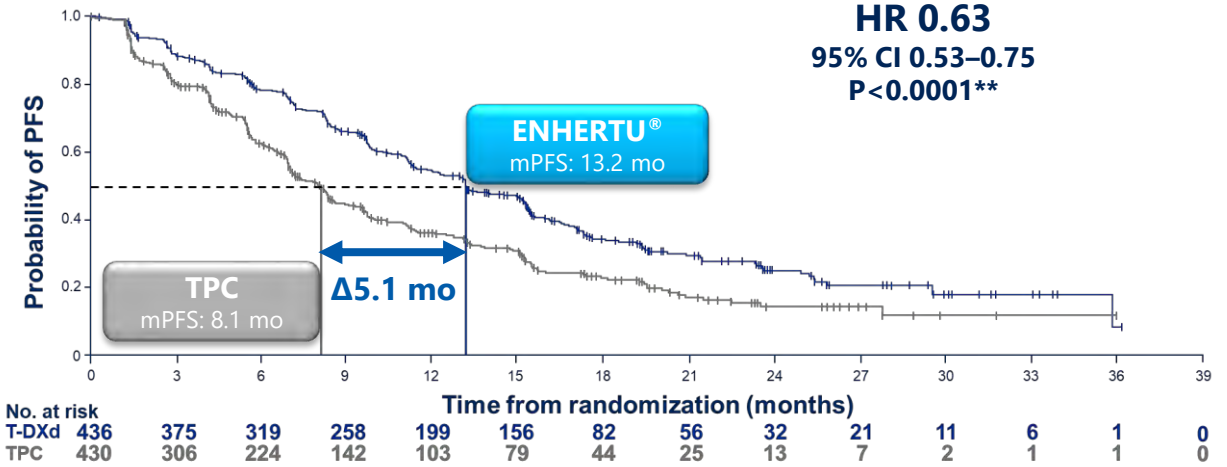
## ENHERTU® demonstrated efficacy in HER2 ultralow as well as HER2 low chemo naïve BC, and is approved in the US and EU

### PFS for HER2 low (BICR)




Data cutoff: March 18, 2024
*P-value of <0.05 required for statistical significance

### PFS for ITT（HER2 low and ultralow） (BICR)




Data cutoff: March 18, 2024
**P-value of <0.015 required for statistical significance

- ENHERTU® demonstrated a statistically significant and clinically meaningful improvement in PFS for chemo naïve HR positive, HER2 low and ultralow metastatic BC. No new safety concerns identified
- Approved for this indication in US in Jan 2025 and in EU in Mar 2025. Expected approval in Japan in FY2025 H1
- Filed in China in Apr 2025
- ENHERTU® is **approved to treat about 90 percent of people with mBC**

BC: breast cancer, BICR: blinded independent central review, CI: confidence interval, HR: hazard ratio, HR: hormone receptor, ITT: intention-to-treat, mPFS: median progression-free survival, PFS: progression-free survival, T-DXd: trastuzumab deruxtecan, ENHERTU®, TPC: treatment of physician's choice

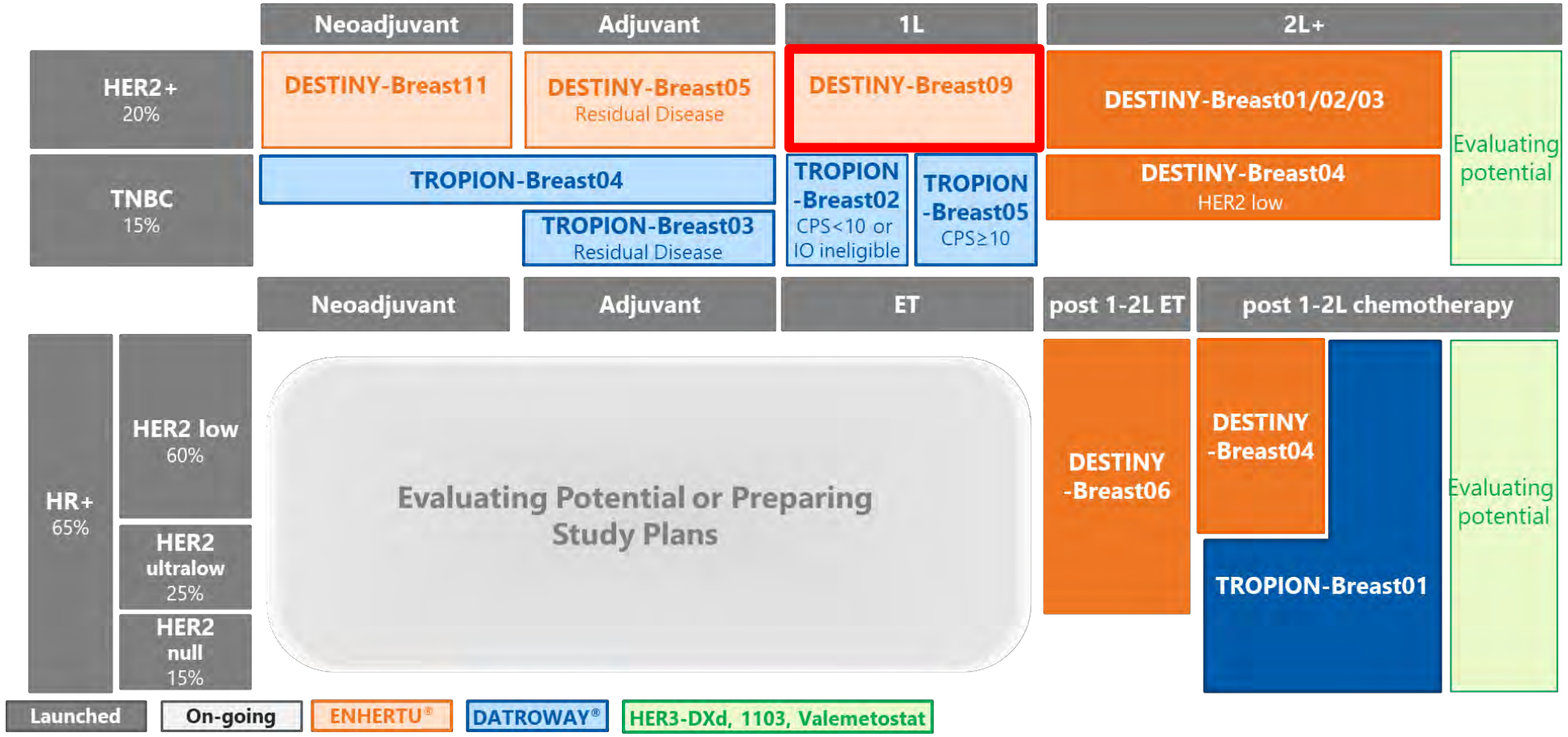
ENHERTU®

# Go Earlier in HER2 Positive Breast Cancer

DESTINY-Breast09 Ph3

Daiichi-Sankyo

## Ph3 study evaluating the efficacy and safety of ENHERTU® in mBC either alone or in combination with pertuzumab vs 1L SOC




CPS: combined positive score, ET: endocrine therapy, HR: hormone receptor, IHC: immunohistochemistry, mBC: metastatic breast cancer, mPFS: median progression-free survival, PFS: progression-free survival, SOC: standard of care, TNBC: triple-negative breast cancer, TPC: treatment of physician's choice

ENHERTU®

# Go Earlier in HER2 Positive Breast Cancer

DESTINY-Breast09 Ph3 Interim Analysis

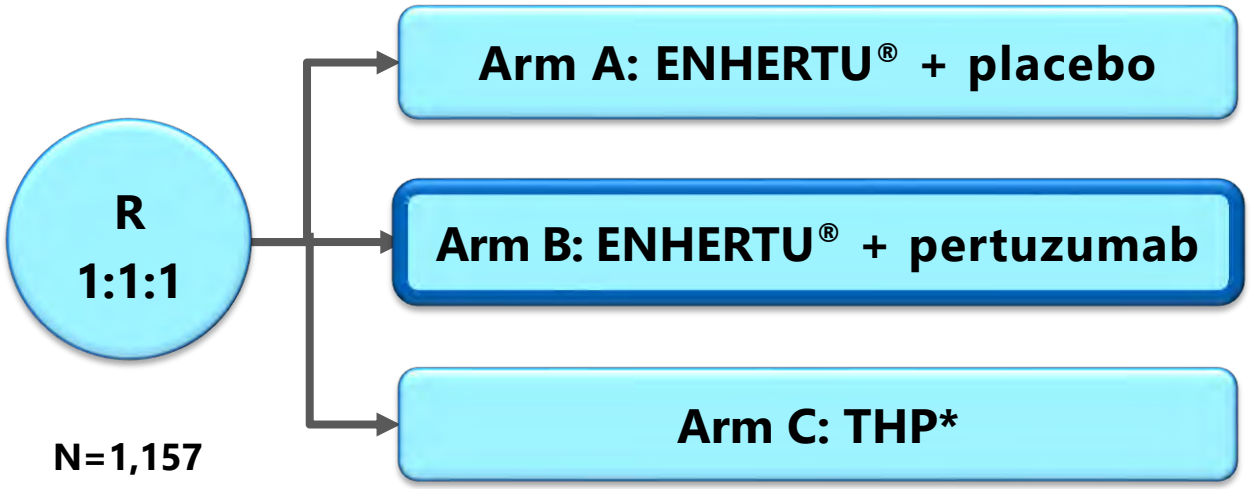
Daiichi-Sankyo

## ENHERTU® + pertuzumab demonstrated highly statistically significant and clinically meaningful improvement in PFS as 1L therapy for patients with HER2+ mBC

### DESTINY-Breast09 Study Design

**Eligible patients**

- Advanced and/or metastatic BC
- HER2 positive (IHC3+ or ISH+) by central confirmation
- No previous chemotherapy or HER2-targeted therapy for advanced or metastatic BC except for 1 previous line of endocrine therapy in the metastatic setting




**Primary endpoint:**
**PFS by BICR**

**Secondary endpoint:**
**PFS by investigator, OS, ORR, DOR, etc.**

*THP: paclitaxel qw
+ trastuzumab q3w
+ pertuzumab q3w

- **The PFS improvement was seen across all pre-specified patient subgroups** with ENHERTU® in combination with pertuzumab
- OS was not mature at the time of this planned interim analysis; however, interim OS data showed an early trend favoring the ENHERTU® combination compared to THP
- The safety profile of ENHERTU® in combination with pertuzumab was consistent with the known profiles of each individual therapy
- ENHERTU® monotherapy arm versus THP remains blinded to patients and investigators and will continue to the final PFS analysis
- Data from the combination arm will be presented at an upcoming medical meeting and shared with regulatory authorities

BC: breast cancer, BICR: blinded independent central review, DOR: duration of response, EFS: event-free survival, IHC: immunohistochemistry, ISH: in situ hybridization, mBC: metastatic breast cancer, ORR: objective response rate, OS: overall survival, PFS: progression-free survival, PK: pharmacokinetics, qw: once weekly, q3W: every 3 weeks, SOC: standard of care, TLR: top line results

ENHERTU®

# Expand Earlier in HER2 Positive Gastric Cancer

Gastric cancer update

Daiichi-Sankyo

## Improving patient outcomes by expanding into earlier lines and building on the success of ENHERTU® in 2L+ HER2 positive GC

| HER2 positive gastric cancer | | |
|---|---|---|
| 1L (PD-L1 CPS≥1) | 2L | 3L |
| **DESTINY-Gastric05* (Ph3)** pembrolizumab+ 5-FU or capecitabine combo | DESTINY-Gastric02 (Ph2) Completed | DESTINY-Gastric01 (Ph2) Completed |
| **ARTEMIDE-Gastric01 (Ph3)** rilvegostomig+ 5-FU or capecitabine combo | **DESTINY-Gastric04 (Ph3) Monotherapy** | DESTINY-Gastric06 (Ph2) China only |

- In Mar 2025, **positive DESTINY-Gastric04 results demonstrated statistically significant and clinically meaningful improvement in OS** primary endpoint
  - Seeking approval in regions where ENHERTU® not currently indicated for 2L, i.e., Japan
  - Securing full approval in regions with conditional approval, i.e., EU and China
  - Data will be presented at ASCO 2025
- Both DESTINY-Gastric05 and ARTEMIDE-Gastric01 started in Mar 2025

*: DESTINY-Gastric05 study will include patients with PD-L1 CPS <1 in the exploratory cohort
ASCO: American Society of Clinical Oncology, CPS: combined positive score, GC: gastric cancer, SOC: standard of care

ENHERTU®

# 1L Treatment for HER2 Overexpressing NSCLC

DESTINY-Lung06 Ph3

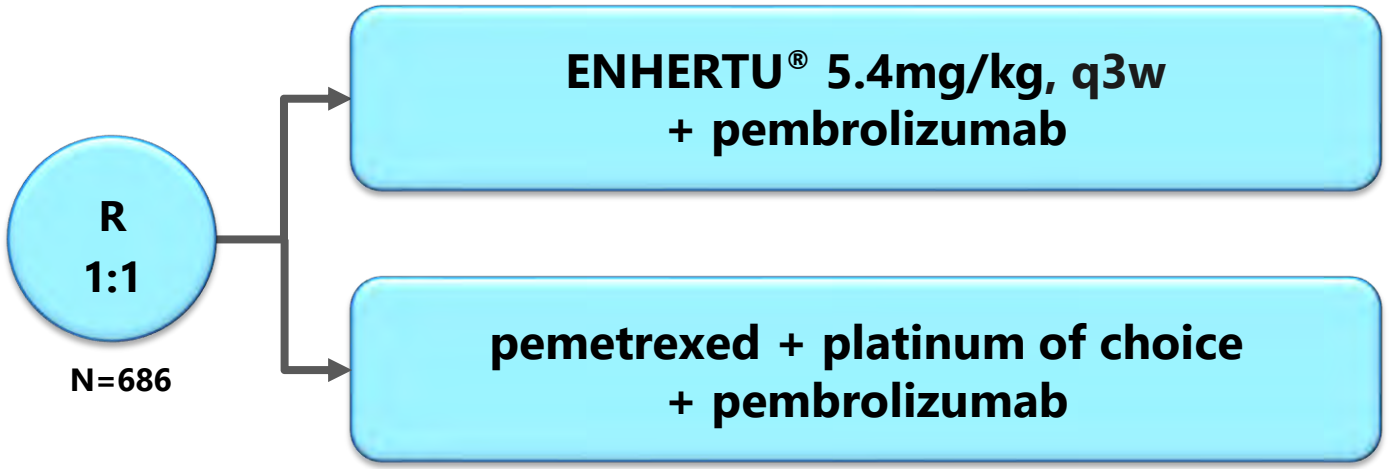
Daiichi-Sankyo

## Expand into earlier treatment lines by combining with current SOC to maximize patient outcomes for HER2 overexpressing NSCLC

### DESTINY-Lung06 Study Design

**Eligible Patients**

- Locally advanced unresectable or metastatic non-squamous NSCLC
- No prior systemic anticancer therapy for advanced/metastatic NSCLC
- HER2 overexpression
- PD-L1 TPS <50%
- No known AGAs




Primary endpoint: PFS (BICR)
Key secondary endpoint: OS

- DESTINY-Lung06 aims to replace standard chemotherapy in 1L SOC with ENHERTU® for HER2 overexpressing and PD-L1 TPS <50% NSCLC
- Plan to start in FY2025 H1

AGA: actionable genomic alteration, BICR: blinded independent central review, IHC: immunohistochemistry, NSCLC: non-small cell lung cancer, OS: overall survival, PFS: progression-free survival, q3w: every 3 weeks, TPS: tumor proportion score

ENHERTU®

# Expansion Beyond DESTINY-PanTumor02

Opportunities in HER2 Expressing tumors

Daiichi-Sankyo

## Building on success of Tumor Agnostic indication, opportunities for ENHERTU® continue to expand

### Expansion of approved countries

- Apr 2024: Approved in the US HER2 positive (IHC 3+) solid tumors with prior systemic treatment and without satisfactory alternative treatment options
- Apr 2025: **Filed in Japan for HER2 expressing recurrent or metastatic solid tumors** based on HERALD*, DESTINY-PanTumor02, DESTINY-CRC02 and DESTINY-Lung01

### Expansion in HER2 Expressing tumors

- Aug 2024: DESTINY-BTC01 Ph3 for HER2 expressing biliary tract cancer 1L started
- Plan to start **DESTINY-Ovarian01 Ph3** in HER2 IHC 3+/2+/1+ ovarian cancer 1L maintenance therapy

*HERALD study: An investigator-initiated Ph2 study evaluating the efficacy and safety of ENHERTU® in multiple solid tumors with HER2 gene amplification of cfDNA
BTC: biliary tract cancer, cfDNA: cell free deoxyribonucleic acid, IHC: immunohistochemistry

# New Challenge in Gynecological Cancers

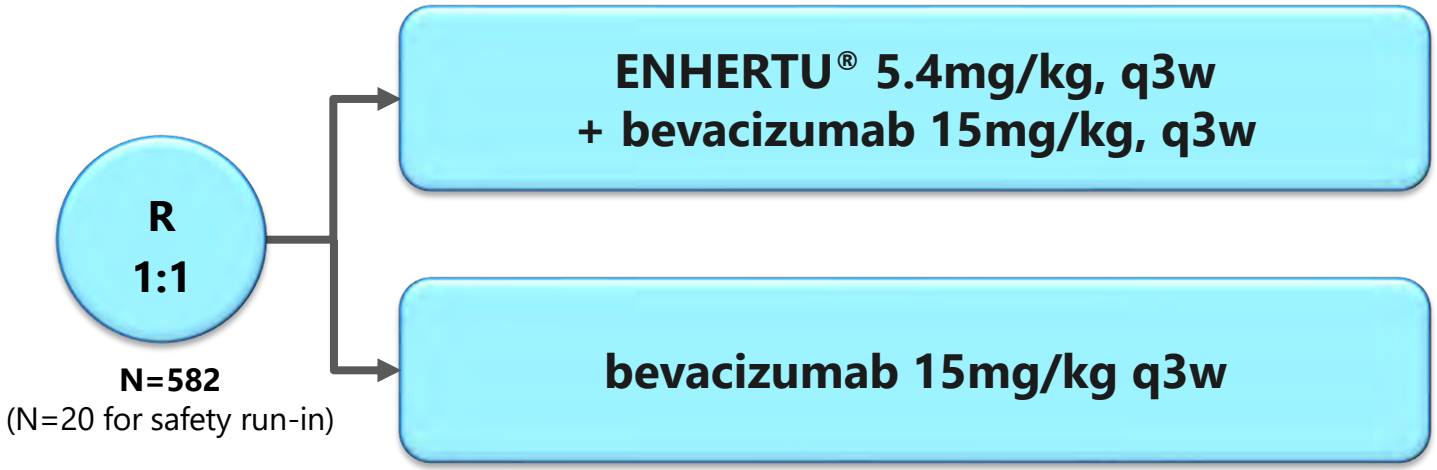
DESTINY-Ovarian01 Ph3

## A new Ph3 study for HER2 expressing ovarian cancer 1L maintenance

### DESTINY-Ovarian01 Study Design

**Eligible Patients**

- Histologically confirmed diagnosis of epithelial high-grade ovarian, fallopian tube or primary peritoneal carcinoma
- Newly diagnosed FIGO Stage III or IV
- HER2 IHC3+, IHC2+ or IHC1+
- Have received standard of care bevacizumab in combination with front line platinum-based chemotherapy
- Without BRCA mutation
- Not eligible for PARPi maintenance




Primary endpoint: PFS by BICR in HER2 IHC 3+/2+ population
Secondary endpoint: OS in HER2 IHC 3+/2+ population,
PFS and OS in HER2 IHC 3+/2+/1+ population

- Observed encouraging signals in heavily pre-treated population in DESTINY-PanTumor02 study (ASCO 2023, ESMO 2023)
  - ✓ Data for ovarian cancer population: cORR: 45.0% (18/40), mDOR: 11.3 mo (95% CI: 4.1, 22), mPFS: 5.9 mo (95% CI: 4.0, 8.3)
- Plan to start in FY2025 H1

ASCO: American Society of Clinical Oncology, BICR: blinded independent central review, CI: confidence interval, cORR: confirmed objective response rate, ESMO: European Society for Medical Oncology, FIGO: International Federation of Gynecology and Obstetrics, IHC: immunohistochemistry, mDOR: median duration of response, mo: month(s), mPFS: median progression-free survival, OS: overall survival, PFS: progression-free survival, q3w: every 3 weeks

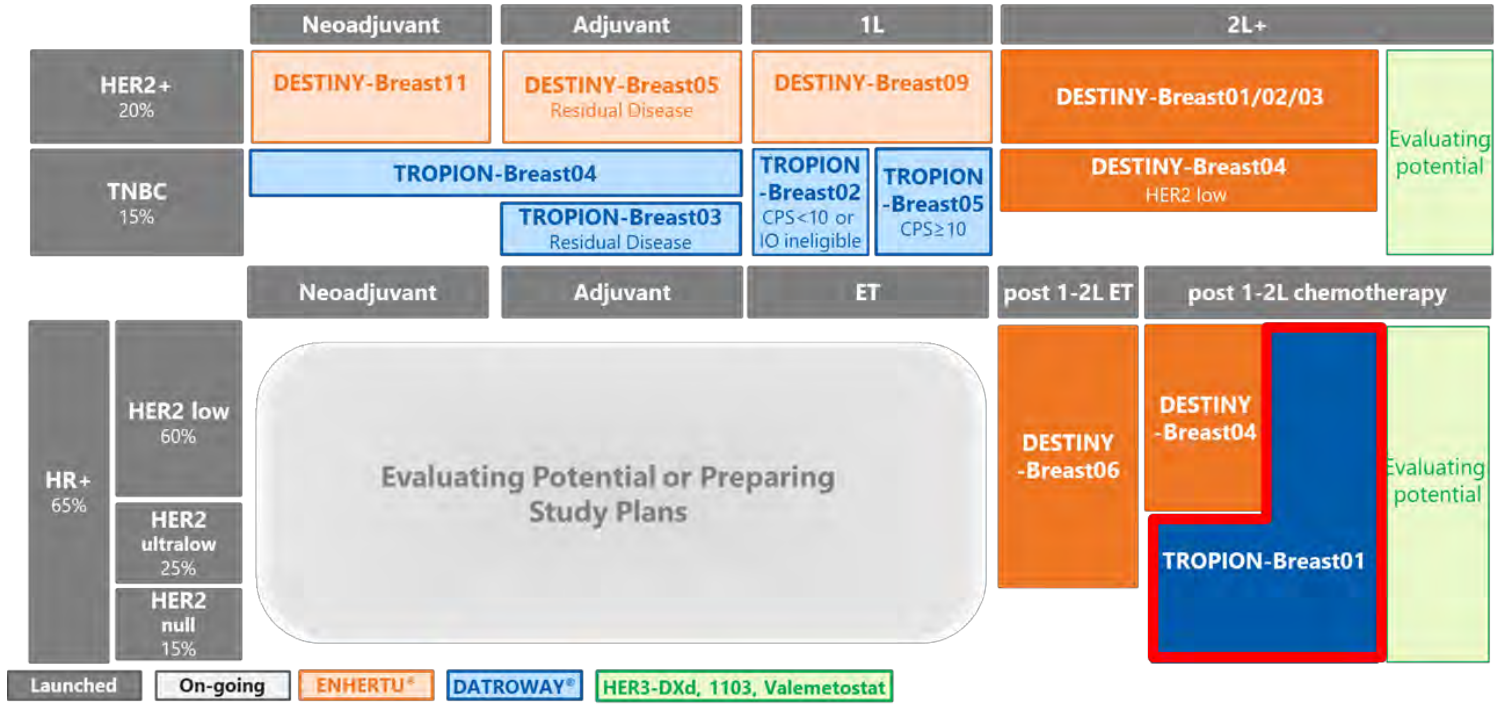
DATROWAY®
(Dato-DXd)

# Progress in FY2024: Breast Cancer

Results based on TROPION-Breast01

Daiichi-Sankyo

## Providing new treatment options for HR positive, HER2 negative breast cancer patients




- DATROWAY® approved in Japan in Dec 2024 and in US in Jan 2025 for HR-positive, HER2 negative (IHC 0, IHC 1+ or IHC 2+/ISH-) post-chemo metastatic BC based on the results of TROPION-Breast01
- Positive CHMP opinion received January 2025 leading to **approval in EU in April 2025**
- TLR of TROPION-Breast02 (TNBC, PD-1/PD-L1 inhibitor ineligible, 1L) is anticipated for FY2025 H1

BC: breast cancer, CHMP: Committee for Medicinal Products for Human Use, CPS: combined positive score, ET: endocrine therapy, HR: hormone receptor, IHC: immunohistochemistry, ISH: *in situ* hybridization, TLR: top line results, TNBC: triple-negative breast cancer

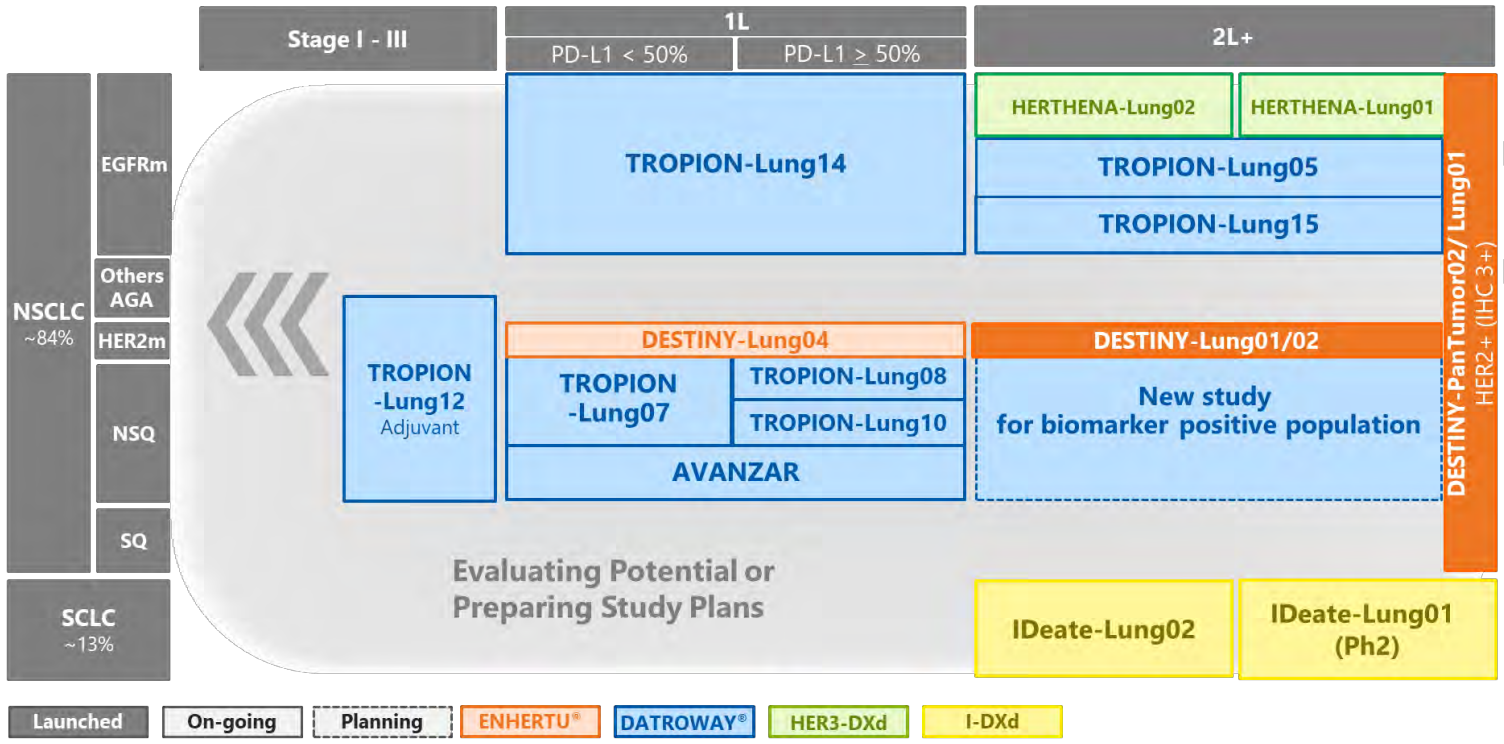
DATROWAY®
HER3-DXd

# Progress in FY2024: NSCLC

HERTHENA-Lung01, HERTHENA-Lung02, TROPION-Lung05 etc.

Daiichi-Sankyo

## Progressing development for EGFR mutated NSCLC




### EGFR mutated NSCLC

- FDA issued CRL for HER3-DXd HERTHENA-Lung01 in June 2024 following inspection of third-party manufacturing facility
- In Sep 2024, HERTHENA-Lung02 met its primary endpoint
- **FDA accepted DATROWAY® submission** with Priority Review for the treatment of patients with EGFR mutated NSCLC who have received prior systemic therapies, including an EGFR-directed therapy based on TROPION-Lung05* in Jan 2025 (PDUFA date: Jul 12, 2025)

### Other NSCLC programs

- Four new Ph3 studies of DATROWAY® started in FY2024
- TLR of AVANZAR Ph3 study for 1L treatment is anticipated in CY2025 H2

* This application was supported by data from TROPION-Lung01 and TROPION-PanTumor01

AGA: actionable genomic alteration, CRL: complete response letter, FDA: U.S. Food and Drug Administration, IHC: immunohistochemistry, PDUFA: prescription drug user fee act, NSQ: non- squamous, NSCLC: non-small cell lung cancer, SCLC: small cell lung cancer, SQ: squamous, TLR: top line results

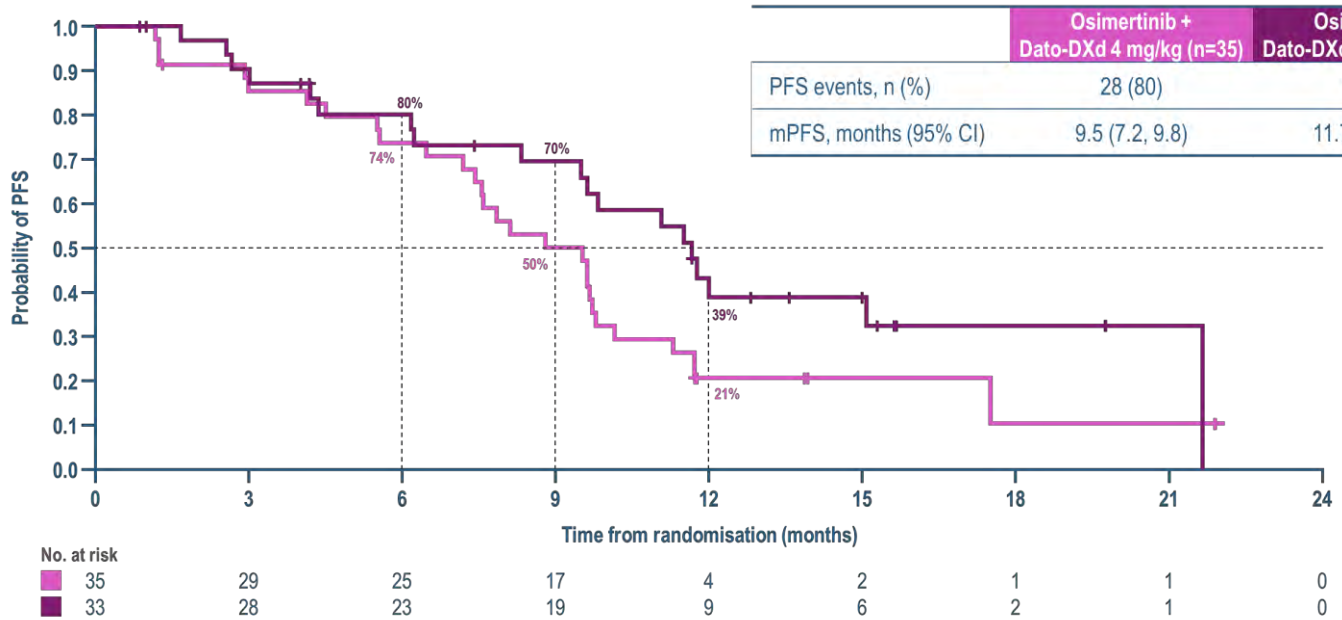
# Progress in EGFR mutated NSCLC

ORCHARD module10 (ELCC 2025)

Daiichi-Sankyo

## DATROWAY® in combination with osimertinib demonstrated promising efficacy in EGFR mutated NSCLC progressed after 1L osimertinib

### Antitumor activity (PFS)




| | Osimertinib + Dato-DXd 4 mg/kg (n=35) | Osimertinib + Dato-DXd 6 mg/kg (n=33) |
|---|---|---|
| PFS events, n (%) | 28 (80) | 19 (58) |
| mPFS, months (95% CI) | 9.5 (7.2, 9.8) | 11.7 (8.3, NC) |

**ORCHARD (Ph2)**

- ✓ EGFR mutated NSCLC progressing on 1L osimertinib monotherapy
- ✓ Evaluate safety and efficacy of combination therapy of osimertinib 80 mg and DATROWAY® (4 mg/kg or 6 mg/kg) in module10
- ✓ Primary endpoint: ORR

Data cut-off: Oct 12, 2024

- mPFS: 9.5 mo (95% CI: 7.2, 9.8), ORR: 43% (80% CI: 31, 55), mDOR: 6.3 mo (95% CI: 3.8, 8.2) in DATROWAY® 4 mg/kg cohort and mPFS: 11.7 mo (95% CI: 8.3, NC), ORR: 36% (80% CI: 25, 49), mDOR*: 20.5 (95% CI: 6.2, NC) in 6 mg/kg cohort
- No new safety signals were identified in either cohort
- Two Ph3 studies, TROPION-Lung14 and TROPION-Lung15 are ongoing to evaluate efficacy of DATROWAY® in combination with osimertinib in EGFR mutated NSCLC

*: mDOR not yet mature for 6 mg/kg cohort CI: confidence interval, Dato-DXd: datopotamab deruxtecan, DATROWAY®, ELCC: European Lung cancer Congress, NC: not calculable, NSCLC: non-small cell lung cancer, mDOR: median duration of response, mo: month(s), mPFS: median progression-free survival, ORR: objective response rate, PFS: progression-free survival

HER3-DXd

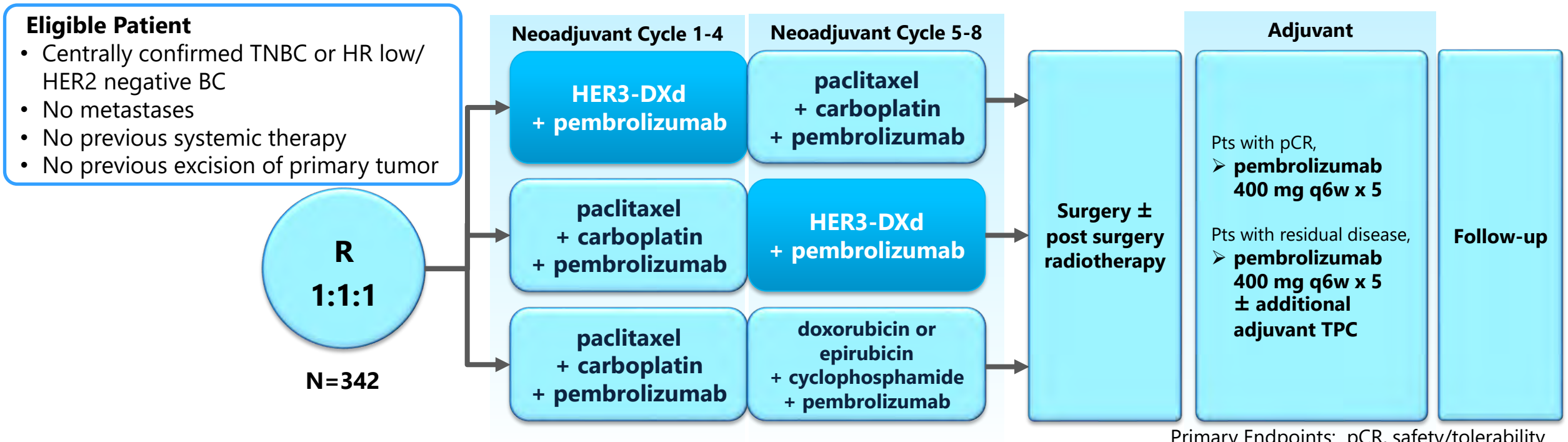
# Enhance Neoadjuvant Treatment in Breast Cancer

HERTHENA-Breast03 Ph2

Daiichi-Sankyo

## Ph2 signal seeking study for pCR improvement by determining optimal sequence of ADC and chemotherapy in neoadjuvant setting

### HERTHENA-Breast03 Study Design (Part 2)




Primary Endpoints: pCR, safety/tolerability
Secondary Endpoints: RCB, EFS, DPDRFS, OS

- HER3-DXd Ph1 study demonstrated promising efficacy in heavily pretreated mTNBC
  - ✓ ORR: 22.6% (95% CI: 12.3, 36.2), mPFS: 5.5 mo (95% CI: 3.9, 6.8), mOS: 14.6 mo (95% CI: 11.2, 17.2) (ASCO 2022)
- Part 2 begins after DLT evaluation for HER3-DXd pembrolizumab combination as safety run-in (Part 1)
- Plan to start in FY2025 H1

ASCO: American Society of Clinical Oncology, BC: breast cancer, CI: confidence interval, DLT: dose limiting toxicity, DPDRFS: Distant Progression or Distant Recurrence-Free Survival, EFS: event-free survival, HR: hormone receptor, mo: month(s), mOS: median overall survival, mPFS: median progression-free survival, mTNBC: metastatic triple negative breast cancer, ORR: objective response rate, OS: overall survival, pCR: pathological complete response, q6w: every 6 weeks, RCB: residual clinical burden, TNBC: triple negative breast cancer, TPC: treatment of physician's choice

Progress towards “Maximize 3ADCs”

**Progress towards “Profit growth for current business and products”**

ASCO 2025

News Flow

I-DXd
R-DXd

# Major Progress in FY2024

## I-DXd and R-DXd demonstrate their significance as 'further growth pillars' supported by the strategic collaboration with MRK*

### I-DXd

- Steady progress for ES-SCLC
  - IDeate-Lung01 Ph2 study is proceeding
  - **IDeate-Lung02 Ph3 study in SCLC** started in Aug 2024
  - Combination study with MK-6070 (gocatamig) started
  - Granted Orphan Drug Designation for SCLC in Japan in Dec 2024
- Expand to tumor types beyond SCLC
  - Plan to start **IDeate-Esophageal01** Ph3 study for pretreated ESCC in FY2025 H1
  - Plan to start **two new studies for mCRPC**
  - Starting with IDeate-PanTumor02, conducting exploratory studies across a wide range of tumor types

### R-DXd

- Steady progress for ovarian cancer
  - **First pivotal Ph2/3 study (REJOICE-Ovarian01)** started in Apr 2024
  - **REJOICE-Ovarian02 Ph1b/2 study** to evaluate combination of R-DXd with either carboplatin, paclitaxel, or bevacizumab is under preparation
  - Granted Orphan Drug Designation for ovarian cancer in EU in Feb 2025
  - Granted Orphan Drug Designation for platinum-resistant ovarian cancer in Japan in Mar 2025
- Exploratory studies across multiple tumor types underway
  - In Jan 2025, REJOICE-PanTumor01 for multiple solid tumors started
  - Studies for ES-SCLC, squamous NSCLC, non-squamous NSCLC, gastrointestinal cancers, etc are ongoing.

*MRK: Merck & Co., Inc., Rahway, NJ, USA

ESCC: esophageal squamous cell carcinoma, ES-SCLC: extensive-stage small cell lung cancer, mCRPC: metastatic castration-resistant prostate cancer, NSCLC: non-small cell lung cancer, SCLC: small cell lung cancer, TLR: top line results

# The Third Ph3 Study

IDeate-Prostate01 Ph3 study (monotherapy)

## New Ph3 study of I-DXd in chemo naive metastatic castration-resistant prostate cancer (mCRPC)

### IDeate-Prostate01 Study Design

**Eligible Patients**

- Metastatic CRPC with ≤2 ARPI treatment
- Prostate cancer progression while on androgen deprivation therapy (or post bilateral orchiectomy) within 6 months before screening
- No requirement on B7-H3 expression status (B7-H3 expression is to be confirmed during the study)


Primary endpoint: OS, rPFS
Secondary endpoint: TFST, OR, DOR etc.

- B7-H3 is highly expressed in metastatic CRPC, and its overexpression is associated with a poor prognosis
- Observed encouraging signals in heavily pre-treated population in Ph1/2 study (ESMO 2023)
  - ✓ cORR: 25.4% (15/73, 95% CI: 15.0, 38.4), mPFS: 5.3 mo (95% CI: 4.1, 6.9), mOS: 13.0 mo (95% CI: 10.3, 16.0), Number of prior treatments, median: 6 (1-11)
- Plan to start in FY2025 H1

ARPI: androgen receptor pathway inhibitors, CI: confidence interval, cORR: confirmed objective response rate, DOR: duration of response, ESMO: European Society for Medical Oncology, mo: month(s), mOS: median overall survival, mPFS: median progression-free survival, OR: objective response, OS: overall survival, rPFS; radiographic progression-free survival, TFST: time to first subsequent therapy

# Expanding Target Indication to mCRPC

IDeate-Prostate02 Ph1/2 (combination therapy)

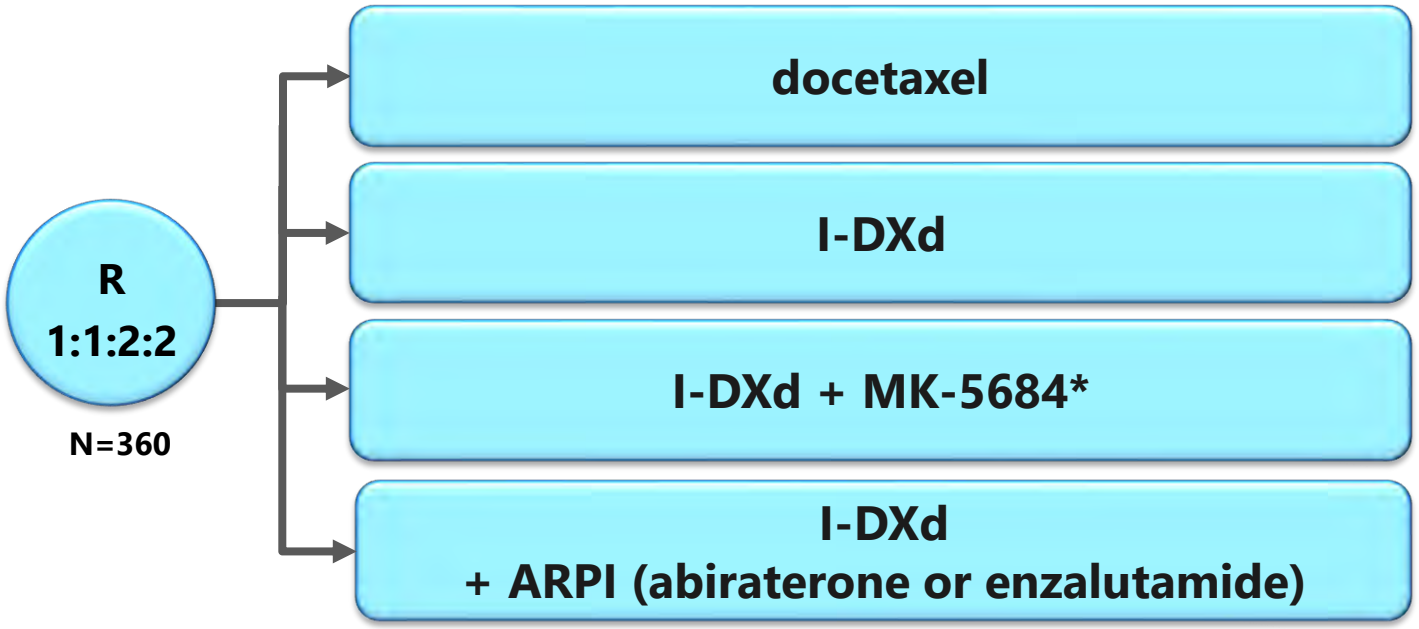
Daiichi-Sankyo

## New Ph1/2 study of I-DXd in chemo naïve metastatic castration-resistant prostate cancer (mCRPC)

### IDeate-Prostate02 Study Design

**Eligible Patients**

- Histologically- or cytologically-confirmed adenocarcinoma of the prostate without small cell histology
- Prostate cancer progression while on androgen deprivation therapy (or post bilateral orchiectomy) within 6 months before screening
- Received 1 or 2 prior ARPI treatment and progressed during or after treatment




Primary outcome measures: safety, PSA response rate
Secondary outcome measures: ORR, rPFS, OS, DOR etc.

- Study will evaluate safety and tolerability of I-DXd, a safe dose level of I-DXd that can be used with other treatments and participant levels of prostate specific antigen (PSA) during treatment
- Plan to start FY2025 H1

*: CYP11A inhibitor developed by MRK, ARPI: androgen receptor pathway inhibitors, DOR: duration of response, ORR: objective response rate, OS: overall survival, rPFS; radiographic progression-free survival

R-DXd

# Exploring Possibilities in Gastrointestinal Cancers

REJOICE-GI01 Ph2

Daiichi-Sankyo

## Plan to start a signal-seeking study in gastrointestinal cancers in addition to REJOICE-PanTumor01 started in January 2025

### REJOICE-GI01 Study Design

**Eligible Patients**

- One of the following cancers:
  - Pancreatic adenocarcinoma (PDAC)
  - Biliary tract cancer (BTC)
  - Colorectal cancer
  - Gastroesophageal adenocarcinoma
- Received prior therapy for the cancer

**PDAC**

**BTC**

**Colorectal cancer**

**Gastroesophageal adenocarcinoma**

N=160

**Outcome Measures**

**Primary:**
ORR
**Secondary:**
safety, DOR, PFS, OS

- Assess safety and efficacy of R-DXd in gastrointestinal cancers
- Plan to start in FY2025 H1

DOR: duration of response, GI: gastrointestinal, ORR: objective response rate, OS: overall survival, PFS: progression-free survival

# Next Wave Progress in FY2024

## Oncology

- **EZHARMIA®** (EZH1/2 inhibitor)
  - Approval for r/r PTCL in Japan (Jun 2024)
  - Started a Ph1b/2 study for NSCLC 1L in combination with pembrolizumab (Oct 2024)
- **VANFLYTA®** (FLT3 inhibitor)
  - Started QuANTUM-Wild Ph3 study for *FLT3*-ITD negative AML (Dec 2024)
- **DS-3939** (TA-MUC1 directed ADC)
  - **Acquired intellectual property rights for anti-TA-MUC1 antibody from Glycotope GmbH (Dec 2024)**
- **DS-2243** (HLA-A*02/NY-ESO directed bispecific T-cell engager)
  - **Started Ph1 study (Mar 2025)**

## Specialty Medicine

- **LIXIANA®** (Factor Xa inhibitor)
  - **Approval for chronic thromboembolic pulmonary hypertension (CTEPH) in Japan (Feb 2025)**
- **TARLIGE®** ($\alpha_2\delta$ ligands)
  - Approval for diabetic peripheral neuropathic pain in China (Jun 2024)

## Vaccine

- **DAICHIRONA®*** (COVID-19 mRNA vaccine)
  - **Approval of vaccine for omicron strain for children aged 5 to 11 years in Japan (Mar 2025)**

**Bold：update from FY2024 Q3**

ADC: antibody-drug conjugate, AML: acute myeloid leukemia, NSCLC: non-small cell lung cancer, PTCL: peripheral T-cell lymphomas, r/r: relapsed/ refractory

* The research and development of DAICHIRONA® FOR INTRAMUSCULAR INJECTION is being conducted through the "Vaccine development project" promoted by the Japan Agency for Medical Research and Development (AMED) and the "Urgent improvement project for vaccine manufacturing systems" supported by the Japanese Ministry of Health, Labour and Welfare (MHLW).

Progress towards “Maximize 3ADCs”

Progress towards “Profit growth for current business and products”

**ASCO 2025**

News Flow

# ASCO Highlights 2025: IR conference call

**Hiroyuki Okuzawa**
President and CEO

**Ken Takeshita**
Head of Global R&D

**Mark Rutstein**
Head of Therapeutic Area
Oncology Development

| | |
|---|---|
| Date and Time | Jun 3, 2025 (Tue) 8:00-9:15am JST/<br>Jun 2, 2025 (Mon) 6:00-7:15pm CDT |
| Meeting style | Virtual (Zoom) |

**Content will be delivered on-demand after the meeting**

Progress towards “Maximize 3ADCs”

Progress towards “Profit growth for current business and products”

ASCO 2025

**News Flow**

# FY2025 News Flow

As of Apr 2025

## Planned major data disclosures

### American Society of Clinical Oncology（ASCO, May 30-Jun 3, 2025）

| | |
|---|---|
| ENHERTU® | **DESTINY-Gastric04: HER2+ GC, 2L, Ph3**<br>**• Primary results** |
| DATROWAY® | **TROPION-Lung02: NSCLC (without AGA), 1L+, pembrolizumab combo, Ph1b**<br>**• Data update** |
| | **TROPION-Lung04: NSCLC (without AGA), 1L/2L, ICI combo, Ph1b**<br>**• First data of rilvegostomig combo cohort** |
| | **NeoCOAST-2: resectable, early-stage NSCLC, neoadjuvant**<br>**• Final analysis of pCR and mPR rates in DATROWAY® combo cohort** |
| HER3-DXd | **HERTHENA-Lung02: EGFR mutated NSCLC, 2L**<br>**• Primary data for PFS** |

## Key data readouts

| | |
|---|---|
| ENHERTU® | DESTINY-Breast11: HER2+ BC, neoadjuvant, Ph3<br>• FY2025 H1 |
| | DESTINY-Breast05*: HER2+ BC, Adjuvant, Ph3<br>• FY2025 H2 |
| | DESTINY-Lung04*: HER2 mutant NSCLC, 1L, Ph3<br>• FY2025 H1 |
| DATROWAY® | TROPION-Breast02*:<br>PD-1/PD-L1 ineligible TNBC, 1L, Ph3<br>• FY2025 H1 |
| | AVANZAR*:<br>TROP2+ NSCLC, 1L, Ph3<br>• CY2025 H2 |
| I-DXd | IDeate-Lung01*:<br>ES-SCLC, 2L+, Ph2<br>• FY2025 H1 |

## Regulatory decisions

| | |
|---|---|
| ENHERTU® | DESTINY-Breast06:<br>HR+/HER2 low or HER2 ultralow, chemo naïve, Ph3<br>• JP: FY2025 H1 |
| DATROWAY® | TROPION-Lung05#: EGFR mutated NSCLC with prior systemic therapies, including an EGFR-directed therapy<br>• US: FY2025 H1 |

#supported by data from TROPION-Lung01, TROPION-PanTumor01

**Bold: update from FY2024 Q3**

Timeline indicated is based on the current forecast and subject to change
※ Timeline for "Planned regulatory filing" indicates expected filing acceptance date
*: event-driven study
AGA: actionable genomic alteration, BC: breast cancer, ES-SCLC: extensive-stage small cell lung cancer, HR: hormone receptor, IHI: immune checkpoint inhibitor, mPR: major pathological response, NSCLC: non-small cell lung cancer, pCR: pathological complete response, PFS: progression-free survival, TNBC: triple negative breast cancer

# Agenda

1. FY2024 Financial Results
2. Business Update
3. R&D Update
4. **5-Year Business Plan Update**
5. FY2025 Forecast
6. Appendix

# Strategic Pillars for the 5-Year Business Plan (FY2021-FY2025)

Daiichi-Sankyo

## Realize 2025 Goal and Shift to Further Growth

**FY2025 Financial Targets**

- Revenue: 1.6 Tr JPY (Oncology > 600.0 Bn JPY)
- Core Operating Profit* Ratio before R&D Expense: 40%
- ROE > 16%
- DOE** > 8%

### Maximize 3ADCs

- Maximize ENHERTU® and Dato-DXd through strategic alliance with AstraZeneca
- Maximize HER3-DXd without a partner
- Expand work force and supply capacity flexibly depending on changes around product potential

### Profit growth for current business and products

- Maximize Lixiana® profit
- Grow Tarlige®, Nilemdo®, etc. quickly
- Transform to profit structure focused on patented drugs
- Profit growth for American Regent and Daiichi Sankyo Healthcare

### Identify and build pillars for further growth

- Identify new growth drivers following 3ADCs
- Select and advance promising post DXd-ADC modalities

### Create shared value with stakeholders

- Patients: Contributing to patients through "Patient Centric Mindset"
- Shareholders: Balanced investment for growth and shareholder returns
- Society: Environment load reduction across the value chain, and actions against pandemic risks
- Employees: Create one DS culture through fostering our core behaviors

- Data-driven management through DX, and company-wide transformation through advanced digital technology
- Agile decision making through new global management structure

*Excluding temporary income and expenses (gains/losses related to sales of fixed assets etc.) from operating income

**DOE: Dividend on Equity = Total dividend amount / Equity attributable to owners of the company

# 5-Year Business Plan: Progress in FY2021-FY2024

## Maximize 3ADCs

- **Maximize product value of ENHERTU®**
  - **Approval of new indication**
    - HER2+ BC 2L, HER2 low BC post-chemo, HR+, HER2 low or HER2 ultralow BC chemo naïve
    - HER2 mutant NSCLC 2L+, HER2+ solid tumors 2L+, etc.
  - **Sales growth in each country/region**
  - **Progress of indication expansion**
- **Maximize product values of DATROWAY®**
  - **Approval and launch**
    - HR+, HER2- BC with prior endocrine-based therapy and chemotherapy
  - **Filing accepted**
    - EGFR mutated NSCLC with prior systemic therapies, including an EGFR-directed therapy
  - **Progress of indication expansion**
- **Strategic collaboration for HER3-DXd, I-DXd, and R-DXd, etc.**
  - **Co-development and co-commercialization with MRK*1**
  - **Co-development and co-commercialization for MK-6070**

## Profit growth for current business and products

- **Growth of current products**
  - **Steady sales expansion of Lixiana®**
    - Increase product value with additional dosage and administration*2
  - **Sales increase of current products in each country/region**
    - Tarlige®, Venofer®, Nilemdo®/Nustendi® etc.
    - Increase product values of current products by additional indication/ formulation
- **Transformation of business structure focused on patented drugs**
  - **Launch of new drug**
    - Emgality®, Ezharmia®, Vanflyta®, Daichirona® , FluMist® etc.
  - **Progress of product divesture after loss of exclusivity in each country/region**
  - **Stock transfer of Daiichi Sankyo Espha Co., Ltd.**
    - Divesture of generic business in Japan
- **Profit growth of American Regent and Daiichi Sankyo Healthcare**
  - **Contribution to consolidated performance through increased revenue and profit**

*1 Merck & Co., Inc., Rahway, NJ, USA; *2 Prevention for stroke and systemic embolism in elderly patients with non-valvular atrial fibrillation and high bleeding risk: ELDERCARE-AF study

Orange: major updates from FY2024

# 5-Year Business Plan: Progress in FY2021-FY2024

## Identify and build pillars for further growth

- **Emerging growth drivers following 3ADCs**
  - **Progress of development for I-DXd (B7-H3-directed ADC)**
    - Started monotherapy Ph3 study for SCLC
    - Started combination therapy with MK-6070 for SCLC
    - Started exploratory studies for various tumor types
  - **Progress of development for R-DXd (CDH6-directed ADC)**
    - Accumulated promising data for OVC
    - Started Ph2/3 study for OVC
    - Started exploratory studies for several types of cancer
  - **Progress of development for DS-3939 (TA-MUC1-directed ADC)**
    - Started clinical study for solid tumor
- **Advancement to select post DXd-ADC modalities**
  - **Started clinical study for DS-9606, an ADC with mPBD payload**
  - **Approval and supply of mRNA COVID-19 vaccine, Daichirona® for intramuscular injection**
- **Established research institutes in the U.S. and EU, and smart research laboratory in the U.S**

## Create shared value with stakeholders

- **Strengthening and enrichment of shareholder returns**
  - **Shareholder returns taking account of profit growth**
    - Increased annual dividend in three consecutive years due to profit growth of ENHERTU®, and received upfront payment related to strategic collaboration with MRK etc
    - Executed two rounds of own shares acquisition from April 2024
- **Actions against pandemic risks**
  - **Supply of Daichirona® for intramuscular injection**
- **Environment load reduction across the value chain**
  - **Progress initiative for environmental issues**
    - Joined RE100, a global initiative aiming to use 100% renewable energy for electricity consumed in business activities
    - Converted electricity consumed in bases in Japan to renewable energy
- **Penetration of Core Behavior for fostering one DS culture**
  - **Further understanding of three Core Behaviors through workshop by management and employees**

mPBD: modified pyrrolobenzodiazepiner, OVC: ovarian cancer, SCLC: small cell lung cancer

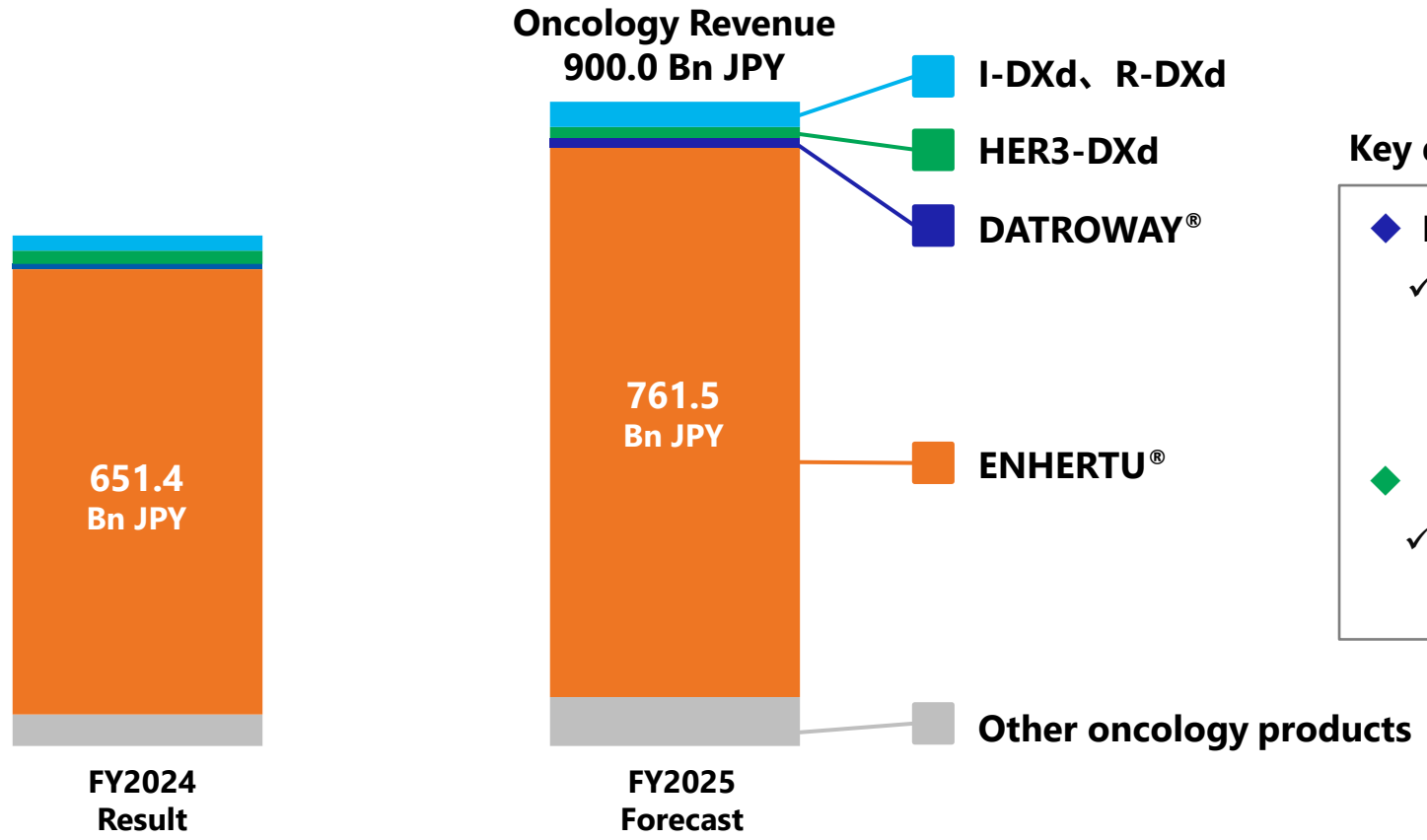
Orange: major updates from FY2024

# Expectation on achieving FY2025 KPIs
(as of Apr. 2025)

| | At the time of planning 5YBP | As of Apr. 2024 | As of Apr. 2025 |
|---|---|---|---|
| Revenue | 1.6 Tr JPY | 2.1 Tr JPY | 2.0 Tr JPY |
| Revenue in Oncology | > 600.0 Bn JPY | > 1.0 Tr JPY | 900.0 Bn JPY |
| Core Operating Profit ratio before R&D expense | 40% | 40% | 40% |
| ROE | > 16% | > 16% | > 16% |
| DOE | > 8% | > 8.5% | > 8.5% |
| Currency exchange rate assumptions | 1 USD=105 JPY, 1 EUR=120 JPY | 1 USD=145 JPY, 1 EUR=155 JPY | 1 USD=140 JPY, 1 EUR=160 JPY |

# Oncology Revenue Forecast
(as of Apr. 2025)

**FY2025 oncology revenue* is forecasted to be 900 Bn JPY, driven by steady growth of ENHERTU®, despite a decline from the April 2024 forecast due to changes in DATROWAY®'s development strategy**




**Key drivers of decline vs. Apr 2024 forecast**

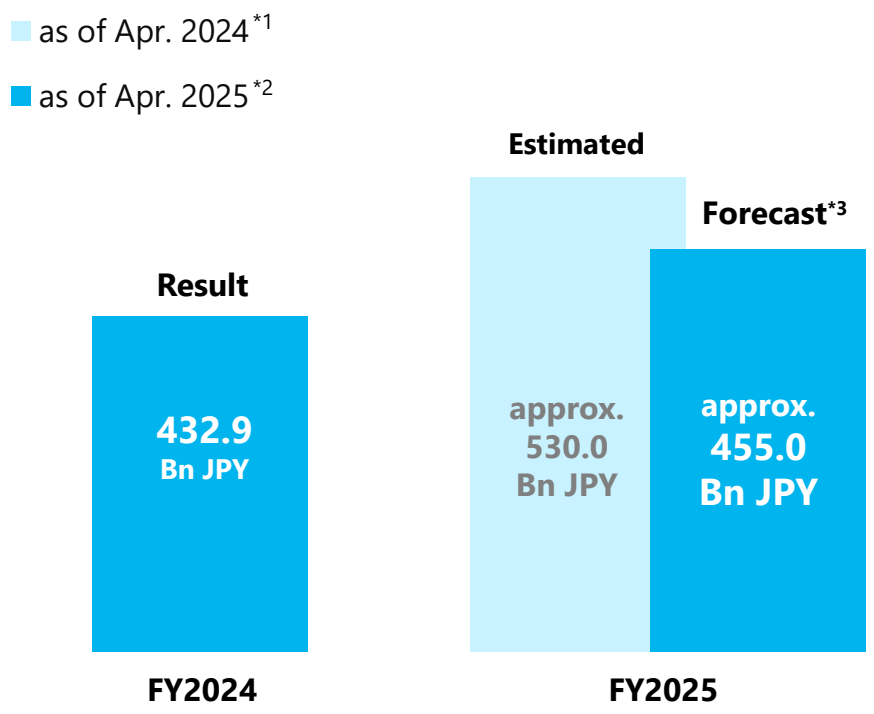
- **DATROWAY®**
  - ✓ The number of eligible patients decreased and launch delayed due to development strategy update on NSCLC (TL01 → TL05 study)
- **HER3-DXd**
  - ✓ Launch delayed due to complete response letter

* Revenue for 5DXd ADCs includes alliance revenue (50% of gross profit from product sales in countries/regions where AstraZeneca and US Merck book sales), upfront payments, development and sales milestones received from both collaborators based on strategic alliance agreements

# R&D Expense Forecast
(as of Apr. 2025)

## FY2025 R&D expense is forecasted to be 455 Bn JPY based on development plan updates

### R&D Expense Trend




Currency exchange rate assumptions
*1: 1 USD=145 JPY、1 EUR=155 JPY
*2: 1 USD=140 JPY、1 EUR=160 JPY

Forecast
*3: as of Apr. 2025

### Key drivers of decline vs. Apr 2024 forecast

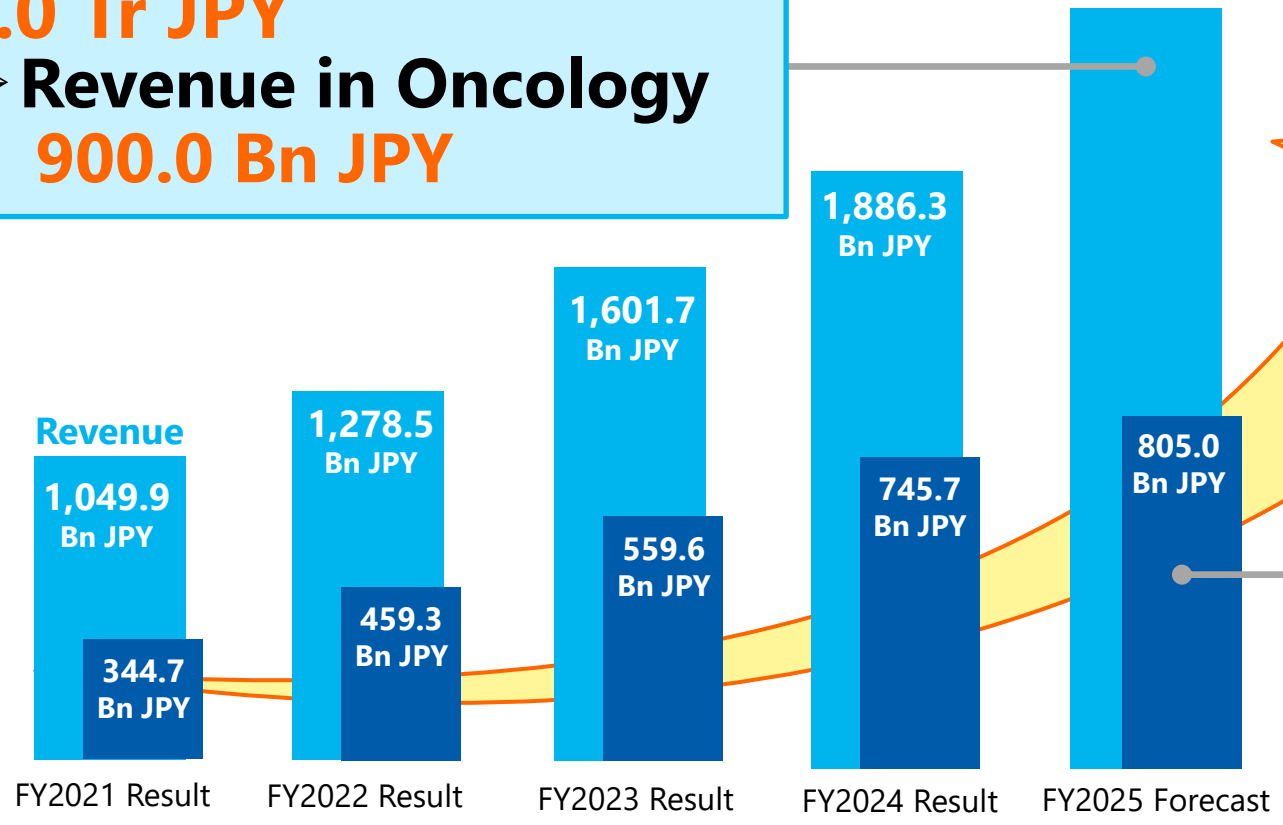
◆ **Clinical development expense**
- ✓ Development plan updated based on strategic collaboration with US Merck

◆ **Medical affairs expense**
- ✓ NSCLC development strategy updated on DATROWAY®
- ✓ Launch delayed on HER3-DXd

# Forecast of FY2025 KPIs
(as of Apr. 2025)

◆**Revenue**
**2.0 Tr JPY**
➢**Revenue in Oncology**
**900.0 Bn JPY**

**Achieve significant revenue/profit growth after investment for DXd ADCs, and shift to a new stage for realizing 2030 vision**



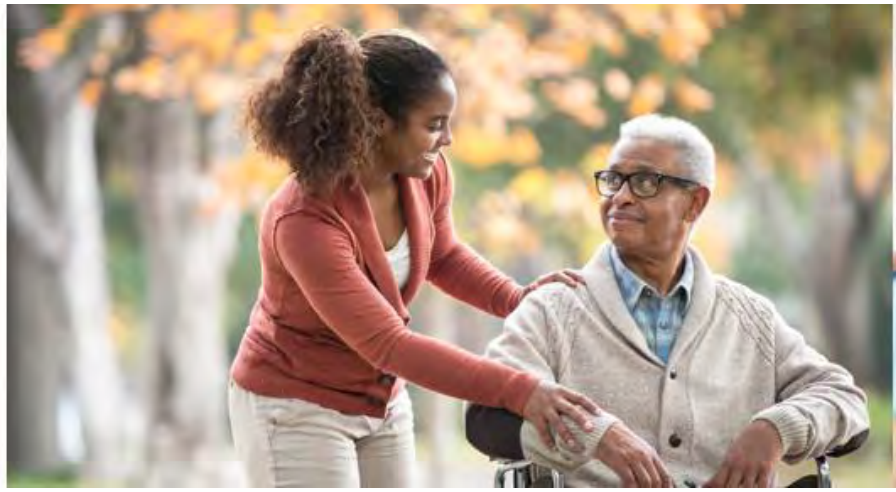

◆**Core Operating Profit* ratio before R&D expense: 40%**

◆**ROE > 16%**

◆**DOE > 8.5%**

FY2025 currency exchange rate assumptions: 1 USD = **140 JPY**, 1 EUR = **160 JPY**
*Excluding temporary income and expenses (gains/losses related to sales of fixed assets etc.) from operating income

# Daiichi Sankyo will contribute to the enrichment of quality of life around the world



# Agenda

1. FY2024 Financial Results
2. Business Update
3. R&D Update
4. 5-Year Business Plan Update
5. **FY2025 Forecast**
6. Appendix

# FY2025 Forecast

(Bn JPY)

| | FY2024 Results | FY2025 Forecast | vs. Forecast |
|---|---|---|---|
| **Revenue** | **1,886.3** | **2,000.0** | **+113.7** |
| Cost of sales *1 | 415.7 | 430.0 | +14.3 |
| SG&A expenses *1 | 724.8 | 765.0 | +40.2 |
| DXd ADC profit share *2 | 226.2 | 265.0 | +38.8 |
| Other SG&A expenses | 498.6 | 500.0 | +1.4 |
| R&D expenses *1 | 432.9 | 455.0 | +22.1 |
| **Core operating profit** *1 | **312.8** | **350.0** | **+37.2** |
| Temporary income *1 | 22.2 | - | -22.2 |
| Temporary expenses *1 | 3.1 | - | -3.1 |
| **Operating profit** | **331.9** | **350.0** | **+18.1** |
| **Profit before tax** | **355.6** | **370.0** | **+14.4** |
| **Profit attributable to owners of the Company** | **295.8** | **300.0** | **+4.2** |

| | | | | |
|---|---|---|---|---|
| Currency Exchange Rate | USD/JPY | 152.57 | 140.00 | -12.57 |
| | EUR/JPY | 163.74 | 160.00 | -3.74 |

**Revenue**
- ↑ : Sales expansion of ENHERTU; Increase in milestone income related to strategic alliance with AstraZeneca and US MRK*
- ↓ : Decrease due to forex impact

* Merck & Co., Inc., Rahway, NJ, USA

**Cost of sales**
- ↑ : Increase in cost of sales driven by sales growth
- ↓ : Decrease due to forex impact

**SG&A expense**
- ↑ : Increase due to profit share from ENHERTU's sales expansion, resource allocation to oncology business, strategic investments in DX / IT and human capital for mid- to long-term growth
- ↓ : Decrease due to forex impact

**R&D expense**
- ↑ : Increase due to R&D investment focused on 5DXd ADCs, expanded medical affairs activities, strengthened R&D structure (e.g. R&D headcount increase)
- ↓ : Decrease due to forex impact

**Temporary income and expense**

FY2024: Gain on stock transfer of DS Espha etc.

**Forex impact (vs FY2024)**

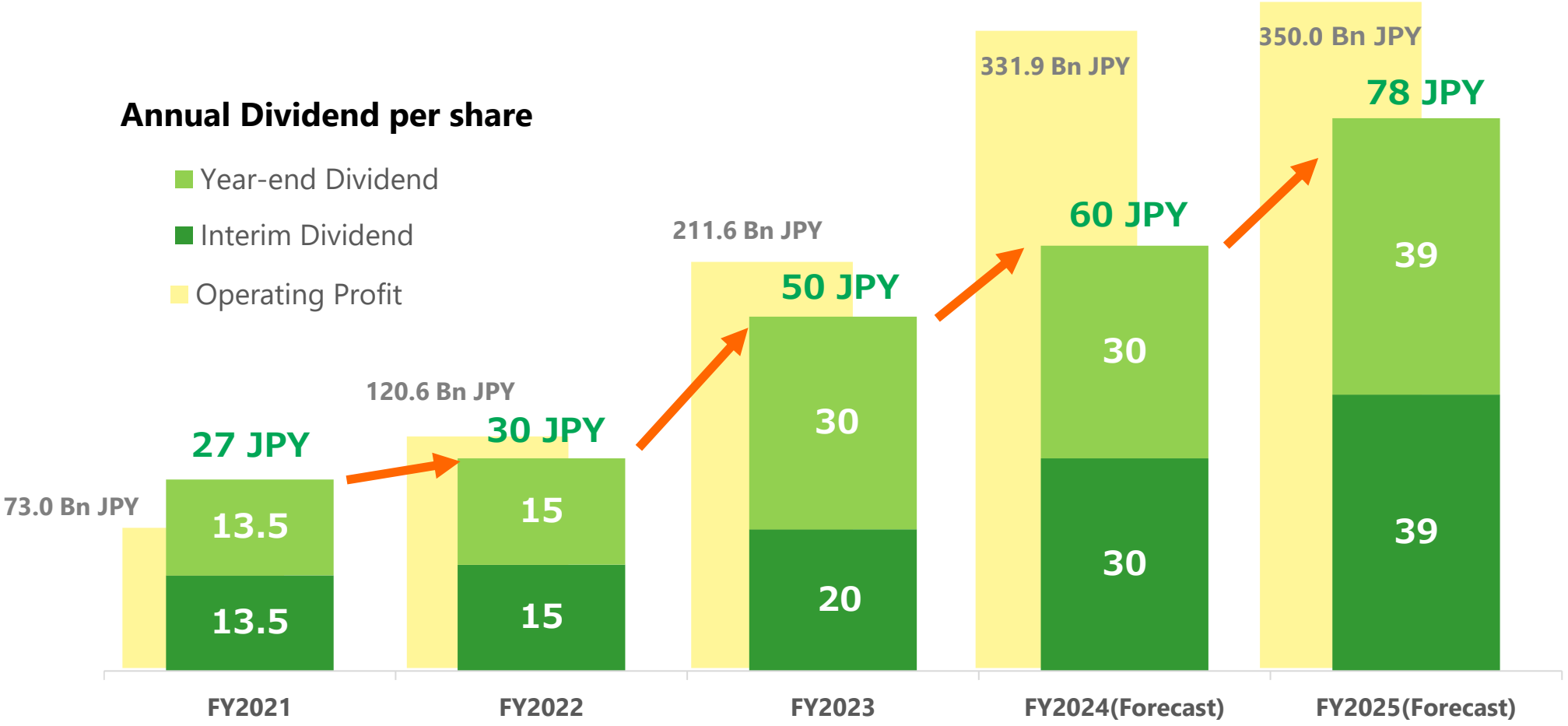
| | | |
|---|---|---|
| **Revenue :** | Approx. | -75.0 Bn JPY |
| **Core operating profit:** | Approx. | -3.5 Bn JPY |

*1 As an indicator of ordinary profitability, "core operating profit" which excludes temporary income and expenses from operating income is disclosed. Income and expenses related to: sale of fixed assets, restructuring (excluding the sales of pipeline and launched products), impairment, loss compensation, reconciliation, and other non-temporary and material gains and losses are included in the "temporary income and expenses". Temporary income and expenses are excluded from results and forecast for cost of sales, SG&A expenses and R&D expenses shown in the list above. The adjustment table from operating profit to core operating profit is stated in the reference data.

*2 DS pays alliance partners 50% of gross profit for the product sales in countries/regions where DS book revenue (excluding Japan) to share profit with the partners.

# FY2025 Annual Dividend Forecast

**Plan to increase annual dividend to 78 JPY per share for FY2025 (up 18 JPY)**
**due to strong performance of ENHERTU® and others**



# Flexible Acquisition of Own Shares (Resolution)

- **Established upper limits for acquiring own shares to take flexible actions based on comprehensive consideration such as share price level and other factors**
- **FY2025 DOE is expected to be over 8.5%**

**Upper limits to acquire own shares**

- Acquisition period: **May. 1, 2025 – Mar. 24, 2026**
- Aggregate amount of acquisition cost: **200 billion JPY (maximum)**
- Total number of shares to be acquired: **80.00 million stocks (maximum)**

# Agenda

1. FY2024 Financial Results
2. Business Update
3. R&D Update
4. 5-Year Business Plan Update
5. FY2025 Forecast
6. **Appendix**

# Revenue: Business Units (incl. Forex Impact)

(Bn JPY)

| | FY2023 Results | FY2024 Results | YoY |
|---|---|---|---|
| Japan Business | 518.9 | 476.9 | -42.0 |
| Daiichi Sankyo Healthcare | 76.0 | 86.7 | +10.7 |
| Oncolgy Business | 334.6 | 463.8 | +129.2 |
| Enhertu | 327.4 | 451.6 | +124.2 |
| Turalio | 5.3 | 6.6 | +1.3 |
| Vanflyta | 1.9 | 4.5 | +2.7 |
| American Regent | 203.4 | 217.2 | +13.8 |
| Injectafer | 50.1 | 53.4 | +3.3 |
| Venofer | 60.9 | 62.0 | +1.1 |
| GE injectables | 81.0 | 89.0 | +8.0 |
| EU Specialty Business | 189.2 | 237.4 | +48.2 |
| Lixiana | 146.2 | 179.0 | +32.8 |
| Nilemdo/Nustendi | 18.4 | 36.9 | +18.5 |
| Olmesartan | 19.6 | 18.3 | -1.3 |
| ASCA (Asia, South and Central America) Business | 184.1 | 211.2 | +27.2 |

| | | | | |
|---|---|---|---|---|
| Currency Exchange Rate | USD/JPY | 144.62 | 152.57 | +7.95 |
| | EUR/JPY | 156.79 | 163.74 | +6.95 |

# Revenue: Major Products in Japan

(Bn JPY)

| | | FY2023 Results | FY2024 Results | YoY |
|---|---|---|---|---|
| **Lixiana** | anticoagulant | **115.6** | **133.0** | **+17.5** |
| **Tarlige** | pain treatment | **45.7** | **55.6** | **+10.0** |
| **Pralia** | Treatment for osteoporosis/ inhibitor of the progression of bone erosion associated with rheumatoid arthritis | **42.8** | **42.2** | **-0.6** |
| **Vimpat** | anti-epileptic agent | **25.7** | **30.4** | **+4.6** |
| **Enhertu** | anti-cancer agent (HER2-directed antibody drug conjugate) | **23.9** | **31.0** | **+7.1** |
| **Ranmark** | treatment for bone complications caused by bone metastases from tumors | **20.4** | **20.1** | **-0.3** |
| **Efient** | antiplatelet agent | **25.6** | **31.5** | **+5.9** |
| **Canalia** | type 2 diabetes mellitus treatment | **15.9** | **15.6** | **-0.3** |
| **Loxonin** | anti-inflammatory analgesic | **15.5** | **12.3** | **-3.2** |
| **Inavir** | anti-influenza treatment | **15.9** | **19.9** | **+4.0** |
| **Minnebro** | antihypertensive agent | **8.3** | **9.6** | **+1.4** |

# 5DXd ADCs Revenue (incl. Forex Impact)

(Unit: Bn JPY)

| | FY2024 Results | YoY | FY2025 Forecast | YoY |
|---|---|---|---|---|
| **ENHERTU®** | **651.4** | **+202.2** | **761.5** | **+110.1** |
| Product Sales | 552.8 | +156.9 | 662.1 | +109.3 |
| Upfront and Milestone Payments, etc. | 98.6 | +45.3 | 99.4 | +0.8 |
| **DATROWAY®** | **7.8** | **+1.4** | **13.0** | **+5.2** |
| Product Sales | 1.4 | +1.4 | 4.7 | +3.2 |
| Upfront and Milestone Payments, etc. | 6.4 | - | 8.3 | +2.0 |
| **HER3-DXd** | **19.8** | **+16.2** | **16.3** | **-3.5** |
| Product Sales | - | - | - | - |
| Upfront and Milestone Payments, etc. | 19.8 | +16.2 | 16.3 | -3.5 |
| **I-DXd** | **15.3** | **+8.8** | **15.1** | **-0.2** |
| Upfront and Milestone Payments, etc. | 15.3 | +8.8 | 15.1 | -0.2 |
| **R-DXd** | **6.7** | **+4.0** | **20.5** | **+13.7** |
| Upfront and Milestone Payments, etc. | 6.7 | +4.0 | 20.5 | +13.7 |
| **5DXd ADCs Total** | **701.1** | **+232.6** | **826.4** | **+125.3** |

# 5DXd ADCs Upfront and Milestone Payments

(Unit: Bn JPY)

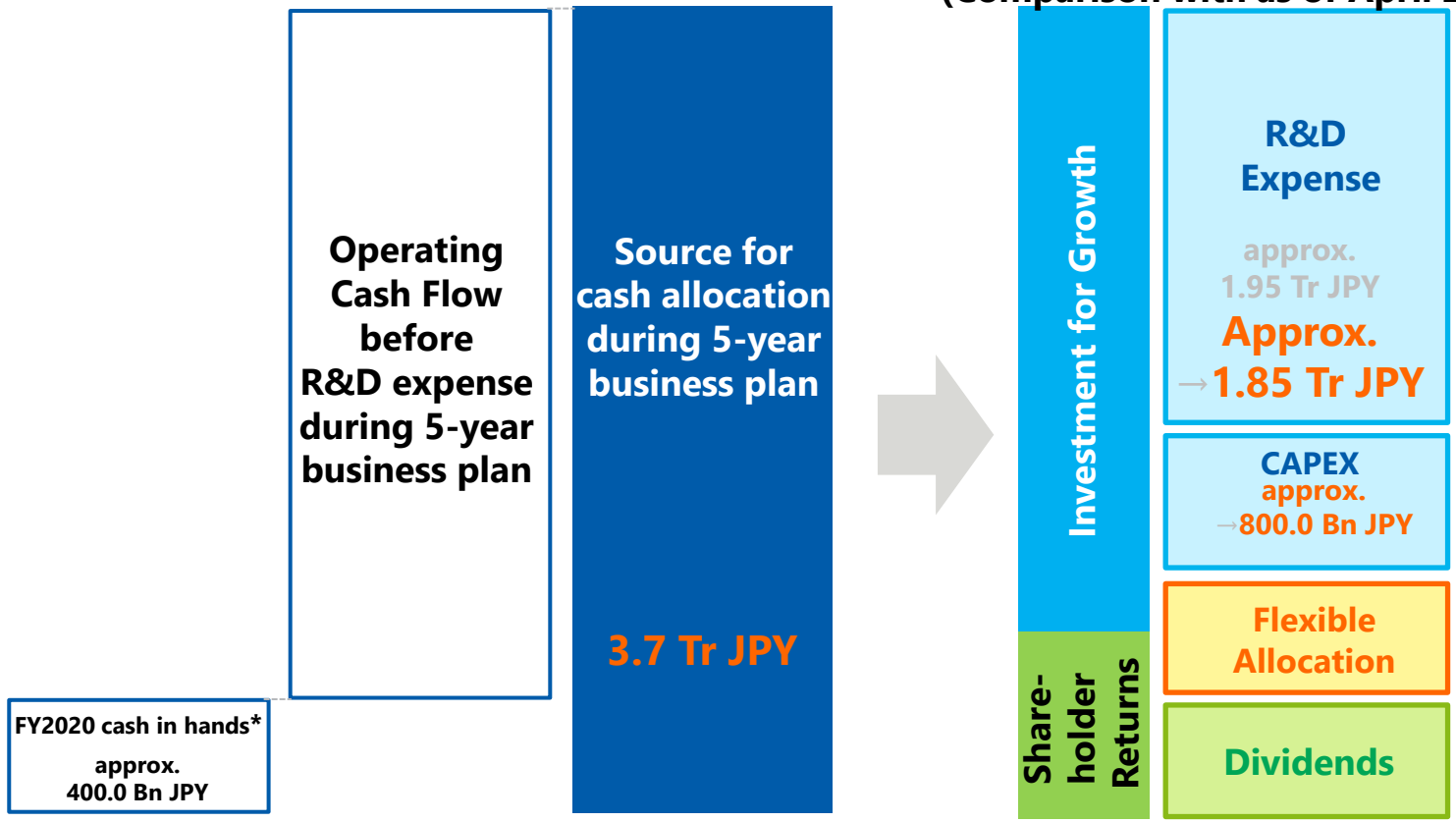
| Asset | Item | FY2024 Results | YoY | FY2025 Forecast | YoY | Total Consideration (as of Mar 2025) |
|---|---|---|---|---|---|---|
| ENHERTU® | Upfront Payment | 10.2 | +0.1 | 10.2 | +0.0 | 149.0 |
| | Regulatory Milestones | 29.2 | +16.9 | 12.7 | -16.5 | 167.7 |
| | Quid Related Payment | 1.2 | +0.0 | 1.2 | - | 17.2 |
| | Sales Milestone | 57.9 | +28.3 | 75.3 | +17.3 | 100.8 |
| DATROWAY® | Upfront Payment | 6.4 | - | 6.4 | - | 115.9 |
| | Regulatory Milestones | - | - | 2.0 | +2.0 | - |
| AZ Alliance Total | | **104.9** | **+45.3** | **107.7** | **+2.8** | **550.5** |
| HER3-DXd | Upfront Payment | 19.0 | +15.5 | 15.8 | -3.3 | 224.9 |
| | Satisfaction of Quid Rights | 0.7 | +0.7 | 0.5 | -0.2 | 7.3 |
| I-DXd | Upfront Payment | 14.7 | +8.1 | 14.7 | - | 225.4 |
| | Satisfaction of Quid Rights | 0.7 | +0.7 | 0.5 | -0.2 | 7.3 |
| R-DXd | Upfront Payment | 6.2 | +3.4 | 20.1 | +13.9 | 112.7 |
| | Satisfaction of Quid Rights | 0.6 | +0.6 | 0.4 | -0.2 | 7.3 |
| US Merck Alliance Total | | **41.8** | **+28.9** | **51.9** | **+10.0** | **584.8** |

* "Quid rights" (worth $150 mil.) that was held under the strategic alliance agreement with US Merck and was appropriated as part of consideration to obtain MK-6070 is booked as deferred revenue

# Well-balanced Investment for Growth and Shareholder Returns
## Cash Allocation

**Increase R&D expense and CAPEX for further growth in future, and increase shareholder returns.**

**Image for cash allocation**
**(Comparison with as of April 2024)**




**Prioritized investment for DXd-ADCs**

**Investment focused on enhancing ADC supply capabilities**

**Flexible allocation depending on pipeline progress for 1) investment to build pillars for further growth (in-house/external); and 2) acquisition of own shares**

**Stable dividends and dividend increase that take account of profit growth**

*Cash in hands excluding working capital

# Major R&D Milestones (ENHERTU®)

As of Apr 2025

| Projecte | | Target indication [phase, study name] | FY2024 H2 | FY2025 H1 | FY2025 H2 |
|---|---|---|---|---|---|
| ENHERTU® | BC | • HER2+, adjuvant* [Ph3, DESTINY-Breast05] | | | • TLR anticipated |
| | | • HR+/HER2 low or HER2 ultralow, chemo naive [Ph3, DESTINY-Breast06] | • Filing accepted（JP/**CN**）<br>• Approved (US/**EU**) | • Regulatory decision anticipated (JP) | |
| | | • HER2+, 1L [Ph3, DESTINY-Breast09] | | **• TLR obtained** | |
| | | • HER2+, neoadjuvant [Ph3, DESTINY-Breast11] | | • TLR anticipated | |
| | GC | • HER2+, 2L [Ph3, DESTINY-Gastric04] | **• TLR obtained** | | |
| | | • HER2+, 1L, pembrolizumab and chemo combo [Ph3, DESTINY-Gastric05] | **• Study started** | | |
| | | • HER2+and PD-L1 CPS≥1, 1L, rilvegostomig and chemo combo [Ph3, ARTEMIDE-Gastric01] | **• Study started** | | |
| | NSCLC | • HER2 mutation, 1L [Ph3, DESTINY-Lung04] | | • TLR anticipated | |
| | | **• HER2 overexpression, 1L, pembrolizumab combo [Ph3, DESTINY-Lung06]** | | **• Study start planned** | |
| | **OVC** | **• HER2 expressing [Ph3, DESTINY-Ovarian01]** | | **• Study start planned** | |

**Bold: update from FY2024 Q3**

BC: breast cancer, CPS: combined positive score, GC: gastric cancer, HR: hormone receptor, NSCLC: non-small cell lung cancer, OVC: ovarian cancer, TLR: Top Line Results

*: Adjuvant therapy for HER2 positive breast cancer patients with residual invasive disease following neoadjuvant therapy

Timeline indicated is based on the current forecast and subject to change

# Major R&D Milestones (DATROWAY®)

As of Apr 2025

| Project | | Target indication [phase, study name] | FY2024 | FY2025 | |
|---|---|---|---|---|---|
| | | | H2 | H1 | H2 |
| DATROWAY® | NSCLC | • EGFR mutated, previously treated (incl. EGFR directed therapy) [Ph2, TROPION-Lung05*] | • Filing accepted (US) | • Regulatory decision anticipated (US) | |
| | | • w/o AGA, durvalumab combo, 1L, [Ph3, AVANZAR] | | • TLR anticipated (CY2025 H2) | |
| | BC | • HR+ and HER2 low or negative, 2/3L [Ph3, TROPION-Breast01] | • Approved (JP/US) | **• Approved (EU)** | |
| | | • TNBC, PD-1/PD-L1 ineligible, 1L [Ph3, TROPION-Breast02] | | • TLR anticipated | |

**Bold: update from FY2024 Q3**

AGA: actionable genomic alterations, BC: breast cancer, HR: hormone receptor, NSCLC: non-small cell lung cancer, TLR: top line results, TNBC: triple-negative breast cancer
* Supported by data from TROPION-Lung01, TROPION-PanTumor01
Timeline indicated is based on the current forecast and subject to change

# Major R&D Milestones (HER3-DXd, I-DXd, R-DXd)

As of Apr 2025

| Project | | Target indication [phase, study name] | FY2024 | FY2025 | |
|---|---|---|---|---|---|
| | | | H2 | H1 | H2 |
| HER3-DXd | BC | **• TNBC, HR low and HER2 negative BC neoadjuvant [Ph2, HERTHENA-Breast03]** | | **• Study start planned** | |
| I-DXd | SCLC | • 2L+ [Dose optimization, Ph2, IDeate-Lung01] | | • TLR anticipated | |
| | ESCC | • 2L [Ph3, IDeate-Esophageal01] | | **• Study start planned** | |
| | **CRPC** | **• Chemo naïve [Ph3, IDeate-Prostate01]** | | **• Study start planned** | |
| R-DXd | **GI cancers** | **• [Ph2, REJOICE-GI01]** | | **• Study start planned** | |

**Bold: update from FY2024 Q3**

BC: breast cancer, cRPC: castration-resistant prostate cancer, ESCC: esophageal squamous cell carcinoma, GI: gastrointestinal, HR: hormone receptor, NSCLC: non-small cell lung cancer, SCLC: small cell lung cancer, TNBC: triple-negative breast cancer, TLR: top line results
Timeline indicated is based on the current forecast and subject to change

# Major R&D Milestones (Next Wave)

As of Apr 2025

| Project | Target indication [phase, study name] | FY2024 | FY2025 | |
|---|---|---|---|---|
| | | H2 | H1 | H2 |
| VANFLYTA® | • ***FLT3*-ITD positive AML, 1L [Ph3, QuANTUM-First]** | • **Filing accepted (CN)** | | |
| MK-6070 (gocatamig) | • SCLC, I-DXd combo, 2L+ [Ph1b/2, MK-6070-002] | • **Study started** | | |
| DS-2243 | • Solid tumors [Ph1] | • **Study started** | | |
| DAICHIRONA® | • COVID-19 mRNA vaccine (mutant strain), children aged 5 to 11 years [Ph2/3] | • **Approved (JP)** | | |

**Bold: update from FY2024 Q3**

AML: acute myeloid leukemia, SCLC: small cell lung cancer,TLR: top line results
Timeline indicated is based on the current forecast and subject to change

# Major R&D Pipeline: 5DXd ADCs ①

As of Apr 2025

Daiichi-Sankyo

## Phase 1

- (US/EU/Asia) HER2 low BC chemo naïve/post chemo DESTINY-Breast08
- (US/EU/Asia) HER2 overexpressing non-squamous NSCLC (durvalumab, volrustomig and rilvegostomig combo) 1L DESTINY-Lung03
- (US/EU) BC, NSCLC (pembrolizumab combo)
- (JP/US) solid tumors TROPION-PanTumor01
- (JP/US/EU/Asia) NSCLC (w/o AGA, pembrolizumab combo) TROPION-Lung02
- (JP/US/EU/Asia) NSCLC (w/o AGA, durvalumab, rilvegostomig, volrustomig and sabestomig combo) TROPION-Lung04
- (JP/US/EU/Asia) NSCLC
- (JP/US/Asia) EGFR mutated NSCLC 1L/2L (osimertinib combo)
- (JP/US) renal cell carcinoma, ovarian cancer

## Phase 1/2

- (US/EU/Asia) HER2+ BC 2L+/1L DESTINY-Breast07
- (JP/US/EU/Asia) HER2 expressing GC combo, 2L+/1L DESTINY-Gastric03
- (US/EU/Asia) TNBC (durvalumab combo) BEGONIA
- (JP/US/EU/Asia) solid tumors (saruparib combo) PETRA
- (US/EU/Asia) TNBC (durvalumab combo) BEGONIA
- (JP/US/EU/Asia) solid tumors (saruparib combo) PETRA
- (US/EU/Asia) CRC, BTC, HCC 2L+ HERTHENA-PanTumor02
- (US/EU/Asia) in prep stageIV NSCLC 1L (pembrolizumab combo) KEYMAKER-U01 substudy 01A
- (JP/US/EU/Asia) HER2+ BC 2L+ HERTHENA-Breast01
- (JP/US) ESCC, CRPC, squamous NSCLC, SCLC, etc. IDeate-PanTumor01
- (JP/US/EU/Asia) solid tumors 2L+ IDeate-PanTumor02
- (JP/US/EU) ES-SCLC 1L IDeate-Lung03
- (TBA) in prep chemo-naïve metastatic CRPC IDeate-Prostate02
- (US/EU/Asia) in prep stageIV NSCLC 1L (pembrolizumab combo) KEYMAKER-U01 substudy 01A
- (TBA) in prep ESCC 1L (pembrolizumab combo) KEYMAKER-U06 substudy 06E
- (US/EU/Asia) ES-SCLC 2L KEYNOTE-B98
- (TBA) in prep ovarian cancer, relapsed after platinum-based chemo. (carboplatin, paclitaxel, bevacizumab combo) REJOICE-Ovarian02

## Phase 2

- (JP/US/EU/Asia) HER2 expressing solid tumors DESTINY-PanTumor02
- (CN) HER2 expressing solid tumors DESTINY-PanTumor03
- (JP/US/EU/Asia) solid tumors TROPION-PanTumor03
- (JP/US/EU/Asia) EGFR mutated NSCLC 2L (osimertinib combo) ORCHARD
- (US/EU/Asia) resectable early-stage NSCLC neoadjuvant (durvalumab combo) NeoCOAST-2
- (JP/US/EU/Asia) solid tumors HERTHENA-PanTumor01
- (US/EU/Asia) in prep high-risk early stage TNBC, HR low and HER2 negative BC neoadjuvant (pembrolizumab combo) HERTHENA-Breast03
- (US/EU/Asia) in prep stageIV NSCLC 1L (pembrolizumab combo) KEYMAKER-U01 substudy 01G
- (JP/US/EU/Asia) ES-SCLC 2L+ IDeate-Lung01
- (TBA) in prep non-squamous NSCLC 2L KEYMAKER-U01 substudy 01H
- (TBA) in prep squamous NSCLC 2L KEYMAKER-U01 substudy 01I
- (US/EU/Asia) in prep gastrointestinal cancers REJOICE-GI01
- (JP/US/EU/Asia) solid tumors REJOICE-PanTumor01
- (TBA) in prep non-squamous NSCLC 2L KEYMAKER-U01 substudy 01H
- (TBA) in prep squamous NSCLC 2L KEYMAKER-U01 substudy 01I

ENHERTU® (T-DXd) / DATROWAY® (Dato-DXd) / HER3-DXd / I-DXd / R-DXd (DS-6000)

Orphan drug designation (designated in at least one country/region among JP, US and EU)

AGA: actionable genomic alterations, BTC: biliary tract cancer, BC: breast cancer, CRC: colorectal cancer, CRPC: castration-resistant prostate cancer, ESCC: esophageal squamous cell carcinoma, ES-SCLC: extensive stage-small cell lung cancer, GC: gastric cancer, HCC: hepatocellular carcinoma, NSCLC: non-small cell lung cancer, SCLC: small cell lung cancer, TBA: to be announced, TNBC: triple negative breast cancer

# Major R&D Pipeline: 5DXd ADCs ②

As of Apr 2025

| Phase 2/3 | Phase 3 | | | Regulatory phase |
|---|---|---|---|---|
| (JP/US/EU/Asia) platinum-resistant ovarian cancer 2L+ REJOICE-Ovarian01 | (JP/US/EU/Asia) HER2+ BC adjuvant*1 DESTINY-Breast05 | (JP) in prep HER2 expressing ovarian cancer 1L maintenance (bevacizumab combo) DESTINY-Ovarian01 | (JP/US/EU/Asia) TNBC (PD-1/PD-L1 inhibitor ineligible) 1L TROPION-Breast02 | (JP/CN) HR+ and HER2 low or HER2 ultralow BC chemo naïve DESTINY-Breast06 |
| | (JP/US/EU/Asia) HER2+ BC 1L DESTINY-Breast09 | (JP/US/EU/Asia) non-squamous NSCLC (w/o AGA, PD-L1 TPS <50%) 1L (pembrolizumab combo) TROPION-Lung07 | (JP/US/EU/Asia) TNBC adjuvant*1 (mono or durvalumab combo) TROPION-Breast03 | (US) EGFR mutated NSCLC (after systemic therapies, incl. EGFR-directed therapy) TROPION-Lung05*2 |
| | (JP/US/EU/Asia) HER2+ BC neoadjuvant DESTINY-Breast11 | (JP/US/EU/Asia) NSCLC (w/o AGA, PD-L1 TPS ≥50%) 1L (pembrolizumab combo) TROPION-Lung08 | (JP/US/EU/Asia) TNBC, HR low and HER2 negative BC neoadjuvant and adjuvant (durvalumab combo) TROPION-Breast04 | (CN) HR+ and HER2 low or negative BC 2/3L TROPION-Breast01 |
| | (JP/EU/Asia) HER2+ GC 2L DESTINY-Gastric04 | (JP/US/EU/Asia) non-squamous NSCLC (w/o AGA, PD-L TC 1≥50%) 1L (rilvegostomig combo) TROPION-Lung10 | (JP/US/EU/Asia) PD-L1 positive TNBC 1L (mono or durvalumab combo) TROPION-Breast05 | (US) EGFR mutated NSCLC 3L HERTHENA-Lung01 |
| | (JP/US/EU/Asia) HER2+ GC 1L (pembrolizumab combo) DESTINY-Gastric05 | (JP/US/EU/Asia) Stage I adenocarcinoma NSCLC adjuvant (rilvegostomig combo) TROPION-Lung12 | (JP/US/EU/Asia) EGFR mutated NSCLC 2L HERTHENA-Lung02 | |
| | (JP/US/EU/Asia) HER2+ and PD-L1 CPS≥1 GC 1L (rilvegostomig combo) ARTEMIDE-Gastric01 | (JP/US/EU/Asia) EGFR mutated NSCLC 1L (osimertinib combo) TROPION-Lung14 | (JP/US/EU/Asia) ES-SCLC 2L IDeate-Lung02 | |
| | (JP/US/EU/Asia) HER2 mutant NSCLC 1L DESTINY-Lung04 | (JP/US/EU/Asia) EGFR mutated NSCLC (progressed on prior EGFR TKI) 2L+ (mono or osimertinib combo) TROPION-Lung15 | (JP/US/EU/Asia) in prep ESCC 2L IDeate-Esophageal01 | |
| | (TBA) in prep HER2 overexpressing non-squamous NSCLC (w/o AGA, PD-L1 TPS < 50%) (pembrolizumab combo) DESTINY-Lung06 | (JP/US/EU/Asia) NSCLC (w/o AGA) 1L (durvalumab combo) AVANZAR | (TBA) in prep chemo-naïve metastatic CRPC IDeate-Prostate01 | |
| | (JP/US/EU/Asia) HER2 expressing BTC 1L (mono or rilvegostomig combo) DESTINY-BTC01 | | | |

ENHERTU® (T-DXd) / DATROWAY® (Dato-DXd) / HER3-DXd / I-DXd / R-DXd (DS-6000)

Project in oncology that is planned to be submitted for approval in some countries/regions based on the results of

Breakthrough Designation (US) / Orphan drug designation (designated in at least one country/region among JP, US

*1 Adjuvant therapy for patients with residual invasive disease following neoadjuvant therapy
*2 Supported by data from TROPION-Lung01, TROPION-PanTumor01

AGA: actionable genomic alterations, BC: breast cancer, BTC: biliary tract cancer, CPS: combined positive score
ES-SCLC: extensive stage-small cell lung cancer, GC: gastric cancer, HR: hormone receptor, NSCLC: non-small cell lung cancer, TKI: tyrosine kinase inhibitor, TC: tumor cells, TNBC: triple negative breast cancer, TPS: tumor proportion score

# Major R&D Pipeline: Next Wave

As of Apr 2025

| Phase 1 | Phase 1/2 | Phase 2 | Phase 3 | Regulatory phase |
|---|---|---|---|---|
| DS-1055 (JP/US)<br>Anti-GARP antibody<br>Solid tumors | DS-3939 (JP/US/EU/Asia)<br>TA-MUC1-directed ADC<br>Solid tumors | EZHARMIA® (EU)<br>EZH1/2 inhibitor<br>BCL | TURALIO® (Asia)<br>CSF-1/KIT/FLT3 inhibitor<br>Tenosynovial giant cell tumor | VANFLYTA® (CN)<br>FLT3 inhibitor<br>*FLT3* -ITD positive AML 1L<br>QuANTUM-First |
| DS-9606 (US/EU)<br>CLDN6-directed ADC<br>Solid tumors | MK-6070 (DS3280) (US)<br>DLL3 directed tri-specific T-cell engager<br>DLL3 expressing advanced cancer | DS-1001 (JP)<br>Mutant IDH1 inhibitor<br>Glioma | VANFLYTA® (JP/US/EU/Asia)<br>FLT3 inhibitor<br>*FLT3* -ITD negative AML 1L<br>QuANTUM-Wild | VN-0102/JVC-001 (JP)<br>Mixed measles-mumps-rubella vaccine |
| DS-1103 (US/EU)<br>Anti-SIRPα antibody<br>HER2 expressing or mutant solid tumors, HER2 low BC (ENHERTU® combo) | MK-6070 (DS3280) (US/EUAsia)<br>DLL3 directed tri-specific T-cell engager<br>ES-SCLC 2L+ (I-DXd combo)<br>MK-6070-002 | TURALIO® (JP)<br>CSF-1/KIT/FLT3 inhibitor<br>Tenosynovial giant cell tumor | | |
| DS-1471 (JP)<br>Anti-CD147 antibody<br>Solid tumors | EZHARMIA® (JP/US/Asia)<br>EZH1/2 inhibitor<br>NSCLC (w/o AGA and PD-L1 TPS ≥50%) 1L (pembrolizumab combo) | DS-1211 (US/EU)<br>TNAP inhibitor<br>Pseudoxanthoma elasticum | | |
| EZHARMIA® (JP/US)<br>EZH1/2 inhibitor<br>HER2+ GC, HER2 low BC (ENHERTU® combo) and non-squamous NSCLC (DATROWAY® combo) | DS-7011 (JP/US/EU/Asia)<br>Anti-TLR7 antibody<br>Systemic lupus erythematosus | | | |
| DS-2243 (US/EU/Asia)<br>HLA-A*02/NY-ESO directed bispecific T-cell engager<br>Solid tumors | DS-2325 (EU)<br>KLK5 inhibitor<br>Netherton syndrome | | | |

Oncology

Specialty medicine

Vaccine

Orphan drug designation (designated in at least one country/region among JP, US and EU)

Rare Pediatric Disease Designation (US)

Fast Track Designation (US)

AGA: actionable genomic alterations, AML: acute myeloid leukemia, BC: breast cancer, BCL: B cell lymphoma, ES-SCLC: extensive-stage small cell lung cancer, GC: gastric cancer, NSCLC: non-small cell lung cancer, TPS: tumor proportion score

Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

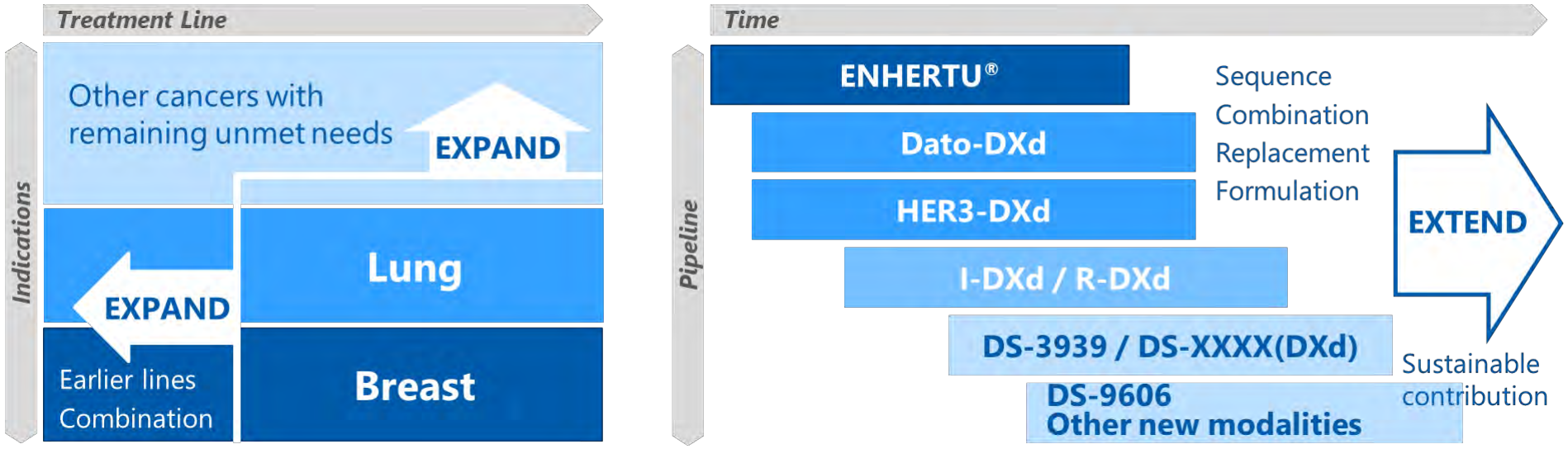
# Science & Technology Day 2024

## DAIICHI SANKYO CO., LTD.

**December 16th, 17th 2024**

# EXPAND & EXTEND to deliver our technology to more patients

## EXPAND and EXTEND




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

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

# Daiichi Sankyo Research Institutes for External Collaboration

**DS Research Laboratories**
**Tokyo, Japan** (Shinagawa, Kasai)

10+Research laboratories
(Wet/Dry)

new

**DS Research Institute Munich**
Located in Daiichi Sankyo Europe

**DS Research Institute Boston**
Located in CIC Cambridge @245 Main

new

## Our Research Institute activities will accomplish the following objectives by deploying top scientists from Research function

- **Form networks** and approach technologies that drive scientific paradigm shifts
- Undertake **sponsored research**, foster startup incubation, and drive technology acquisition
- **Cultivate talent** to enhance global insights and perspectives

ENHERTU®

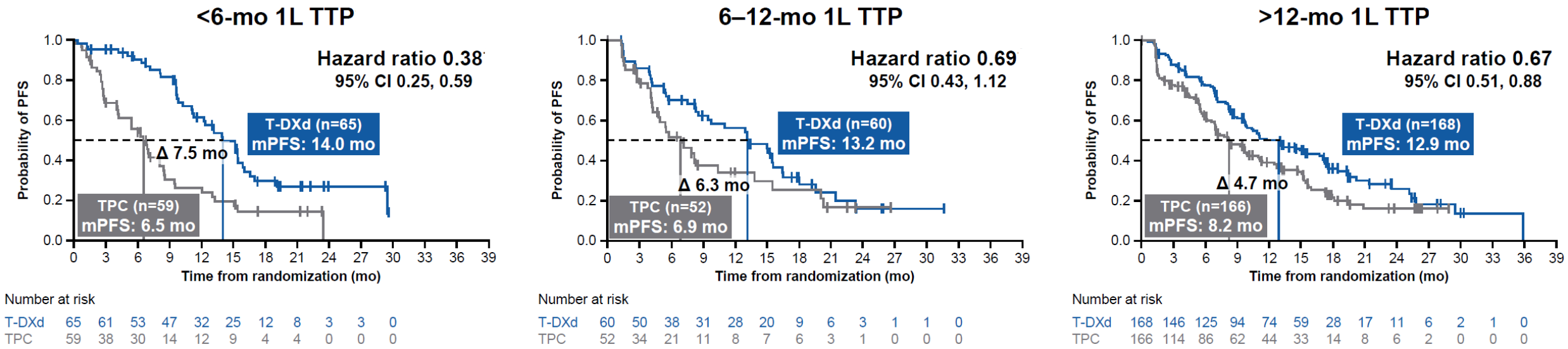
# DESTINY-Breast06: PFS in Exploratory Subgroup Analysis

SABCS 2024

Daiichi-Sankyo

## ENHERTU® improved PFS vs TPC regardless of time to progression on 1L endocrine therapy + CDK4/6i

<TTP subgroups>




- ENHERTU® demonstrated a clinically meaningful efficacy benefit vs TPC regardless of time to progression (TTP) on 1L ET + CDK4/6i (mPFS 12.9–14.0 mo with ENHERTU®)
  - ✓ This included patients with rapid (<6-mo) progression on 1L ET + CDK4/6i

CI: confidence interval, ET: endocrine therapy, mo: months, (m)PFS: (median) progression-free survival, PD: progressive disease, T-DXd: trastuzumab deruxtecan, TPC: treatment of physician's choice

ENHERTU®

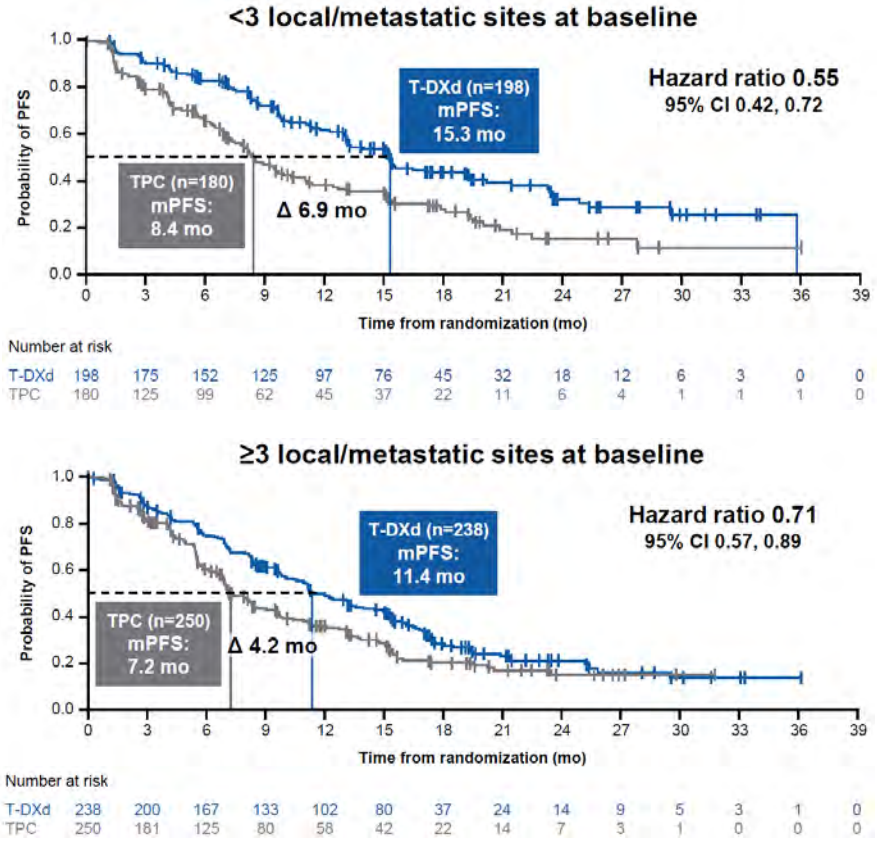
# DESTINY-Breast06: PFS in Exploratory Subgroup Analysis

SABCS 2024

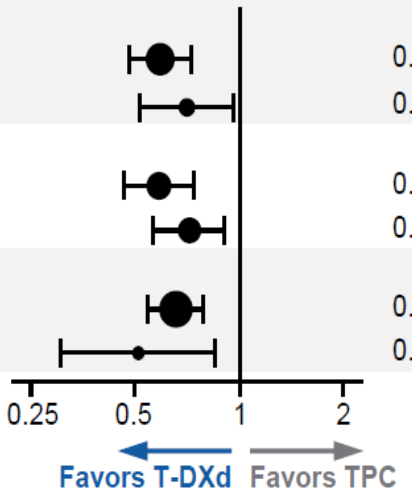
Daiichi-Sankyo

## PFS benefit with ENHERTU® was observed regardless of disease burden, with notable efficacy in patients with lower disease burden

**<Disease burden subgroups>**




| | Median PFS, mo (95% CI) | | Hazard ratio (95% CI) |
|---|---|---|---|
| | T-DXd | TPC | |
| **Liver metastases** | | | |
| Yes (n=579) | 12.2 (10.4, 13.5) | 7.0 (6.4, 8.1) | 0.59 (0.48, 0.72) |
| No (n=287) | 16.5 (13.2, 19.4) | 11.3 (8.3, 15.2) | 0.70 (0.51, 0.96) |
| **Baseline tumor size** | | | |
| >Median (n=432) | 12.0 (9.9, 15.2) | 7.1 (6.5, 8.3) | 0.57 (0.45, 0.72) |
| ≤Median (n=434) | 15.0 (13.1, 16.1) | 9.7 (7.5, 13.2) | 0.71 (0.55, 0.90) |
| **Visceral disease** | | | |
| Yes (n=740) | 13.1 (11.1, 15.1) | 7.9 (6.9, 8.5) | 0.65 (0.55, 0.78) |
| No (n=126) | 23.3 (13.1, NE) | 11.3 (6.9, 15.7) | 0.51 (0.30, 0.85) |




- ENHERTU® also demonstrated efficacy regardless of disease burden, with notable efficacy in patients with lower disease burden (mPFS 15.0–23.3 mo with ENHERTU® )

CI: confidence interval, ET: endocrine therapy, mo: months, NE, not evaluable, (m)PFS: (median) progression-free survival, T-DXd: trastuzumab deruxtecan, TPC: treatment of physician's choice

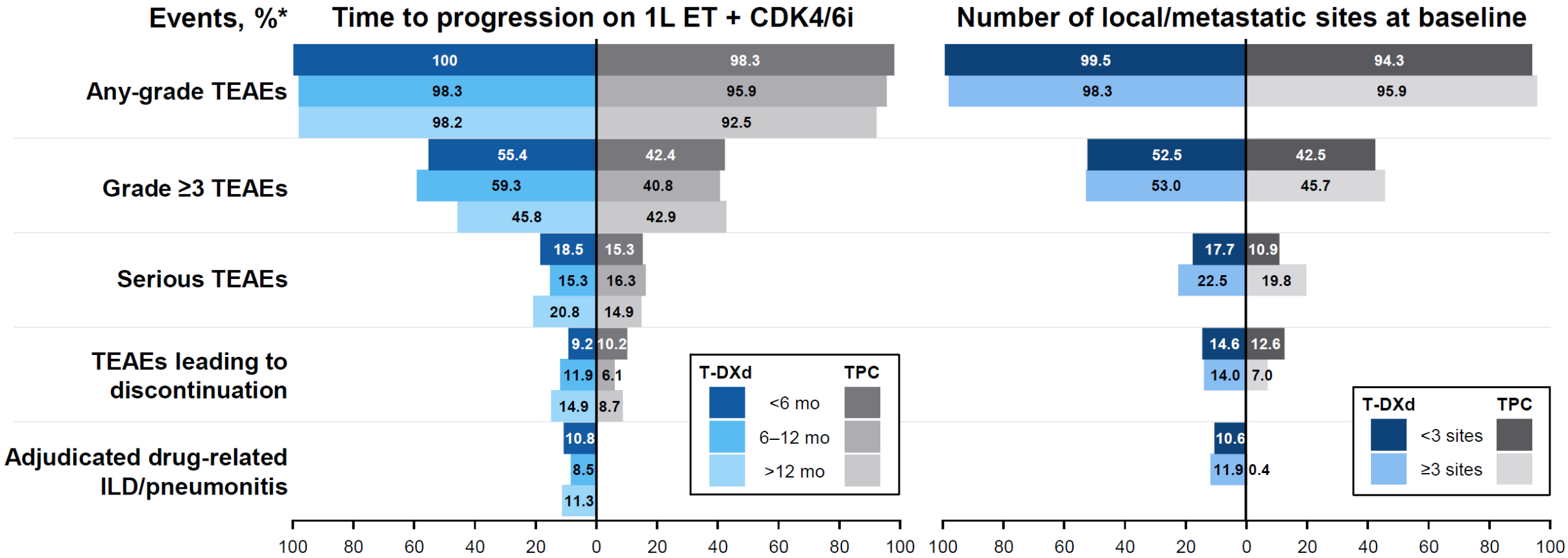
ENHERTU®

# DESTINY-Breast06: Safety in Exploratory Subgroups

SABCS 2024

Daiichi-Sankyo

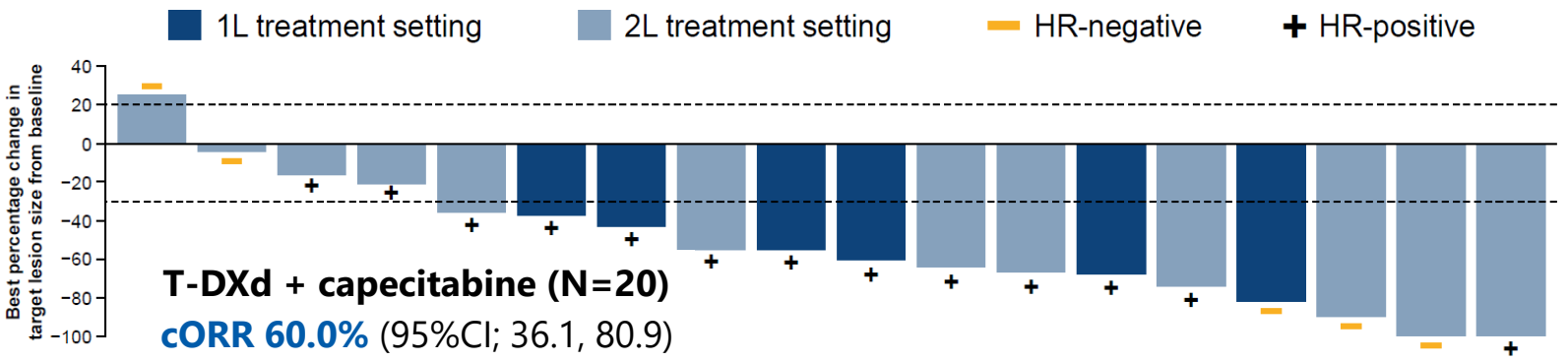
## Safety profiles for ENHERTU® and TPC in TTP and disease burden subgroups in line with overall safety population†




*Includes AEs with an onset date or worsening on or after the date of first dose and up to and including 47 days following the date of last dose of study medication or before the initiation of the first subsequent cancer therapy (whichever occurs first); includes ILD/pneumonitis with an onset date or worsening on or after the date of first dose; †overall safety population (T-DXd vs TPC): any TEAEs, 98.8% vs 95.2%; Grade ≥3 TEAEs, 52.8% vs 44.4%; serious TEAEs, 20.3% vs 16.1%; TEAEs leading to discontinuation, 14.3% vs 9.4%; adjudicated drug-related ILD, 11.3% vs 0.2%
AE: adverse event, ET: endocrine therapy, ILD: interstitial lung disease, mo: months, T-DXd: trastuzumab deruxtecan, TEAE: treatment-emergent adverse event, TPC: treatment of physician's choice, TTP: time to progression

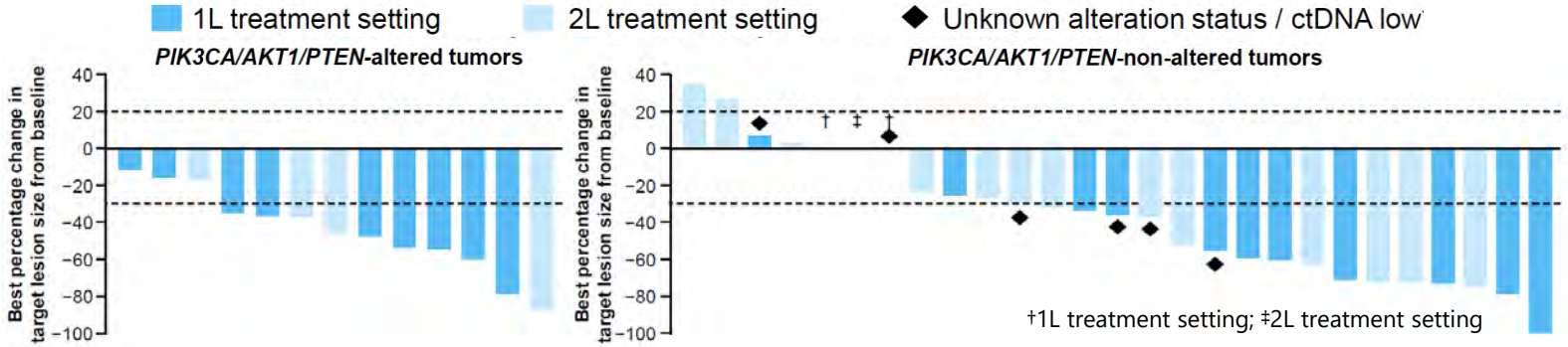
# ENHERTU® + capecitabine or capivasertib are tolerable and active in patients with HER2 low mBC, potentially supporting further investigation

## Efficacy




**T-DXd + capecitabine (N=20)**

**cORR 60.0%** (95%CI; 36.1, 80.9)




**T-DXd + capivasertib (N=40)**

**cORR 60.0%** (95%CI; 43.3, 75.1)

- **cORR** in patients with ***PIK3CA/AKT1/PTEN*-altered tumors** was **76.9%** (n=10/13; 95% CI 46.2, 95.0)
- **cORR** in patients with ***PIK3CA/AKT1/PTEN*-non-altered tumors** was **52.4%** (n=11/21; 95% CI 29.8, 74.3)
- **cORR** in patients with an **unknown** and **ctDNA low** status was **50.0%** (n=1/2) and **50.0%** (n=2/4), respectively

**DESTINY-Breast08 Study :**

A Ph1b study to investigate safety, tolerability, PK and preliminary anti-tumor activity of ENHERTU® in combination with other therapeutics in patients with HER2 low mBC

- ENHERTU® in combination with capecitabine or capivasertib demonstrated preliminary antitumor activity in patients with HER2-low mBC
- The safety profiles for ENHERTU® plus capecitabine and ENHERTU® plus capivasertib were generally consistent with the known safety profile of each agent

ctDNA: circulating tumor deoxyribonucleic acid, mBC: metastatic breast cancer, CI: confidence interval, HR: hormone receptor, PK: pharmacokinetics, cORR: confirmed objective response rate, SABCS: San Antonio Breast Cancer Symposium, T-DXd: trastuzumab deruxtecan

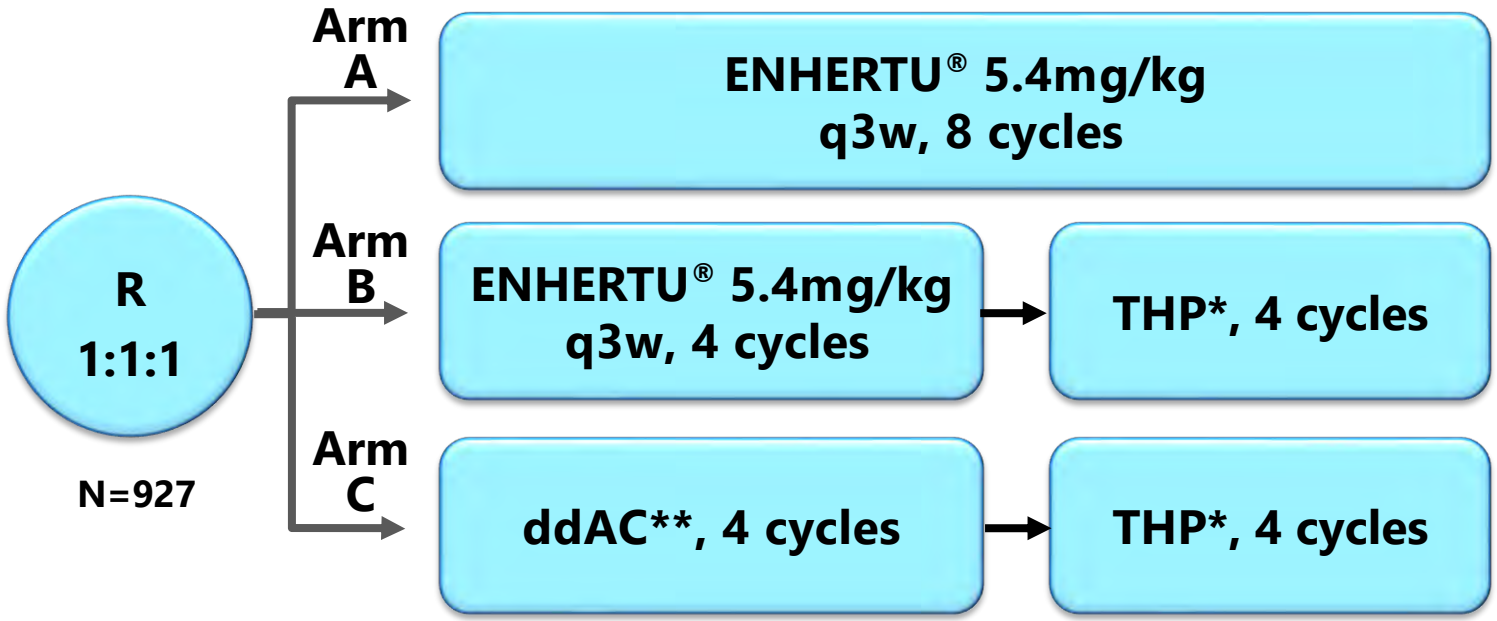
ENHERTU®

# DESTINY-Breast11 Study

## Ph3 study of ENHERTU® monotherapy or ENHERTU® followed by THP vs. ddAC-THP in neoadjuvant setting for high-risk HER2-positive early-stage BC

**Key Eligibility Criteria**

- HER2-positive locally advanced BC
- HR positive or negative
- Histologically documented HER2 positive early BC participants, including clinical stage at presentation (based on mammogram or breast MRI assessment): T0-4 (inclusive of inflammatory breast cancer), N1-3, M0 or ≥ T3, N0, M0 as determined by the AJCC staging system, 8th edition




* THP: paclitaxel qw + trastuzumab q3w + pertuzumab q3w

** ddAC: doxorubicin + cyclophosphamide q2w

Primary endpoint: pCR

Secondary endpoint: EFS, OS

## TLR anticipated in FY2025 H1

AJCC: American Joint Committee on Cancer, BC: breast cancer, EFS: event-free survival, HR: hormone receptor, MRI: Magnetic Resonance Imaging, OS: overall survival, pCR: pathological complete response, qw: once weekly, q2w: every 2 weeks, q3w: every 3 weeks, TLR: top line results

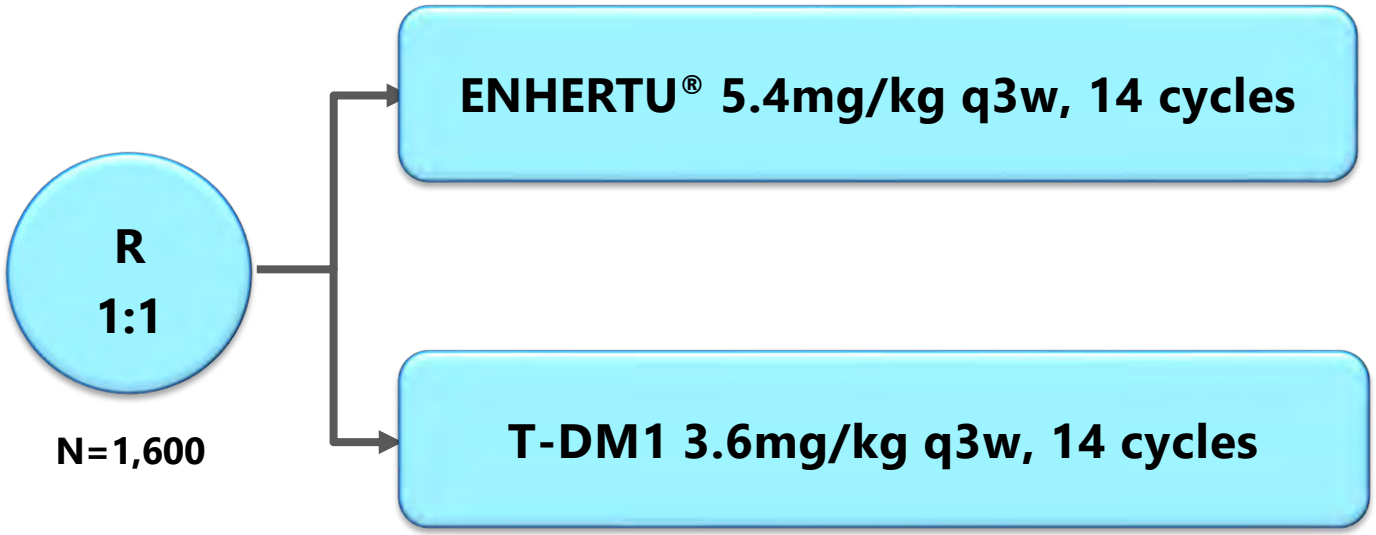
ENHERTU®

# DESTINY-Breast05 Study

## Ph3 study of ENHERTU® vs. T-DM1 in high-risk HER2 positive participants with residual invasive BC following neoadjuvant therapy

**Key Eligibility Criteria**

- HER2 positive BC (IHC3+ or ISH+ as confirmed by a central laboratory) histologically
- Completion of neoadjuvant systemic chemotherapy and HER2-directed treatment
- Adequate excision: surgical removal of all clinically evident disease in the breast and lymph nodes
- Pathologic evidence of residual invasive carcinoma in the breast and/or axillary lymph nodes following completion of neoadjuvant therapy meeting high-risk criteria




**Primary endpoint: IDFS,**

**Secondary endpoint: DFS, OS, DRFI, BMFI, safety and tolerability, PK, ADA**

## TLR anticipated in FY2025

ADA: anti-drug antibody, BC: breast cancer, BMFI: brain metastases-free interval, DFS: disease-free survival, DRFI: distant recurrence-free interval, IDFS: invasive disease-free survival, IHC: immunohistochemistry, ISH: in situ hybridization, OS: overall survival, pCR: pathological complete response, PK: pharmacokinetics, q3W: every 3 weeks, TLR: top line results

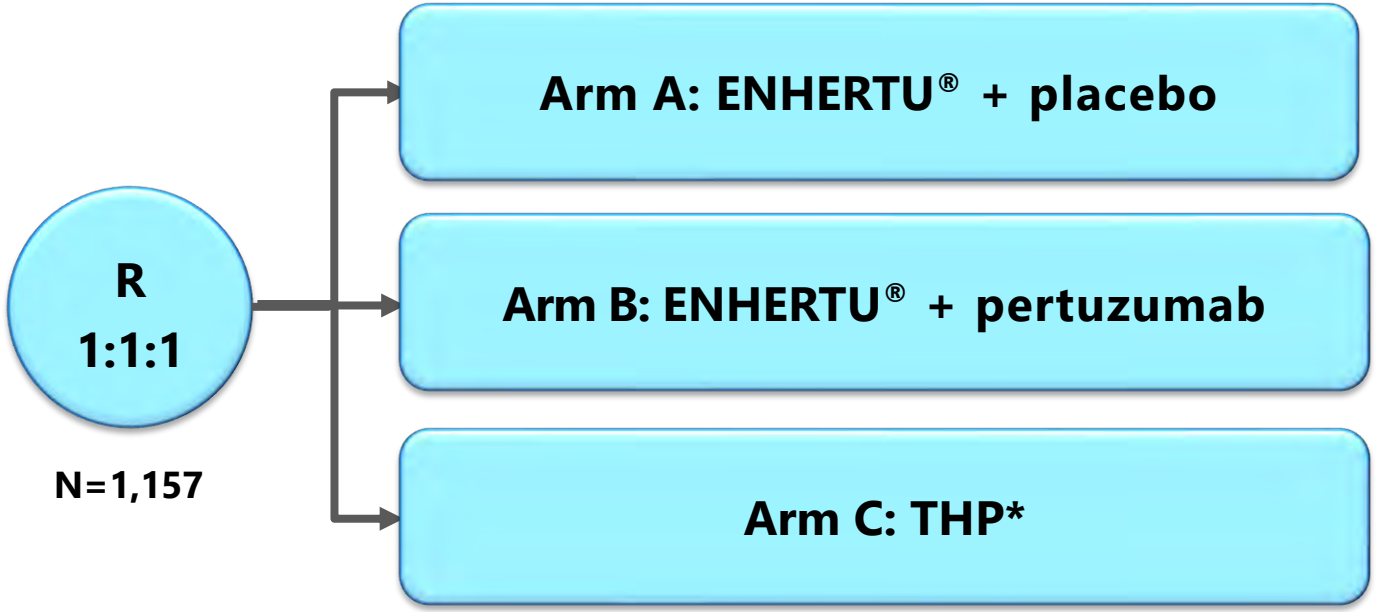
ENHERTU®

# DESTINY-Breast09 Study

## Ph3 study of ENHERTU® monotherapy or in combination with pertuzumab vs. SOC in 1L setting for HER2 positive BC

**Key Eligibility Criteria**

- Advanced and/or metastatic BC
- HER2 positive (IHC3+ or ISH+) by central confirmation
- No previous chemotherapy or HER2-targeted therapy for advanced or metastatic BC except for 1 previous line of endocrine therapy in the metastatic setting




*THP: paclitaxel qw + trastuzumab q3w + pertuzumab q3w

**Primary endpoint: PFS by BICR**
**Secondary endpoint: PFS by investigator, OS, ORR, DOR, PK, safety and tolerability etc.**

## TLR anticipated in FY2025

BC: breast cancer, BICR: blinded independent central review, DOR: duration of response, EFS: event-free survival, IHC: immunohistochemistry, ISH: in situ hybridization, ORR: objective response rate, OS: overall survival, PFS: progression-free survival, PK: pharmacokinetics, qw: once weekly, q3W: every 3 weeks, SOC: standard of care, TLR: top line results

Dato-DXd

# Pooled Analysis of TROPION-Lung01 and TROPION-Lung05

ESMO Asia 2024

Daiichi-Sankyo

## 117 patients with EGFRm NSCLC who received Dato-DXd in TL01 and TL05 study were included in the pooled analysis

**TROPION-Lung05 (Phase II study)**

- **Presence of ≥1 actionable genomic alteration** (*EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
  - ≥1 line of targeted therapy
  - 1–2 prior cytotoxic agent–containing therapies including Pt-CT in the metastatic setting
  - Radiographic disease progression after most recent therapy

**TROPION-Lung01 (Phase III study)**

- **In those with actionable genomic alterations** (*EGFR*, *ALK*, *ROS1*, *NTRK*, *BRAF*, *MET* exon 14 skipping, or *RET*)
  - 1–2 prior approved targeted therapies + Pt-CT, and ≤1 anti–PD-(L)1 mAb
  - No prior docetaxel

R 1:1

**Dato-DXd** 6 mg/kg Q3W[a] **(N=137)**

**Dato-DXd** 6 mg/kg Q3W[b] **(N=299)**

**Docetaxel** 75 mg/m$^2$ Q3W[b] **(N=305)**

***EGFR*m Pool: N=117**

**TROPION-Lung05 (n=78)**

**TROPION-Lung01 (n=39)**

**Endpoints:**

- ORR per BICR
- BOR per BICR
- DCR per BICR
- DOR per BICR
- PFS per BICR
- OS
- Safety

[a]Data cut off: December 14, 2022; [b]Data cut off: March 1, 2024 (OS and safety) or March 29, 2023 (all other efficacy endpoints).
BICR: blinded independent central review, BOR: best overall response, CT: chemotherapy, DCR: disease control rate, DOR: duration of response, ESMO: European Society for Medical Oncology, NSCLC: non-small cell lung cancer, ORR: overall response rate, OS: overall survival, PFS: progression-free survival, Pt-CT: platinum-based chemotherapy, Q3W: once every 3 weeks

Dato-DXd

# Pooled Analysis of TROPION-Lung01 and TROPION-Lung05

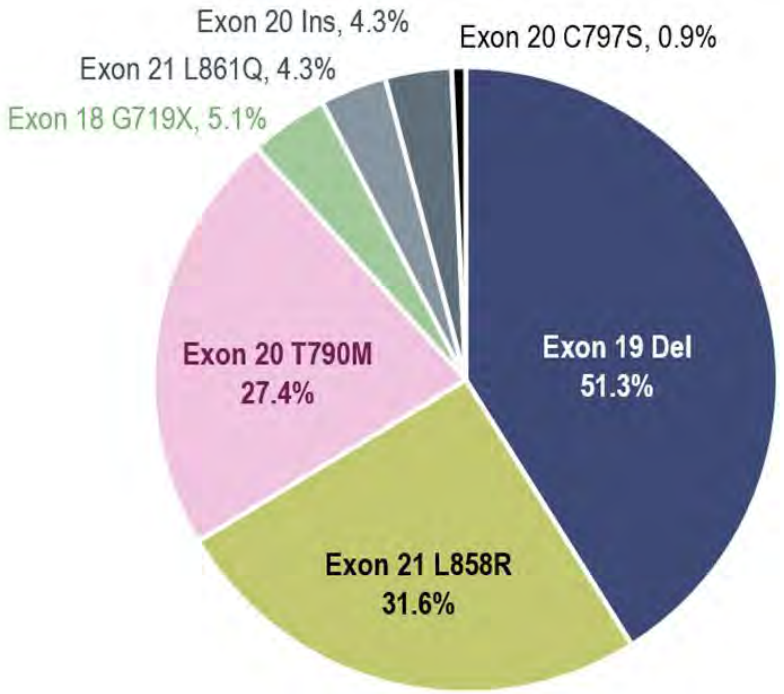
ESMO Asia 2024

Daiichi-Sankyo

## Demographics and Baseline Characteristics

| Characteristic | *EGFR*m Pool (N=117) | TROPION-Lung05 (N=78) | TROPION-Lung01 (N=39) |
|---|---|---|---|
| Median age (range), years | 63 (36–81) | 63 (36–77) | 62 (39–81) |
| Sex, female, n (%) | 73 (62.4) | 52 (66.7) | 21 (53.8) |
| Race, n (%) | | | |
| Asian | 81 (69.2) | 55 (70.5) | 26 (66.7) |
| White | 27 (23.1) | 20 (25.6) | 7 (17.9) |
| Black or African American | 1 (0.9) | 0 | 1 (2.6) |
| Other/missing | 8 (6.8) | 3 (3.8) | 5 (12.8) |
| ECOG PS, n (%) | | | |
| 0 | 39 (33.3) | 24 (30.8) | 15 (38.5) |
| 1 | 78 (66.7) | 54 (69.2) | 24 (61.5) |
| Smoker[a], n (%) | 55 (47.0) | 34 (43.6) | 21 (53.8) |
| Nonsquamous histology[b], n (%) | 115 (98.3) | 77 (98.7) | 38 (97.4) |
| Brain metastasis at study entry, n (%) | 36 (30.8) | 21 (26.9) | 15 (38.5) |
| Median lines systemic therapy (range)[c] | 3 (1–5) | 3 (1–5) | 2 (1–5) |
| Prior osimertinib[d], n (%) | 96 (82.1) | 61 (78.2) | 35 (89.7) |
| First line | 47 (40.2) | 27 (34.6) | 20 (51.3) |
| Second line | 34 (29.1) | 20 (25.6) | 14 (35.9) |

*EGFR* Mutational Profile (N=117)[e]




[a]Current/former; [b]Adenocarcinoma and other nonsquamous types; [c]Prior lines in the locally advanced/metastatic setting; [d]Additional patients may have received osimertinib as third line or later therapy; [e]Analyses based on local testing reported by investigators in the electronic case report form. Patients may have ≥1 *EGFR* mutation with or without a non-*EGFR* mutation. Other mutation types identified alongside *EGFR* were *ALK* rearrangement, n=2; *ROS1* rearrangement, n=2; *NTRK* fusion, n=1; *MET* amplification, n=5; *MET* Exon 14 skipping, n=1.
Del: deletion, ECOG PS: Eastern Cooperative Oncology Group Performance Status, ESMO: European Society for Medical Oncology, Ins: insertion

Dato-DXd

# Pooled Analysis of TROPION-Lung01 and TROPION-Lung05

ESMO Asia 2024

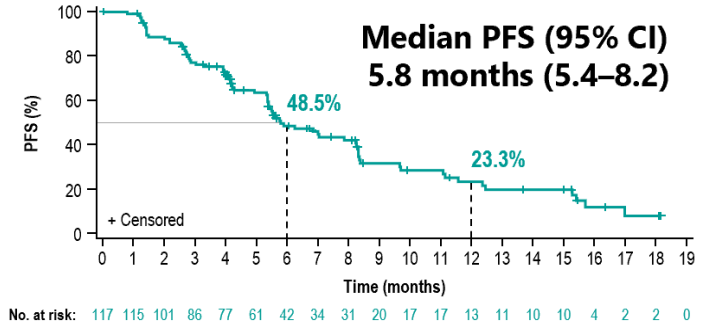
Daiichi-Sankyo

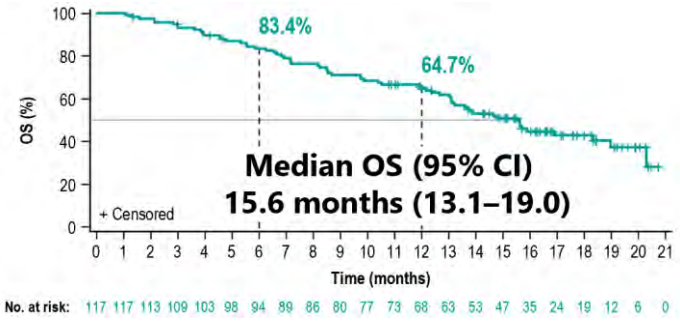
## Dato-DXd is a potential treatment option for patients with EGFRm NSCLC in the second-line and later settings

### Efficacy

| Response | *EGFR*m Pool (N=117) | Prior Osimertinib (N=96) |
|---|---|---|
| **Confirmed ORR,**[a] n (%) [95% CI] | 50 (**42.7**) [33.6–52.2] | 43 (**44.8**) [34.6–55.3] |
| **BOR,** n (%) | | |
| CR | 5 (**4.3**) | 4 (**4.2**) |
| PR | 45 (**38.5**) | 39 (**40.6**) |
| SD | 48 (41.0) | 37 (38.5) |
| Non-CR/Non-PD | 3 (2.6) | 2 (2.1) |
| PD | 12 (10.3) | 10 (10.4) |
| NE | 4 (3.4) | 4 (4.2) |
| **Median DOR,** months (95% CI) | **7.0** (4.2–9.8) | **6.9** (4.2–9.8) |
| **DCR,**[b] n (%) [95% CI] | 101 (**86.3**) [78.7–92.0] | 82 (**85.4**) [76.7–91.8] |
| **Median PFS,** months (95% CI) | **5.8** (5.4–8.2) | **5.7** (5.4–7.9) |
| **Median OS,** months (95% CI) | **15.6** (13.1–19.0) | **14.7** (13.0–18.3) |

**PFS and OS in the *EGFR*m Pool (N=117)**




■ **Robust clinical activity:**

- ORR: 42.7% (95% CI: 33.6–52.2); median DOR: 7.0 mo (range: 4.2–9.8); median PFS: 5.8 mo; median OS: 15.6 mo
- Outcomes for patients with prior osimertinib treatment were similar to the overall pooled population

[a]CR+PR; [b]CR+PR+SD or non-CR/non-PD.

BICR: blinded independent central review, BOR: best overall response, CI: confidence interval, CR: complete response, DCR: disease control rate, DOR: duration of response, ESMO: European Society for Medical Oncology, NE: not evaluable, ORR: overall response rate, OS: overall survival, PFS: progression-free survival, PD: progressive disease, PR: partial response, SD: stable disease.

Dato-DXd

# Pooled Analysis of TROPION-Lung01 and TROPION-Lung05

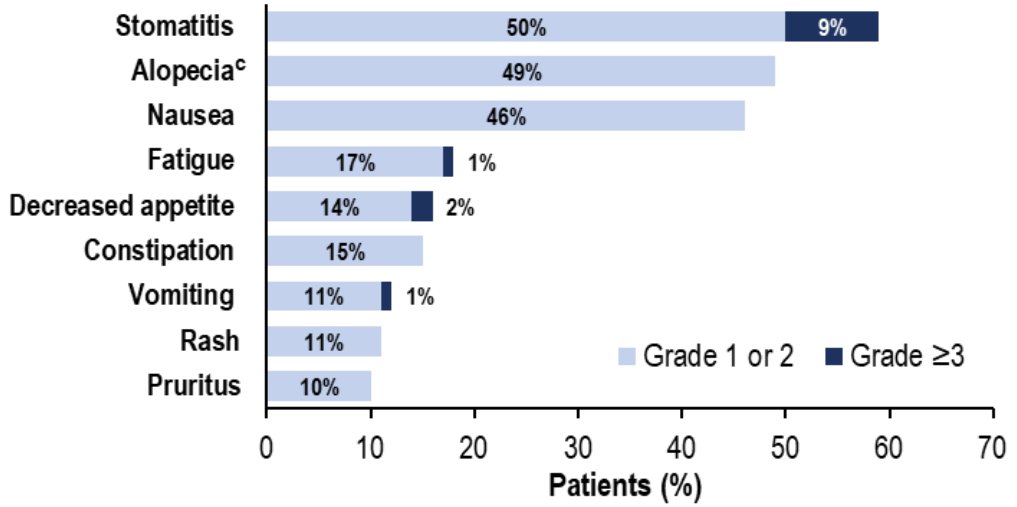
ESMO Asia 2024

Daiichi-Sankyo

## Dato-DXd is a potential treatment option for patients with EGFRm NSCLC in the 2L and later settings

### Safety

| | *EGFR*m Pool (N=117) |
|---|---|
| **TRAEs, n (%)** | 111 (95) |
| Grade ≥3 | 27 (23) |
| **Associated with dose reduction** | 26 (22) |
| **Associated with dose delay** | 27 (23) |
| **Associated with treatment discontinuation** | 6 (5) |
| **Associated with death** | 0 (0) |
| **Serious TRAEs** | 9 (8) |
| **AESIs[a], n (%)** | |
| **Stomatitis/oral mucositis** | 81 (69) |
| Grade 3[b] | 11 (9) |
| **Ocular surface events** | 38 (32) |
| Grade 3[b] | 3 (3) |
| **Adjudicated drug-related ILD** | 5 (4) |
| Grade 3[b] | 1 (1) |



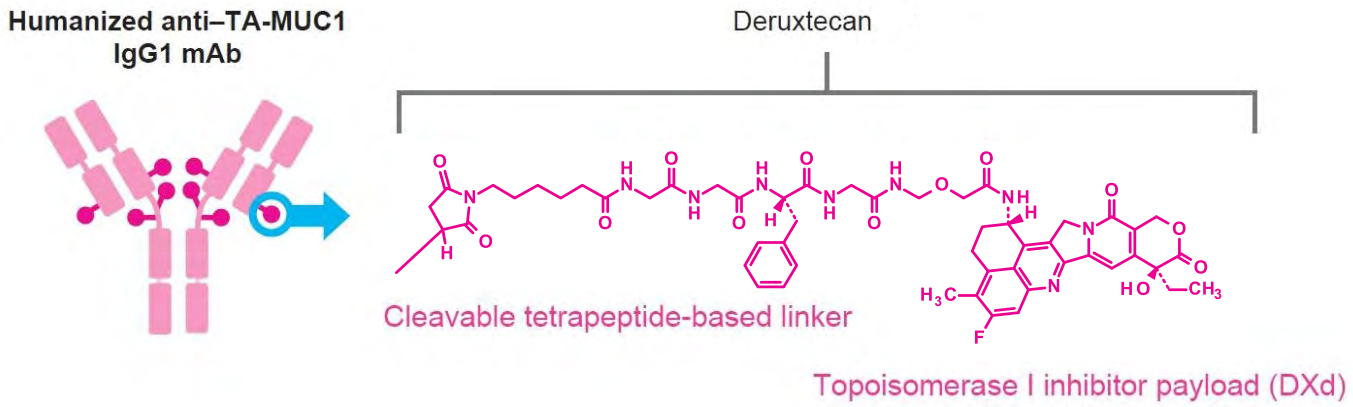

■ **A manageable safety profile with no new safety signals**

- Low rates of serious TRAEs or TRAEs leading to treatment discontinuations
- Grade ≥2 stomatitis/oral mucositis seen in ~1/3 patients was effectively managed with dose reductions/delays, and no treatment discontinuations due to stomatitis occurred
- No grade 4 or 5 ILD events

[a]AESIs listed are treatment emergent and include all preferred terms that define the medical concept. Some patients may have had >1 event. [b]No grade 4 or 5 events occurred. [c]Includes an event incorrectly reported as grade 3 per CTCAE grades.

AESI: adverse event of special interest, CTCAE: Common Terminology Criteria for Adverse Events, ILD: interstitial lung disease, NSCLC: non-small cell lung cancer, TRAE: treatment-related adverse event

# DS-3939 is the 6th DXd ADC and Directed Against TA-MUC1




## What is TA-MUC1?

- MUC1 is a transmembrane glycoprotein that is highly glycosylated in normal tissues and is localized to the apical membrane of epithelial surfaces.
- In cancers, MUC1 loses cell polarity and is redistributed over the cell surface and within the cytoplasm. Glycosylation of MUC1 is dysregulated in cancers and predominantly modified with shorter glycans, leading to the emergence of aberrantly glycosylated MUC1, known as tumor-associated MUC1 (TA-MUC1).
- TA-MUC1 is overexpressed in **broad range of tumors** including NSCLC, BC, UC, OVC, BTC and PDAC

## DS-3939 features

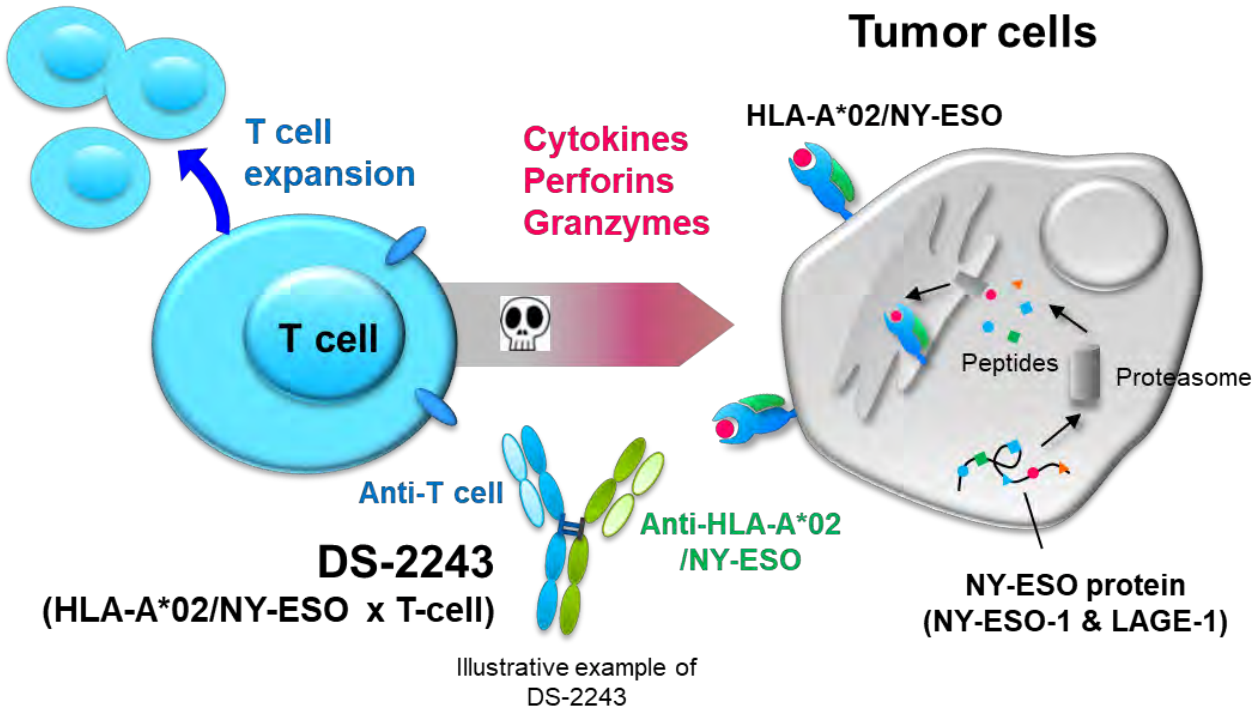
- High drug-to-antibody ratio ≈8
- DS-3939 specifically binds to TA-MUC1 by recognizing both the tumor specific glycan and backbone peptide moieties
- DS-3939 exhibited tumor regression against various preclinical in vivo models and also induced tumor regression after treatment of other FDA approved ADCs in xenograft model

BC; breast cancer, BTC: biliary tract cancer, FDA: Food and Drug Association, NSCLC: non-small cell lung cancer, OVC: ovarian cancer, PDAC: Pancreatic invasive ducatal adenocarcinoma, UC: urothelial cancer

# DS-2243 Overview

## A Potential First-in-Class Bispecific T-cell Engager (Bi-TCE) Targeting HLA-A*02/NY-ESO Tumors

### Mode of Action




Illustrative example of DS-2243

- **Cutting-Edge Bi-TCE:** Engineered to selectively engage both tumor antigens and T-cells, driving a targeted and potent immune response.
- **Tumor-Specific Targeting**: Precise targeting through the HLA-A*02/NY-ESO complex mediated by NY-ESO, a highly tumor-specific antigen. NY-ESO is only expressed in the testis in normal tissue, where it is present without HLA-A molecules.
- **Broad Applicability**: High/moderate frequency of NY-ESO expression observed in Synovial Sarcoma, Myxoid/Round Cell Liposarcoma, NSCLC, UC etc.
- **Promising Efficacy**: Exhibits robust anti-tumor activity and significant combination therapy potential in preclinical studies.

NSCLC: non-small cell lung cancer, UC: urothelial cancer

# TROP2 Normalized Membrane Ratio (NMR) measured by Quantitative Continuous Scoring (QCS)

## QCS is a novel computational pathology approach that precisely quantifies and locates targets like TROP2

**1 IHC with TROP2 Assay**

**2 Whole Slide Imaging**

**3 Automated Image Analysis (QCS)**

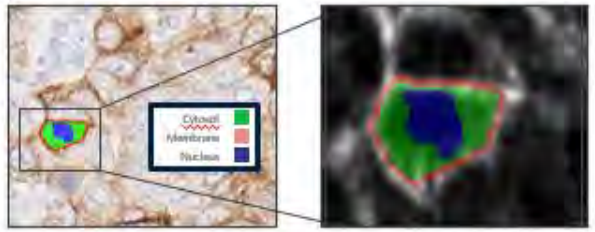
**4 Patient Biomarker Status Determination**

\+ ≥75% of tumor cells with TROP2 NMR ≤0.56

\- <75% of tumor cells with TROP2 NMR ≤0.56*

**Differentiates tumor from non-tumor**

**Measures OD in each tumor cell**



Membrane and cytoplasm optical density (OD)

**Calculates TROP2 NMR for every tumor cell**

$$\frac{\text{Membrane OD}}{\text{Membrane OD + Cytoplasm OD}}$$

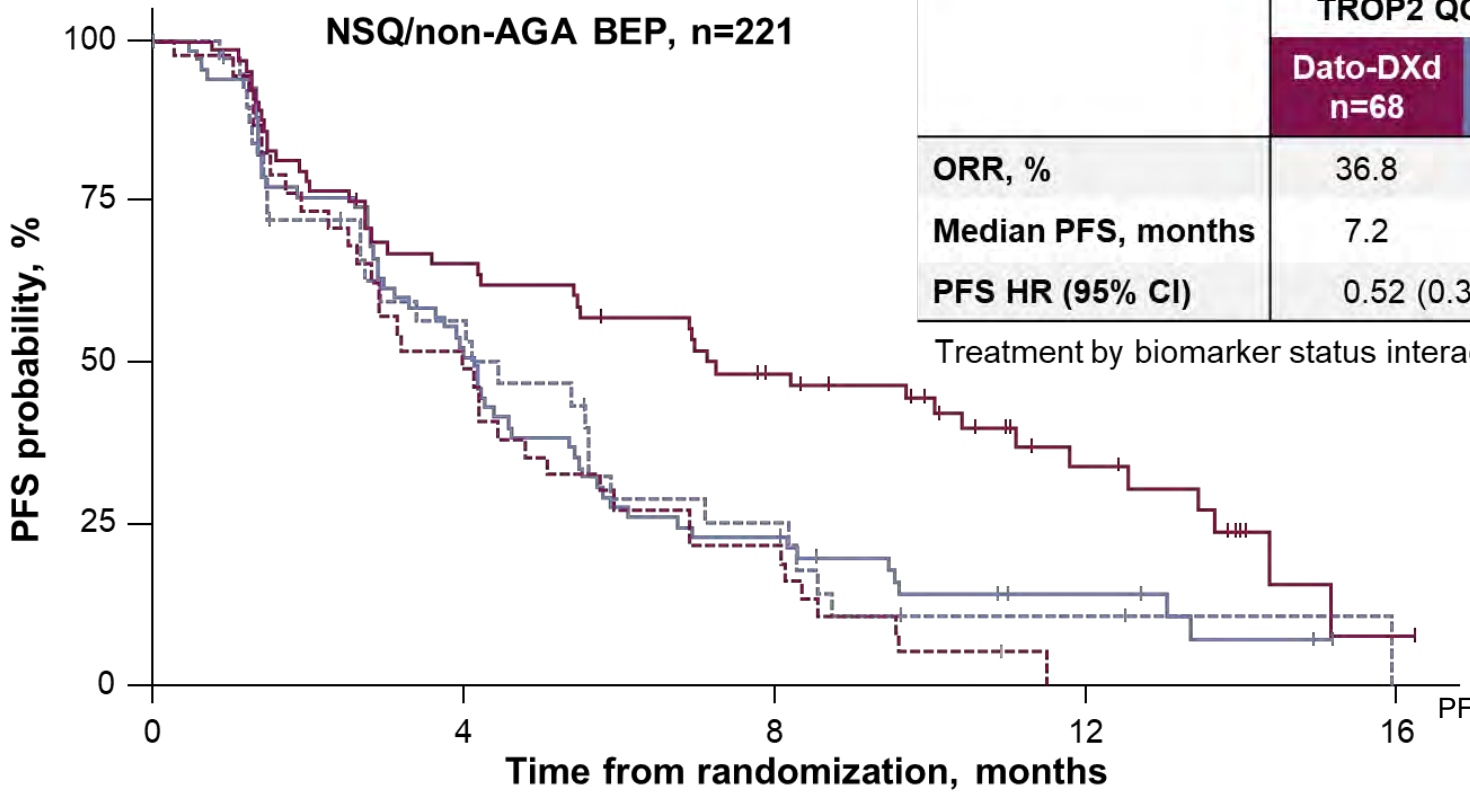
*Lower NMR → higher cytoplasm proportion*

Dr Marina Chiara Garassino | Normalized Membrane Ratio of TROP2 by Quantitative Continuous Scoring is Predictive of Clinical Outcomes in TROPION-Lung01

IHC; immunohistochemistry

# NSQ/non-AGA BEP: Efficacy by TROP2 QCS-NMR Status

## TROP2 QCS-NMR positivity is predictive for longer PFS with Dato-DXd in the NSQ/non-AGA biomarker-evaluable population




| | TROP2 QCS-NMR+ | | TROP2 QCS-NMR– | |
|---|---|---|---|---|
| | Dato-DXd n=68 | Docetaxel n=72 | Dato-DXd n=40 | Docetaxel n=41 |
| ORR, % | 36.8 | 15.3 | 22.5 | 12.2 |
| Median PFS, months | 7.2 | 4.1 | 4.0 | 4.4 |
| PFS HR (95% CI) | 0.52 (0.35–0.78) | | 1.22 (0.74–2.00) | |

Treatment by biomarker status interaction: p=0.0098

Data cutoff: March 29 2023

PFS HR (95% CI) by TROP2 QCS-NMR status (+ vs -) within treatment:
- ✓ Dato-DXd: 0.40 [0.25-0.64]
- ✓ Docetaxel:0.94 [0.60-1.49]

- AVANZAR and TROPION-Lung10 have the potential to clinically validate the TROP2 QCS biomarker for Dato-DXd
- An additional trial in patients with biomarker-positive tumors in the 2L NSQ NSCLC setting is planned

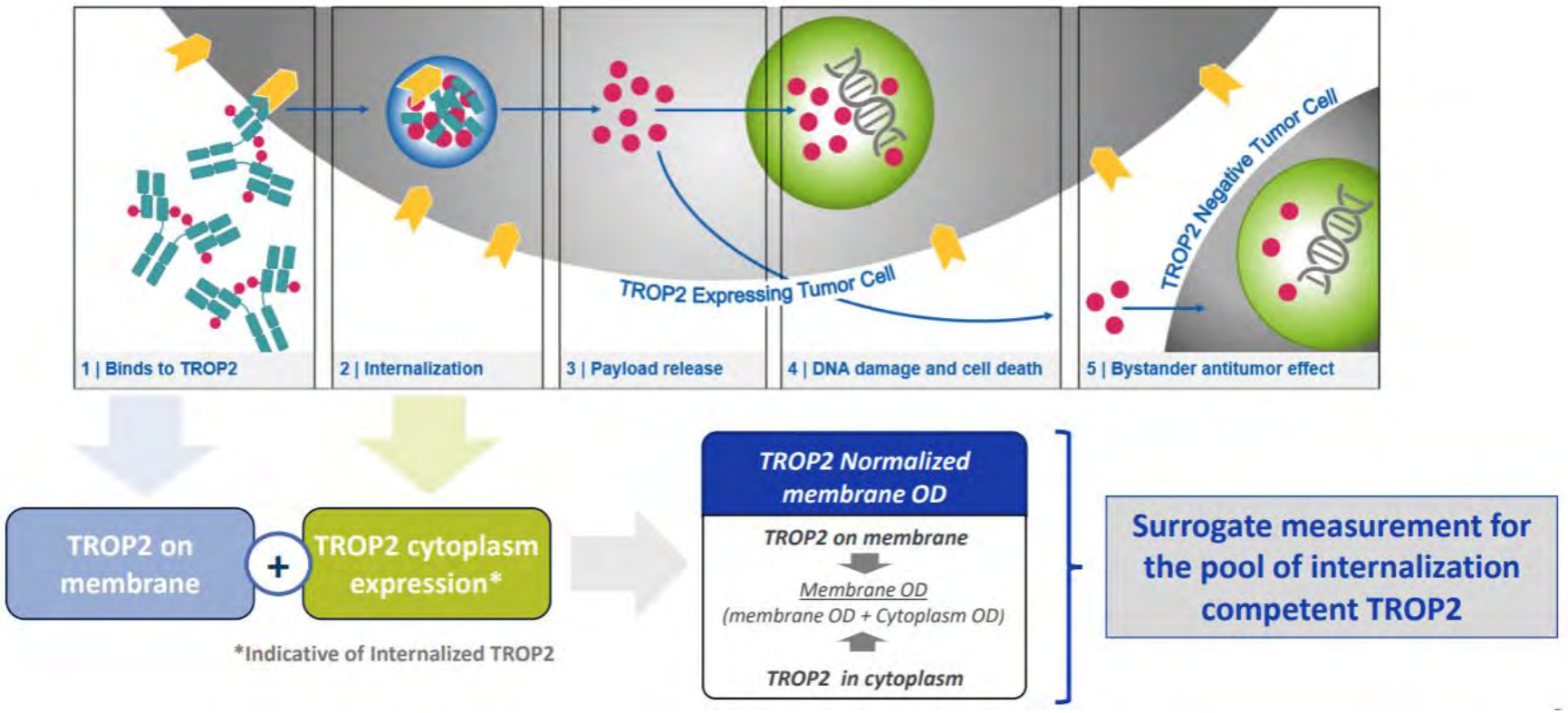
AGA; actionable genomic alteration, BEP; biomarker evaluable population, CI: confidence interval, HR; hazard ratio, NMR; Normalized Membrane Ratio, NSCLC; non-small cell lung cancer, NSQ; non-squamous, ORR; objective response rate, PFS; progression free survival, QCS; Quantitative Continuous Scoring,

# QCS in Dato-DXd

A success case of hypothesis-driven predictive biomarker discovery

## Hypotheses

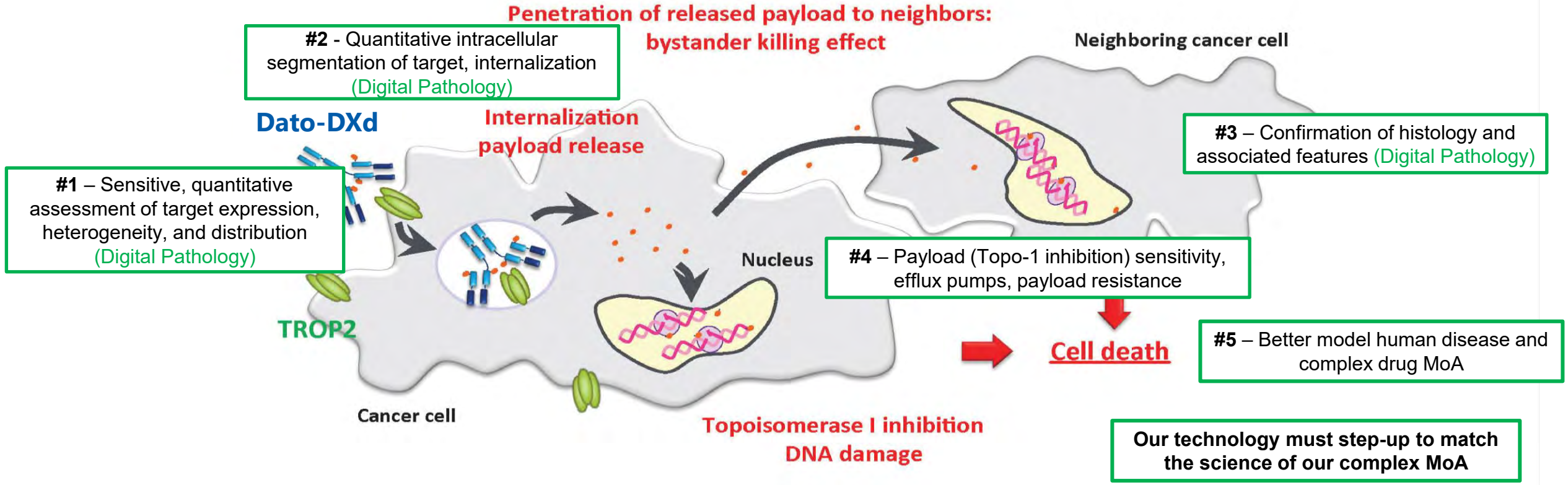
1. Precise, quantitative measurement of TROP2 in the membrane and cytoplasm, and their relationship, predict efficacy of Dato-DXd in NSCLC
2. Increased cytoplasmic expression of TROP2 identify a greater pool of cytoplasmic TROP2 capable of internalizing Dato-DXd bound to TROP2 and predict efficacy of Dato-DXd in NSCLC




NSCLC; non-small cell lung cancer, OD; optical density, QCS; quantitative continuous scoring,

# Predictive Biomarkers from Focus on ADC Mechanism of Action

## The mechanism of action (MoA) is more complex for DXd ADCs than conventional targeted therapies




- For conventional targeted therapies, a predictive biomarker often derives from target expression
- Target expression along with attention to key steps in the MoA may bring more success predicting efficacy
- Access to large datasets with clinical results will be critical

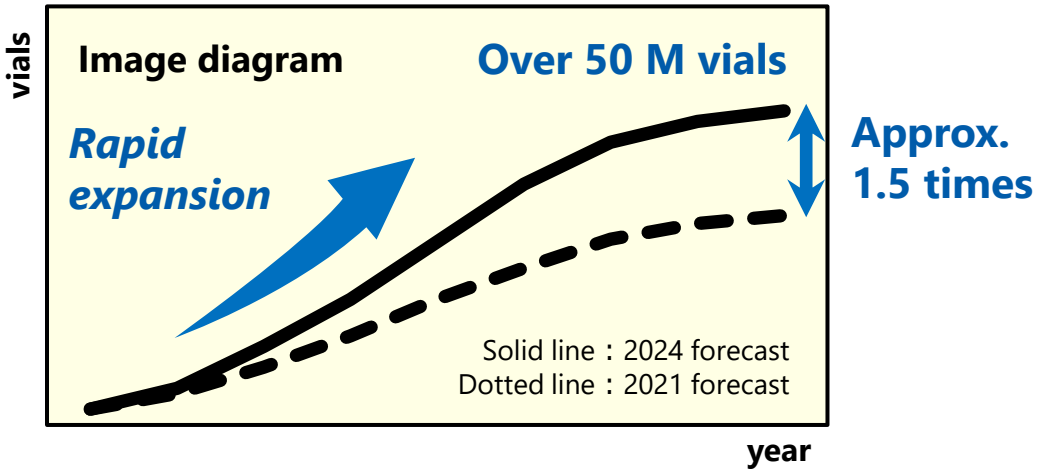
# Rapid Expansion of Demand for 5DXd ADCs

## With strong progress of clinical development, the overall demand forecast for 5DXd ADCs has significantly increased.

- Strong progress of Enhertu®, Product sales forecast for FY2024 : 508.4 Bn yen
- The emergence of a new growth driver following 3ADC (3ADCs ➡ 5DXd ADCs)
- Strategic partnership with AstraZeneca (Enhertu®, Dato-DXd) and US Merck* (HER3-DXd, I-DXd, DS-6000)

* Merck & Co., Inc., Rahway, NJ, USA

- A demand of over 50 M vials*1 is expected for 5DXd ADCs in total.（Approx. 1.5 times*2 increased compared to the original demand forecast in the 5-Year Business Plan (FY2021-FY2025)）




*1 Number of vials required per year at peak time (Total of 5DXd ADCs)
*2 Comparison with number of vials required per year at peak time calculated in the 5-Year Business Plan

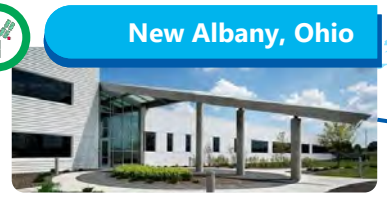
**It is essential to establish a supply system that can meet peak demand for 5DXd ADCs in total (Over 50 M vials)**

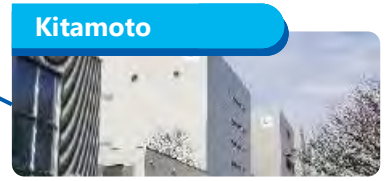
# Enhancement of Supply Capacity through Capital Investment in in-house and CMOs














**Promoted capital investment of approx. 600 Bn yen*1 globally, including in-house and CMOs**

**Supply capacity expected to meet peak demand for the 5 DXd ADCs in total**

**Sites executing or considering capital investment for ADCs**

*1 The total amount of capital investment related to ADCs planned in the 5-Year Business Plan

CMO; contract manufacturing organization

# History of the Daiichi Sankyo Group

## A History as a Partner to Patients for over 100 years

**1899**

**1899**
Launched *Taka-Diastase*®, a digestive enzyme agent, based on Taka-Diastase digestive enzyme discovered on a fungus by Dr. Jokichi Takamine

**1902**
Adrenalin, an adrenal cortex hormone agent

**1910**

**1910**
Dr. Umetaro Suzuki, a future Sankyo scientific adviser, made the world's first discovery of vitamin B1 (*Orizanin*®) in rice bran and established a foundation for the theory of vitamins

**1915**
Dr. Shozaemon Keimatsu (founder of Arsemin Shokai, the predecessor organization of Daiichi Pharmaceutical) began domestic manufacturing of Salvarsan, a therapeutic drug for syphilis

**1980**

**1985**
*Loxonin*®, an anti-inflammatory analgesic

**1990**

**1989**
*Mevalotin*®, hypercholesterolemia treatment

**1993**
*Cravit*®, a broad-spectrum oral antimicrobial agent

**2000**

**2002**
Olmesartan (*Olmetec*® in Japan, *Benicar*® in the United States), an antihypertensive agent

**2009**
*Efient*®, an antiplatelet agent

**2010**

**2010**
*Inavir*®, anti-influenza treatment

**2011**
*Lixiana*®, an anticoagulant
*Tarlige*®, pain treatment

**2020**

**2020**
*Enhertu*®, an anti-cancer agent (HER2 directed antibody drug conjugate)


**2030**

**1899~: Sankyo Co., Ltd.**

**1910~: Daiichi Pharmaceutical Co., Ltd.**

**2005~: Daiichi Sankyo Co., Ltd.**

# Becoming an Innovative Global Healthcare Company with Strengths in S&T

SCIENCE & TECHNOLOGY

## Human Resources

- Diverse range of talents with high levels of expertise
- Technologies originated from craftspersonship
- Scientific assessment capabilities
- Desire for innovation
- High levels of engagement

## Core Technologies

- Proprietary ADC technology platform
- Medicinal chemistry, protein engineering, drug evaluation, computational science, and translational research

## Corporate Culture

- A corporate culture in which employees respect each other as a specialist in science, and exchange opinions in a free and open-minded manner, regardless of positions and tenure
- A culture that promotes the transmission of experience and technologies for creating medicines

Driving Force for Value Creation

**Science & Technology**

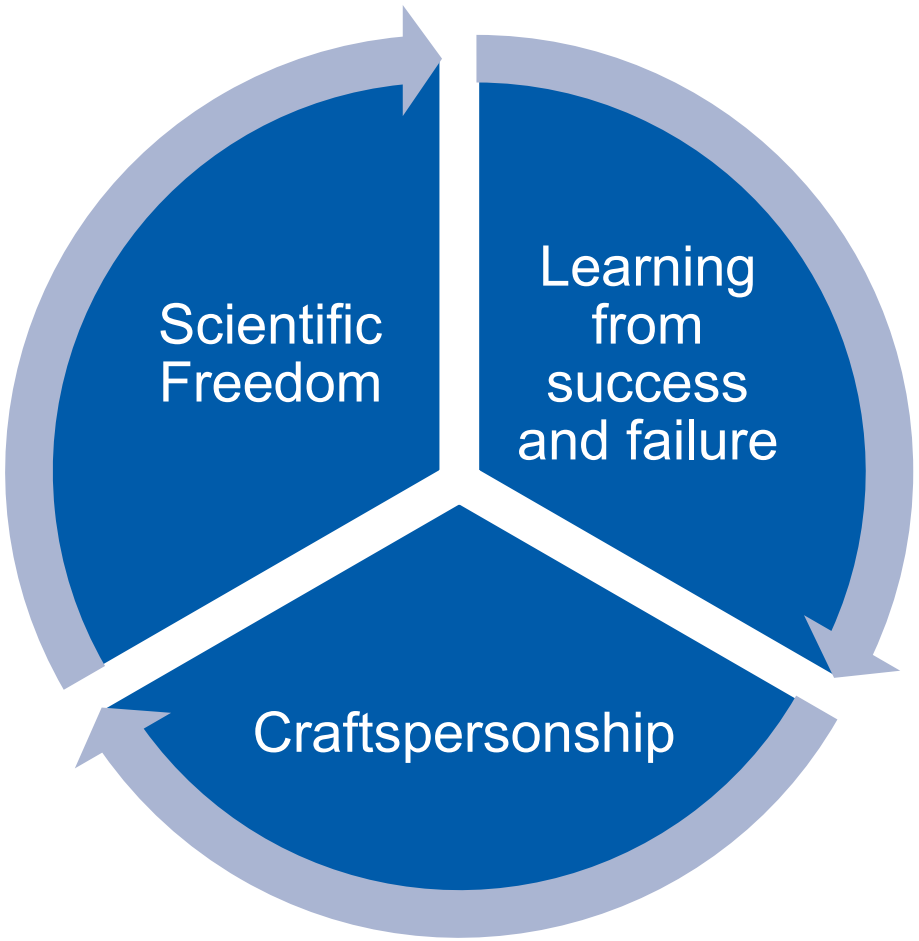
S&T SCIENCE & TECHNOLOGY


## Business Innovations Driven by New Drugs

The innovation resulting from the new drugs created through our strengths in S&T is not limited to research, but also drives further innovation and new opportunities throughout each function of the value chain and the business as a whole.

# To what do you attribute your success with Enhertu and your DXd ADC? What makes your R&D process so special?

We attribute our strong science and technology to a special culture with three overlapping concepts:



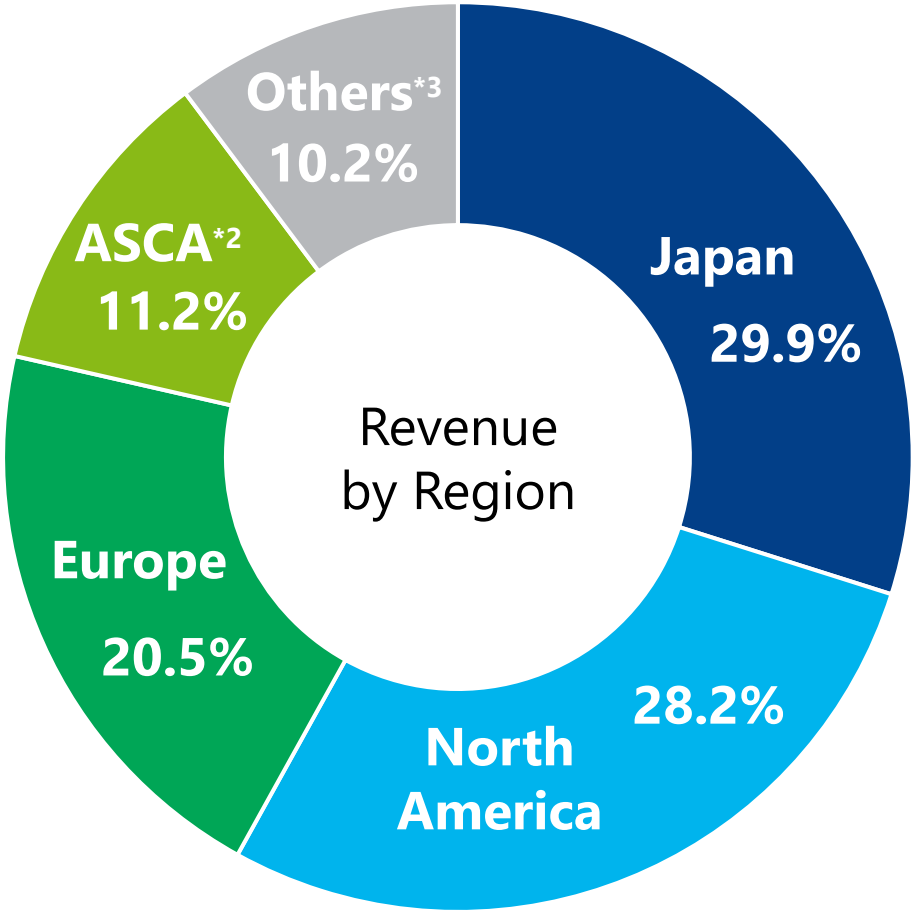

- **Scientific Freedom**
  - We value scientific freedom to explore questions, share knowledge, and communicate openly, while also acting responsibly.
  - Our environment promotes psychological safety, where anyone can discuss and propose ideas without fear.
- **Learning from Success and Failure**
  - The culture in our labs encourage taking intelligent risks and learning from what transpires whether it succeeds or fails.
  - We believe in testing new ideas boldly, embracing challenges, and applying our learnings to continuously improve.
- **Craftspersonship**
  - When exceptional researchers perform in a culture based on the concepts above, they can work with a craftsperson mindset:
  - At the heart of our work is a dedication to quality and careful craftspersonship, a tradition we've upheld for over a century.

# Overview of Daiichi Sankyo

## Overview of FY2024 consolidated P&L

(Bn JPY)

| | FY2024 Results | | | |
|---|---|---|---|---|
| | | to revenue | vs FY2023 | |
| **Revenue** | **1,886.3** | **100.0%** | **+17.8%** | **+284.6** |
| **Cost of sales** *1 | **415.7** | **22.0%** | | **+1.0** |
| **SG&A expenses** *1 | **724.8** | **38.4%** | | **+97.5** |
| **R&D expenses** *1 | **432.9** | **22.9%** | | **+68.5** |
| **Core operating profit** *1 | **312.8** | **16.6%** | **+60.2%** | **+117.6** |
| **Operating profit** | **331.9** | **17.6%** | **+56.9%** | **+120.3** |
| **Profit attributable to owners of the Company** | **295.8** | **15.7%** | **+47.3%** | **+95.0** |




*1 As an indicator of ordinary profitability, "core operating profit" which excludes temporary income and expenses from operating income is disclosed.
Income and expenses related to sale of fixed assets, restructuring (excluding the sales of pipeline and launched products), impairment, loss compensation, reconciliation, and other non-temporary and material gains and losses are included in the "temporary income and expenses".
Temporary income and expenses are excluded from results and forecast for cost of sales, SG&A expenses and R&D expenses shown in the list above.

*2 Asia, South & Central America

*3 Revenue related to upfront and milestone payments based on ENHERTU® and DATROWAY® strategic alliance agreements with AstraZeneca, and HER3-DXd, I-DXd and R-DXd strategic alliance agreement with Merck & Co., Inc., Rahway, NJ, USA.

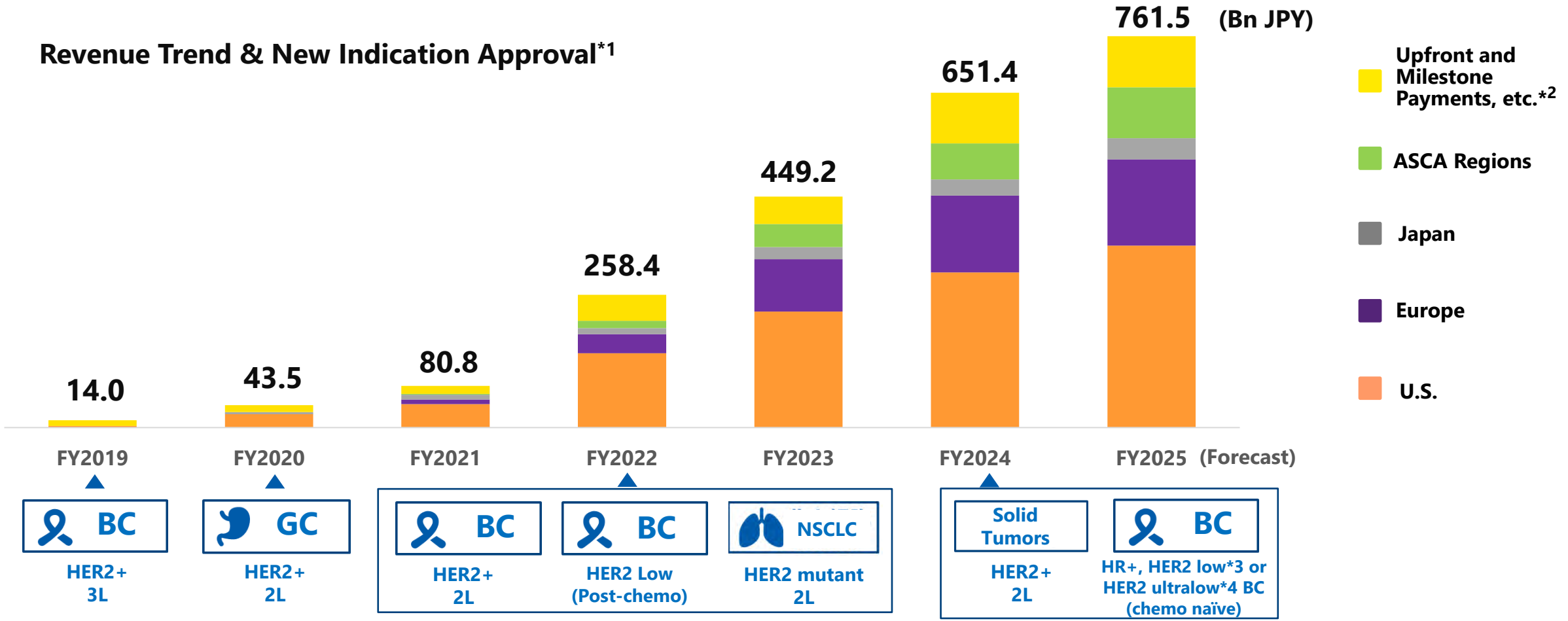
# 5 DXd ADCs financial impact

# ENHERTU®: Revenue growth since Launch

ENHERTU trastuzumab deruxtecan

Daiichi-Sankyo

**Revenue is growing steadily by solid market penetration (increase in market share) and expansion of sales regions and indications (increase in eligible patients)**




*1 U.S. approval timing, **2 Amount booked as revenue for each fiscal year, *3 IHC 1+ or IHC 2+/ISH-, *4 IHC 0 with membrane staining
ASCA: Asia, South and Central America, BC: breast cancer, GC: gastric cancer, HR: hormone receptor, NSCLC: non-small cell lung cancer

# 5DXd ADCs Revenue (incl. Forex Impact)

(Unit: Bn JPY)

| | FY2024 Results | YoY | FY2025 Forecast | YoY |
|---|---|---|---|---|
| **ENHERTU®** | **651.4** | **+202.2** | **761.5** | **+110.1** |
| Product Sales | 552.8 | +156.9 | 662.1 | +109.3 |
| Upfront and Milestone Payments, etc. | 98.6 | +45.3 | 99.4 | +0.8 |
| **DATROWAY®** | **7.8** | **+1.4** | **13.0** | **+5.2** |
| Product Sales | 1.4 | +1.4 | 4.7 | +3.2 |
| Upfront and Milestone Payments, etc. | 6.4 | - | 8.3 | +2.0 |
| **HER3-DXd** | **19.8** | **+16.2** | **16.3** | **-3.5** |
| Product Sales | - | - | - | - |
| Upfront and Milestone Payments, etc. | 19.8 | +16.2 | 16.3 | -3.5 |
| **I-DXd** | **15.3** | **+8.8** | **15.1** | **-0.2** |
| Upfront and Milestone Payments, etc. | 15.3 | +8.8 | 15.1 | -0.2 |
| **R-DXd** | **6.7** | **+4.0** | **20.5** | **+13.7** |
| Upfront and Milestone Payments, etc. | 6.7 | +4.0 | 20.5 | +13.7 |
| **5DXd ADCs Total** | **701.1** | **+232.6** | **826.4** | **+125.3** |

# 5DXd ADCs Upfront and Milestone Payments

(Unit: Bn JPY)

| Asset | Item | FY2024 Results | YoY | FY2025 Forecast | YoY | Total Consideration (as of Mar 2025) |
|---|---|---|---|---|---|---|
| ENHERTU® | Upfront Payment | 10.2 | +0.1 | 10.2 | +0.0 | 149.0 |
| | Regulatory Milestones | 29.2 | +16.9 | 12.7 | -16.5 | 167.7 |
| | Quid Related Payment | 1.2 | +0.0 | 1.2 | - | 17.2 |
| | Sales Milestone | 57.9 | +28.3 | 75.3 | +17.3 | 100.8 |
| DATROWAY® | Upfront Payment | 6.4 | - | 6.4 | - | 115.9 |
| | Regulatory Milestones | - | - | 2.0 | +2.0 | - |
| AZ Alliance Total | | **104.9** | **+45.3** | **107.7** | **+2.8** | **550.5** |
| HER3-DXd | Upfront Payment | 19.0 | +15.5 | 15.8 | -3.3 | 224.9 |
| | Satisfaction of Quid Rights | 0.7 | +0.7 | 0.5 | -0.2 | 7.3 |
| I-DXd | Upfront Payment | 14.7 | +8.1 | 14.7 | - | 225.4 |
| | Satisfaction of Quid Rights | 0.7 | +0.7 | 0.5 | -0.2 | 7.3 |
| R-DXd | Upfront Payment | 6.2 | +3.4 | 20.1 | +13.9 | 112.7 |
| | Satisfaction of Quid Rights | 0.6 | +0.6 | 0.4 | -0.2 | 7.3 |
| US Merck Alliance Total | | **41.8** | **+28.9** | **51.9** | **+10.0** | **584.8** |

* "Quid rights" (worth $150 mil.) that was held under the strategic alliance agreement with US Merck and was appropriated as part of consideration to obtain MK-6070 is booked as deferred revenue

# 5DXd ADCs Consideration of Strategic Collaborations

As of Mar 31, 2025

| Asset | Item | Consideration (Mn USD) | Received Amount (Mn USD) | Remained Amount (Mn USD) | <FYI>Received Amount (Bn JPY) |
|---|---|---|---|---|---|
| ENHERTU | Upfront Payment | 1,350 | 1,350 | - | 149.0 |
| | Regulatory Milestones | 3,725 | 1,275 | 2,450 | 167.7 |
| | Quid Related Payment | 150 | 150 | - | 17.2 |
| | Sales Milestones | 1,825 | 688 | 1,138 | 100.8 |
| | **ENHERTU Total** | **7,050** | **3,463** | **3,588** | **434.6** |
| Dato-DXd | Upfront Payment | 1,000 | 1,000 | - | 115.9 |
| | Regulatory Milestones | 1,000 | - | 1,000 | - |
| | Sales Milestones | 4,000 | - | 4,000 | - |
| | **Dato-DXd Total** | **6,000** | **1,000** | **5,000** | **115.9** |
| **AZ Alliance Total** | | **13,050** | **4,463** | **8,588** | **550.5** |
| HER3-DXd | Upfront Payment | 1,500 | 1,500 | - | 224.9 |
| | RD Expenses Related Refundable Upfront Payments | 500 | 500 | - | 75.1 |
| | Satisfaction of Quid Rights | 50 | 50 | - | 7.3 |
| | Sales Milestones | 5,500 | - | 5,500 | - |
| | **HER3-DXd Total** | **7,550** | **2,050** | **5,500** | **307.3** |
| I-DXd | Upfront Payment | 1,500 | 1,500 | - | 225.4 |
| | RD Expenses Related Refundable Upfront Payments | 500 | 500 | - | 75.1 |
| | Satisfaction of Quid Rights | 50 | 50 | - | 7.3 |
| | Sales Milestones | 5,500 | - | 5,500 | - |
| | **I-DXd Total** | **7,550** | **2,050** | **5,500** | **307.8** |
| DS-6000 (R-DXd) | Upfront Payment | 1,500 | 750 | 750 | 112.7 |
| | Satisfaction of Quid Rights | 50 | 50 | - | 7.3 |
| | Sales Milestones | 5,500 | - | 5,500 | - |
| | **R-DXd Total** | **7,050** | **800** | **6,250** | **120.0** |
| **US Merck Alliance Total** | | **22,150** | **4,900** | **17,250** | **735.1** |

Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

# HER3-DXd, I-DXd (DS-7300), R-DXd (DS-6000) Strategic Collaboration with Merck & Co., Inc., Rahway, NJ, USA

# Why a Strategic Collaboration?

Daiichi-Sankyo

**Our Mission**

**Purpose**
Contribute to the enrichment of quality of life around the world

**Mission**
Create innovative pharmaceuticals addressing diverse medical needs

**Internal/external environmental changes**

**Enhanced capacity, resources and capabilities have become necessary to maximize DXd-ADC franchise**

**Strategic collaboration will help us deliver on the promise of our next three DXd-ADCs by potentially enabling us to reach more patients more quickly than we could on our own**

# What We Aim to Achieve through Strategic Collaboration

Daiichi-Sankyo

## Leverage collaborator's capacity, resources and capabilities

- Develop **more aggressive development plans** targeting **broader patient populations**
- **Accelerate development timelines** and **mitigate risk of delays**
- Gain opportunity to **contribute to patients in more countries/regions**

## Further expand resources to create favorable cycle for sustainable growth

- **Optimal resource allocation** for new growth drivers following 5DXd-ADCs, post DXd-ADC modalities, etc.
  - DS-3939 (TA-MUC1 directed ADC), DS-XXXX (7th DXd-ADC)
  - DS-9606 (2nd generation ADC), New concept ADC, etc.
  - Early stage research projects

**Create more corporate and product value through strategic collaboration**

# Why Merck & Co., Inc., Rahway, NJ, USA?

Daiichi-Sankyo

## A world-leading oncology company with KEYTRUDA® as a foundation

- **Remarkable experience** in oncology, **proven expertise** in immuno-oncology
- **Strong capabilities and capacity, resources** in development
- Oncology business in **numerous countries/regions and tumor types**

KEYTRUDA® (pembrolizumab) Injection 100 mg

**A collaborator that is best-positioned to help us in our goal of establishing new standards of care across multiple tumor types**

## Extensive experience with strategic collaboration

A collaborator with **multiple successful global strategic collaborations,** gives us the highest probability **to achieve our goals**

## High valuation and commitment for success

A collaborator with **highest valuation for 3 products (HER3-DXd, I-DXd and R-DXd),** and **commitment for success** among the companies that expressed interest

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Rahway, NJ, USA

# Overview of Strategic Collaboration

- **Co-development and co-commercialization of HER3-DXd, I-DXd (DS-7300), R-DXd (DS-6000) with Merck & Co., Inc., Rahway, NJ, USA (MRK)**
  - **Maximize the value of 3 products by accelerating and expanding development**
  - **Allocate resource rapidly with flexibility** to new growth drivers following 5DXd-ADCs, post DXd-ADC modalities, etc.

## Development

- **Co-development** as monotherapy and combination therapy for **HER3-DXd, I-DXd (DS-7300), R-DXd (DS-6000)**

- **MRK** will be responsible for **75%** of **the first 2 Bn USD** of R&D expenses for each product, and the companies will share R&D expenses **equally thereafter**

## Manufacturing

- **Daiichi Sankyo** will **manufacture** and **supply** all 3 products

## Commercial

- **Global (excluding Japan):**
  The companies will **co-promote** and **share gross profit** and **promotional expenses etc.**
- **Japan:**
  **Daiichi Sankyo** will **solely commercialize** and **pay royalty** to MRK
- **Sales booking**
  **Daiichi Sankyo** will book product sales in **all countries/regions where Daiichi Sankyo has local operations (including Japan)**

# Financial Terms for Strategic Collaboration

Daiichi-Sankyo

## Up to 22.0 Bn USD (3,300.0 Bn JPY) in total (1USD=150JPY)

### Upfront payments 4.5 Bn USD (675.0 Bn JPY) : 1.5 Bn USD×3 products

| | HER3-DXd | I-DXd (DS-7300) | R-DXd (DS-6000) | **Total** |
|---|---|---|---|---|
| Upon contract execution | 0.75 Bn USD | 1.5 Bn USD | 0.75 Bn USD | **3.0 Bn USD** |
| 12 months after execution | 0.75 Bn USD | - | - | **0.75 Bn USD** |
| 24 months after execution | - | - | 0.75 Bn USD | **0.75 Bn USD** |
| **Total** | **1.5 Bn USD** | **1.5 Bn USD** | **1.5 Bn USD** | **4.5 Bn USD** |

MRK may elect not to pay the two upfront payments of 0.75 Bn USD each that are due after 12 months and after 24 months, respectively. If MRK opts out of HER3-DXd and/or R-DXd, the upfront payments already paid will be retained by DS and rights related to such products will be returned to DS

- Received upfront payments **will be deferred and booked as revenue** considering the estimated exclusivity period

### R&D expenses related refundable upfront payments 1.0 Bn USD (150.0 Bn JPY) : 0.5 Bn USD×2 products (HER3-DXd,I-DXd)

- MRK will be responsible for 75% of the first 2 Bn USD of R&D expenses for each product (MRK to bear 0.5 Bn USD more than DS compared to equal share)
  - ✓ 0.5 Bn USD for HER3-DXd and I-DXd, respectively to be paid upon contract execution as R&D expenses related refundable upfront payments (Pro-rated portion may be refundable in the event of early termination of development for both products).
    As for R-DXd, 75% of R&D expenses will be paid by MRK as they are incurred
  - ✓ **Accounting treatment is not yet determined**

### Sales milestones Up to 16.5 Bn USD (2,475.0 Bn JPY) : Up to 5.5 Bn USD×3 products

- Received sales milestones **will be booked as revenue in the year of achievement**

# How R&D Expenses will be Shared, and How Cash will be Paid

◆ **How R&D expenses for 3 products will be shared between the companies**

① **MRK will be responsible for 75% of the first 2 Bn USD of R&D expenses for each product** (MRK will bear 0.5 Bn USD (25% of 2 Bn USD) more than DS compared to 50% : 50% share)

② **MRK and DS will share R&D expenses equally thereafter for each product**

◆ **How cash for R&D expenses of 0.5 Bn USD (25% of the first 2 Bn USD) , which MRK will bear more than DS compared to 50% : 50% share, will be paid**

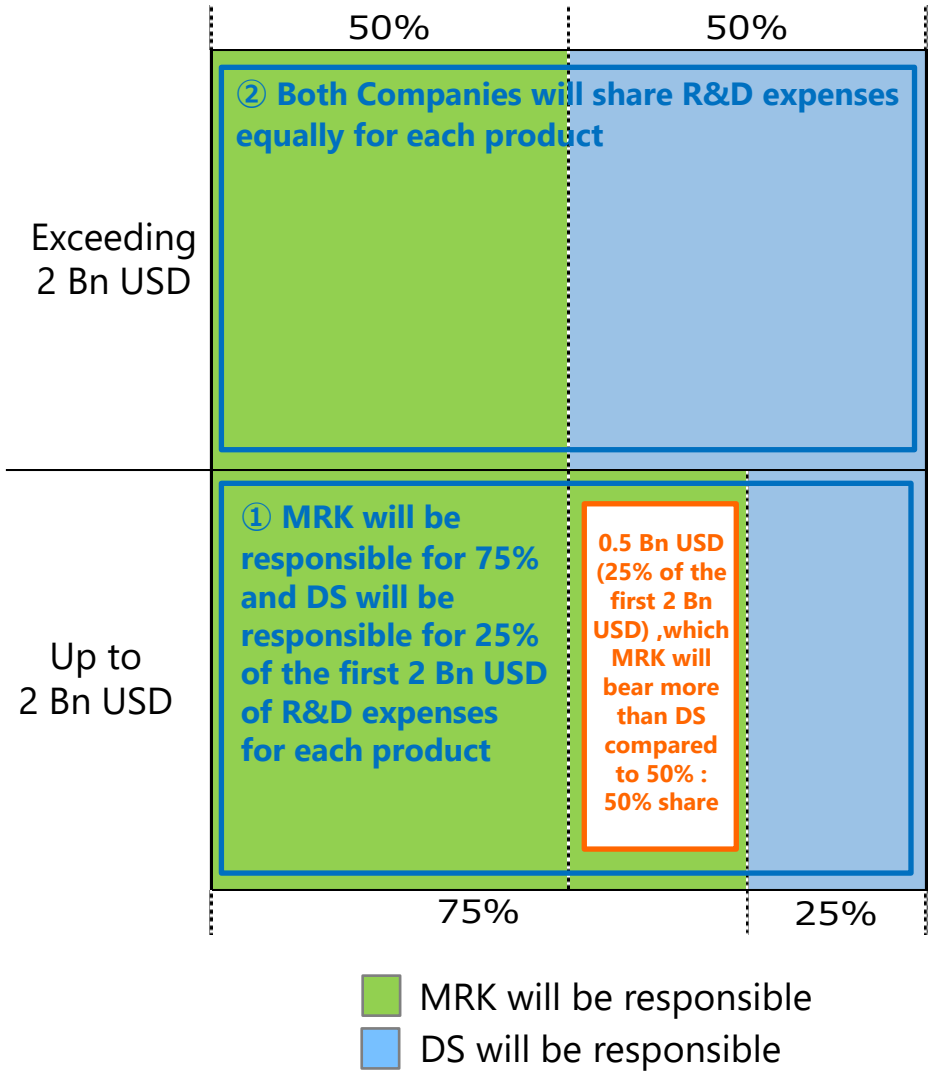
✓ **HER3-DXd, I-DXd (DS-7300)**

- **Will be paid upon contract execution** as "R&D expenses related refundable upfront payments" (Pro-rated portion may be refundable in the event of early termination of development for both products)
- Amount equivalent to 25% of R&D expenses will be appropriated from "R&D expenses related refundable upfront payments" as they are incurred

✓ **R-DXd (DS-6000)**

- **Will not be paid upon contract execution** as "R&D expenses related refundable upfront payments"
- To be paid as R&D expenses are incurred

**R&D expenses for each product**



Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

# 5-Year Business Plan (FY2021–FY2025)

# 5-Year Business Plan (FY2021-FY2025) for Sustainable Growth

We will achieve our 2025 Goal, **Global Pharma Innovator with Competitive Advantage in Oncology**, and will shift to further growth towards our 2030 Vision


**As of FY2020**

- Oncology business launched
- Edoxaban growing
- Regional value being enhanced
- AZ strategic alliance
- Increased RD investment

**2030 Vision**

**Innovative Global Healthcare Company Contributing to the Sustainable Development of Society**

- Global top 10 in Oncology
- Additional growth pillars being source of revenue and profit
- New products being source of profit in each business unit
- Contributing to sustainable development of society through our business

# Strategic Pillars for the 5-Year Business Plan (FY2021-FY2025)

## Achieve 2025 Goal and Shift to Further Growth

**FY2025 Financial Targets**

- Revenue: 1.6 Tn JPY (Oncology > 0.6 Tn JPY)
- Core Operating Profit* Ratio before R&D Expense: 40%
- ROE > 16%
- DOE** > 8%

### Maximize 3ADCs

- Maximize ENHERTU® and Dato-DXd through strategic alliance with AstraZeneca
- Maximize HER3-DXd without a partner
- Expand work force and supply capacity flexibly depending on changes around product potential

### Profit growth for current business and products

- Maximize Lixiana® profit
- Grow Tarlige®, Nilemdo®, etc. quickly
- Transform to profit structure focused on patented drugs
- Profit growth for American Regent and Daiichi Sankyo Healthcare

### Identify and build pillars for further growth

- Identify new growth drivers following 3ADCs
- Select and advance promising post DXd-ADC modalities

### Create shared value with stakeholders

- Patients: Contributing to patients through "Patient Centric Mindset"
- Shareholders: Balanced investment for growth and shareholder returns
- Society: Environment load reduction across the value chain, and actions against pandemic risks
- Employees: Create one DS culture through fostering our core behaviors

- Data-driven management through DX, and company-wide transformation through advanced digital technology
- Agile decision making through new global management structure

*Excluding temporary income and expenses (gains/losses related to sales of fixed assets etc.) from operating income

**DOE: Dividend on Equity = Total dividend amount / Equity attributable to owners of the company

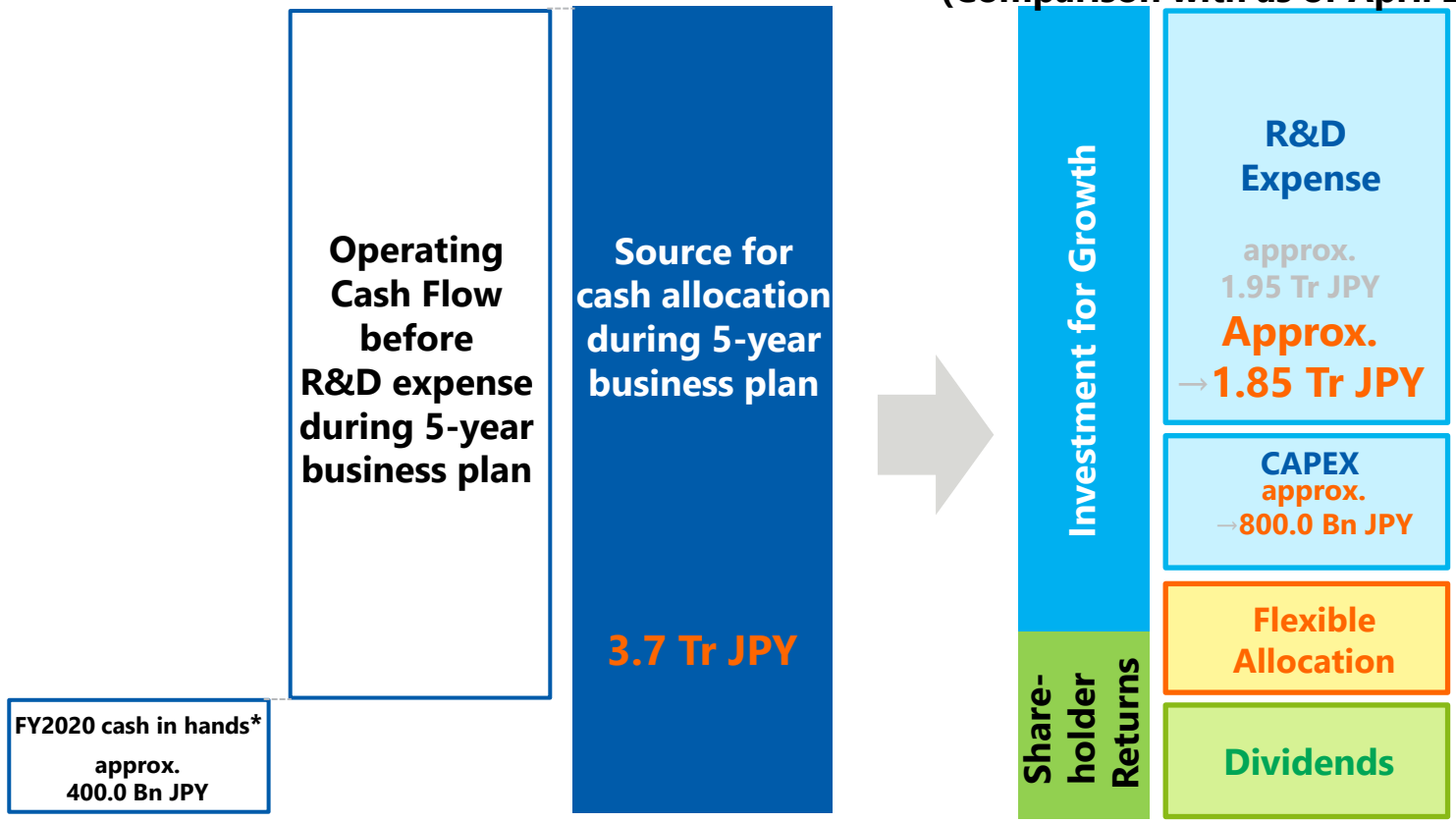
# Expectation on achieving FY2025 KPIs
(as of Apr. 2025)

| | At the time of planning 5YBP | As of Apr. 2024 | As of Apr. 2025 |
|---|---|---|---|
| Revenue | 1.6 Tr JPY | 2.1 Tr JPY | 2.0 Tr JPY |
| Revenue in Oncology | > 600.0 Bn JPY | > 1.0 Tr JPY | 900.0 Bn JPY |
| Core Operating Profit ratio before R&D expense | 40% | 40% | 40% |
| ROE | > 16% | > 16% | > 16% |
| DOE | > 8% | > 8.5% | > 8.5% |
| Currency exchange rate assumptions | 1 USD=105 JPY, 1 EUR=120 JPY | 1 USD=145 JPY, 1 EUR=155 JPY | 1 USD=140 JPY, 1 EUR=160 JPY |

# Well-balanced Investment for Growth and Shareholder Returns
## Cash Allocation

**Increase R&D expense and CAPEX for further growth in future, and increase shareholder returns.**

**Image for cash allocation**
**(Comparison with as of April 2024)**




**Prioritized investment for DXd-ADCs**

**Investment focused on enhancing ADC supply capabilities**

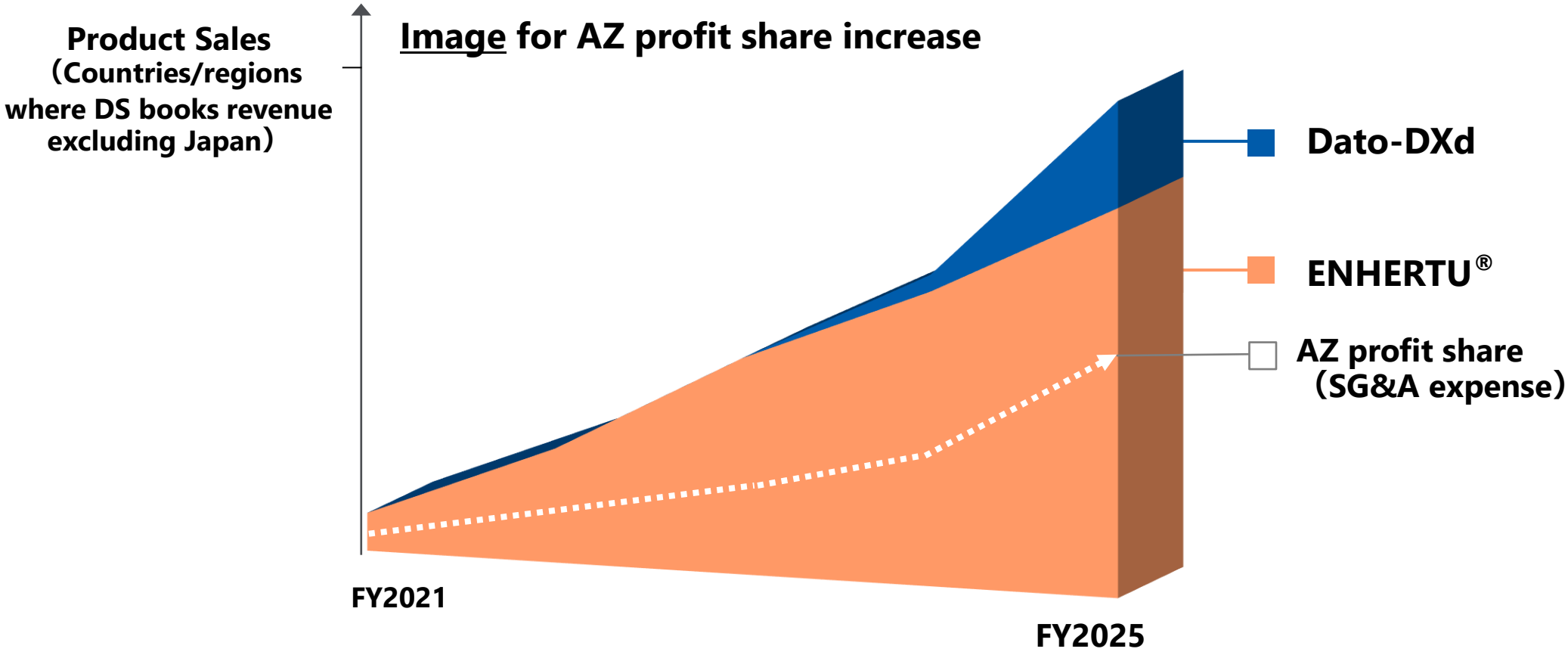
**Flexible allocation depending on pipeline progress for 1) investment to build pillars for further growth (in-house/external); and 2) acquisition of own shares**

**Stable dividends and dividend increase that take account of profit growth**

*Cash in hands excluding working capital

# Profit Share Increase for ENHERTU® and Dato-DXd

**SG&A expenses will increase along with the increase in profit share* of ENHERTU® and Dato-DXd product sales growth based on the strategic alliance with AZ**

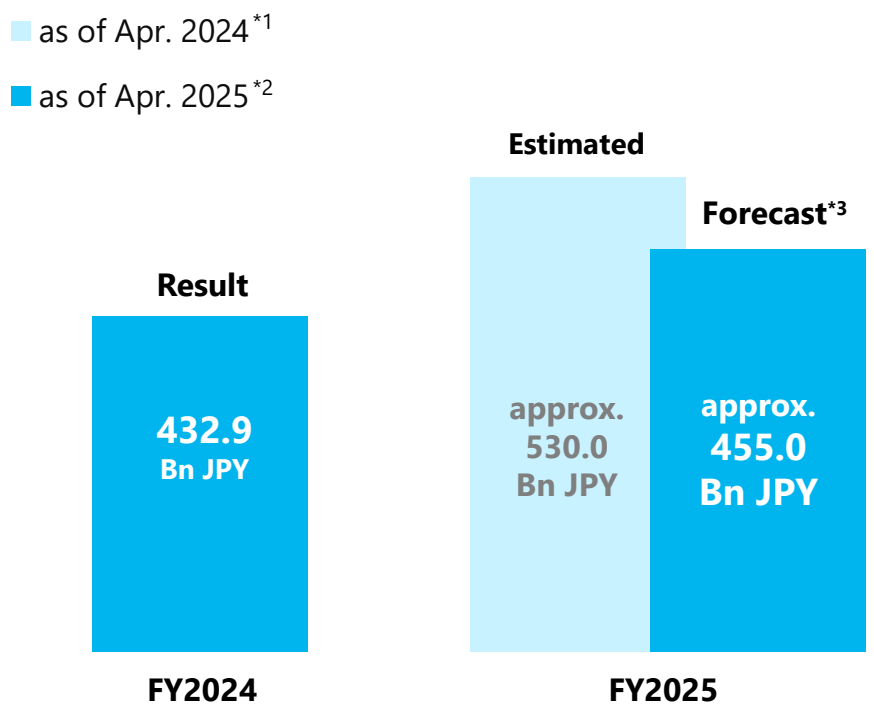



*DS pays AZ 50% of gross profit for the product sales in countries/regions where DS book revenue (excluding Japan) to share profit with AZ

# R&D Expense Forecast
(as of Apr. 2025)

## FY2025 R&D expense is forecasted to be 455 Bn JPY based on development plan updates

### R&D Expense Trend




Currency exchange rate assumptions
*1: 1 USD=145 JPY、1 EUR=155 JPY
*2: 1 USD=140 JPY、1 EUR=160 JPY

Forecast
*3: as of Apr. 2025

### Key drivers of decline vs. Apr 2024 forecast

◆ **Clinical development expense**
- ✓ Development plan updated based on strategic collaboration with US Merck

◆ **Medical affairs expense**
- ✓ NSCLC development strategy updated on DATROWAY®
- ✓ Launch delayed on HER3-DXd

# 3ADCs launch plan

## Realize maximizing the product values of 3ADCs through expanding the indications

### ~FY2020

**ENHERTU®**

- DESTINY-Breast01
- DESTINY-Gastric01

### 5-Year Business Plan (FY2021-FY2025)

**ENHERTU®**

- DESTINY-Breast03
- DESTINY-Breast04
- DESTINY-Breast06
- DESTINY-Breast09
- DESTINY-Breast11
- DESTINY-Gastric02
- DESTINY-Lung01/02
- DESTINY-Lung04
- DESTINY-PanTumor02*

**Dato-DXd**

- TROPION-Lung01
- TROPION-Breast01
- TROPION-Breast02

**HER3-DXd**

- HERTHENA-Lung01
- HERTHENA-Lung02

### FY2026 & Beyond

**ENHERTU®**

- DESTINY-Breast05
- DESTINY-Gastric04
- Combo with DS internal asset, I/O or targeted therapy in BC and NSCLC
- Other cancer types

**Dato-DXd**

- TROPION-Lung07
- TROPION-Lung08
- TROPION-Breast03
- Combo with I/O in BC and NSCLC etc.
- Other cancer types

**HER3-DXd**

- Combo with targeted therapy in NSCLC
- Other cancer types

Major study only (ref., appendices)

Already approved indications

Studies with updated timeline from the estimation in Apr 2023

* Submission data package includes DESTINY-CRC02 and DESTINY-Lung01 study

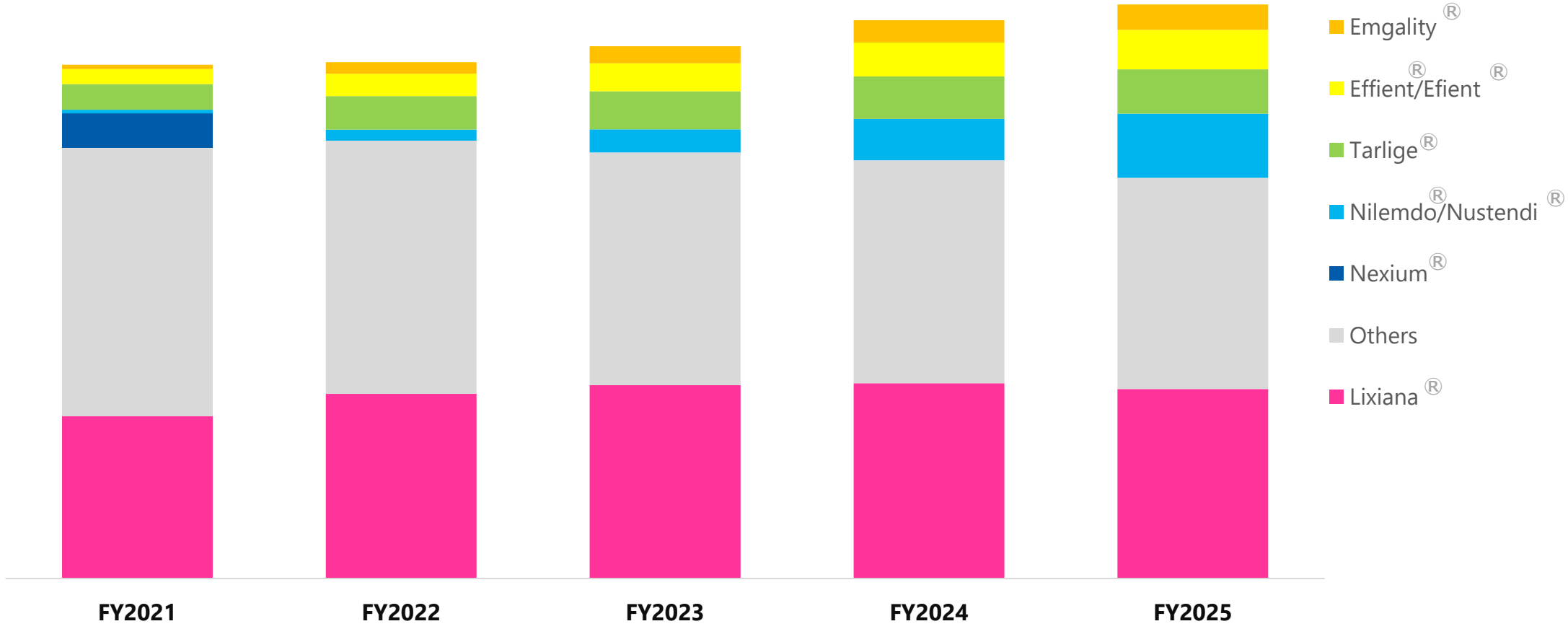
Timeline indicated is based on the current forecast and subject to change.

ADC: antibody-drug conjugate, BC: breast cancer, I/O: immuno-oncology, NSCLC: non-small cell lung cancer

# Grow Tarlige®, Nilemdo®, and Other Products

## We will also aim for sustainable growth in our business outside of oncology

### Image for consolidated revenue growth

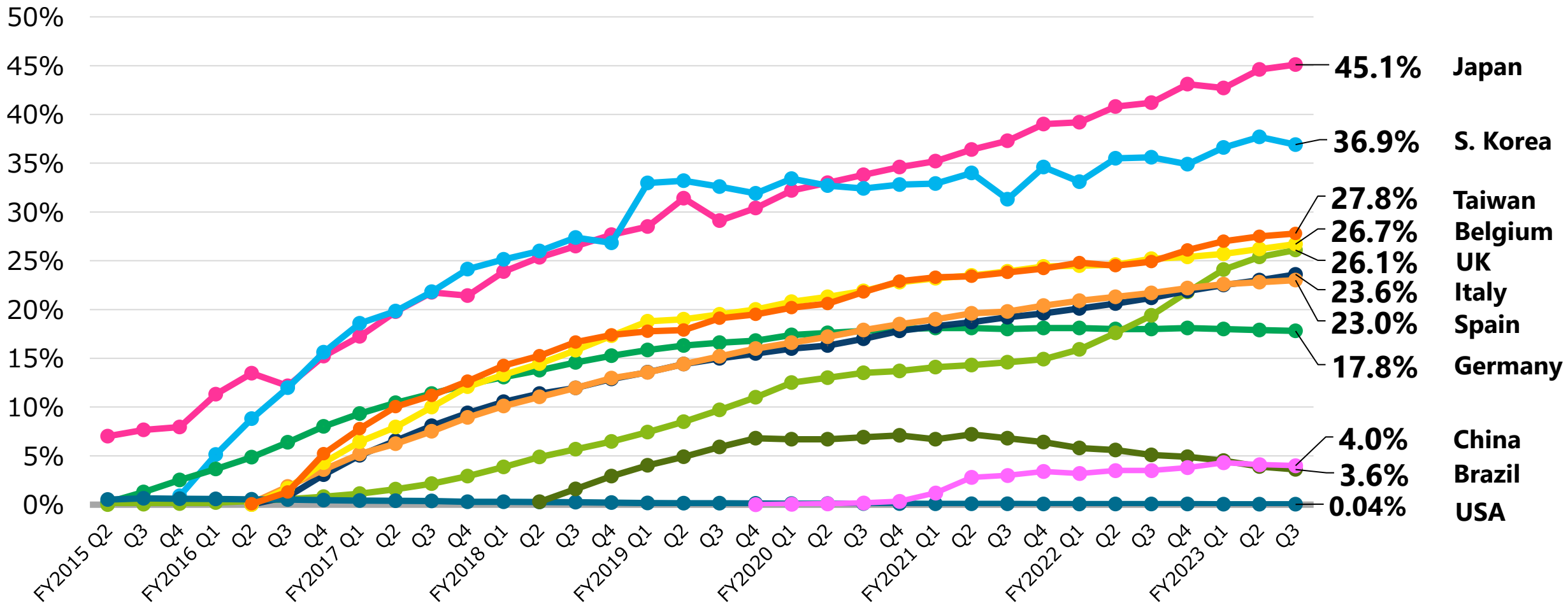


# LIXIANA®: Growth in Each Country/Region

Volume

Daiichi-Sankyo

**Global revenue FY2023 results: 287.7 Bn JPY (YoY +43.8 Bn JPY)**



# Investment in the US Business

## American Regent, Inc. acquired HBT Labs, Inc. (August 2022)

### Overview of HBT Labs, Inc.

- Business
  - **Research and development, manufacturing, sales and marketing** etc. of **generic (GE) injectables**
- Launched product
  - Mitotic inhibitor **Abraxane®** (generic name: paclitaxel) **authorized generic**
    - The company sells Abraxane AG supplied by Bristol Myers Squibb (Celgene)
- Major pipeline
  - Mitotic inhibitor **paclitaxel**
    - **Abraxane GE** originally developed by HBT
    - Approved by FDA (July 2022)
    - Planned to be Launched in FY2022 4Q
  - Atypical antipsychotic **aripiprazole (GE)**
  - Local anesthetic **bupivacaine (GE)**
- Headquarter and plant California, USA
- Number of employees 83

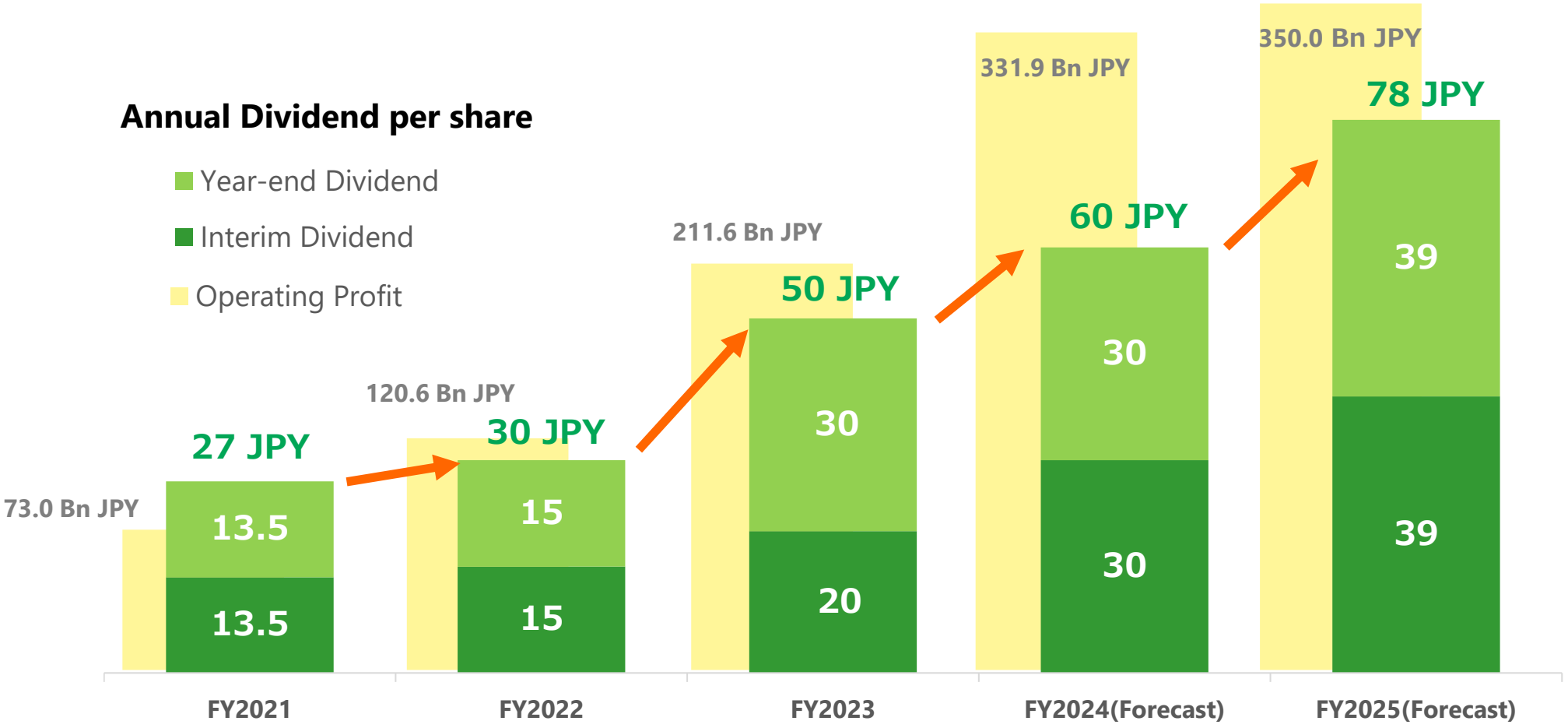
### Background, Purpose, Terms of Contract

- Background
  - For mid-to-long-term growth of ARI, it is necessary to **strengthen the product portfolio of GE injectables**
- Purpose
  - Contribution to sales revenue and profit by **paclitaxel**
  - HBT's advanced manufacturing technology will enable ARI to expand its **GE injectable pipeline**, including oncology
- Terms of contract
  - Upfront payment **225 Mn USD (30.0 Bn JPY)**
  - Milestone payment **20 Mn USD** (maximum)
    - 10 Mn USD to each launch for aripiprazole and bupivacaine
  - Royalty payment
    - Payment of 10% and 6%, respectively, for 3 years after the launch of aripiprazole and bupivacaine

**Aiming for further growth by strengthening the product portfolio through synergies with HBT Labs, Inc.**

# FY2025 Annual Dividend Forecast

**Plan to increase annual dividend to 78 JPY per share for FY2025 (up 18 JPY)**
**due to strong performance of ENHERTU® and others**



# Flexible Acquisition of Own Shares (Results)

- **Acquired own shares to strengthen and enhance shareholder returns**
- **FY2025 DOE is expected to be over 8.5%**

| | |
|---|---|
| **Apr. 2024 Resolution** | ➢ Acquisition period: **Apr. 26, 2024 – Jan. 9, 2025**<br>➢ Aggregate amount of acquisition cost: **200 billion JPY (maximum)**<br>➢ Total number of shares to be acquired: **38.71 million stocks (maximum)**<br>➢ Completed the cancellation of all of acquired own shares |
| **Feb. 2025 Resolution** | ➢ Acquisition period: **Mar. 3, 2025 – Apr. 8, 2025**<br>➢ Aggregate amount of acquisition cost: **50 billion JPY (maximum)**<br>➢ Total number of shares to be acquired: **13.97 million stocks (maximum)**<br>➢ Scheduled to cancel all of acquired own shares on May 30, 2025. |

# Flexible Acquisition of Own Shares (Resolution)

- **Established upper limits for acquiring own shares to take flexible actions based on comprehensive consideration such as share price level and other factors**
- **FY2025 DOE is expected to be over 8.5%**

**Upper limits to acquire own shares**

- Acquisition period: **May. 1, 2025 – Mar. 24, 2026**
- Aggregate amount of acquisition cost: **200 billion JPY (maximum)**
- Total number of shares to be acquired: **80.00 million stocks (maximum)**

# Daiichi Sankyo created and launched innovative drugs from its own research laboratories

Daiichi-Sankyo

EST. 2007

pravastatin

levofloxacin

olmesartan

laninamivir

prasugrel

edoxaban

mirogabalin

trastuzumab deruxtecan

valemetostat

DAICHIRONA®

Shinagawa, 1908

Kasai,1938

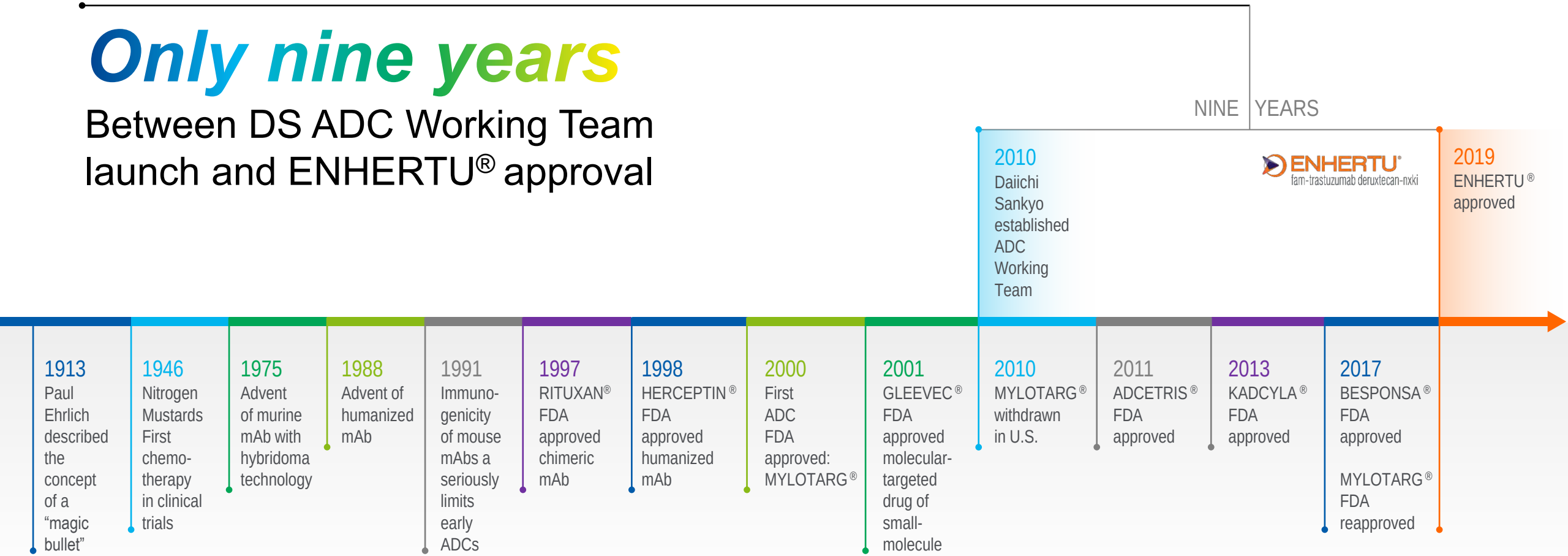
Shinagawa

Kasai

# Swift. Decisive. Courageous.

## *Only nine years*

Between DS ADC Working Team launch and ENHERTU® approval




History of ADCs

Source: *Nakada T. et al., Chem Pharm Bull (Tokyo). 2019*

ADC: antibody-drug conjugate, mAb: monoclonal antibody

# Long history behind the birth of DXd ADC

1990 | 2000 | 2010 | 2020 → **5 DXd ADCs & Next Wave**

**Sankyo Co., Ltd.**

**Biologics**

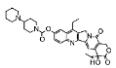
**1990s**
Humanization
Small-scale manufacturing (Anti CD95, anti-DR5)

**2000s**
Establishment of mAb screening / Expansion of mAb portfolio / Establishment of large-scale manufacturing / M&A (Denosumab etc.)

**Daiichi Pharmaceutical Co., Ltd.**

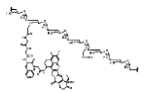
**Topo I inhibitors**

**1980s**
Irinotecan（CPT-11）
Co-development w/ Yakult



**1990s**
Potent Top I inhibitor, Exatecan（Ph3 terminated）

**2000s**
R&D of DDS（DE-310, Ph1 terminated）



**2007 merged**

**Cross-functional activity for ADC research**

**R&D of ENHERTU®**

| 2013 | 2015 | 2019 |
|---|---|---|
| Preclinical studies | Clinical trial initiated | 1st indication approved |

**Our research culture includes…**

- Great history of delivering unique value for patients
- Insatiable passion in the pursuit of new science & technology
- Emphasis creativity and insistence on perfection

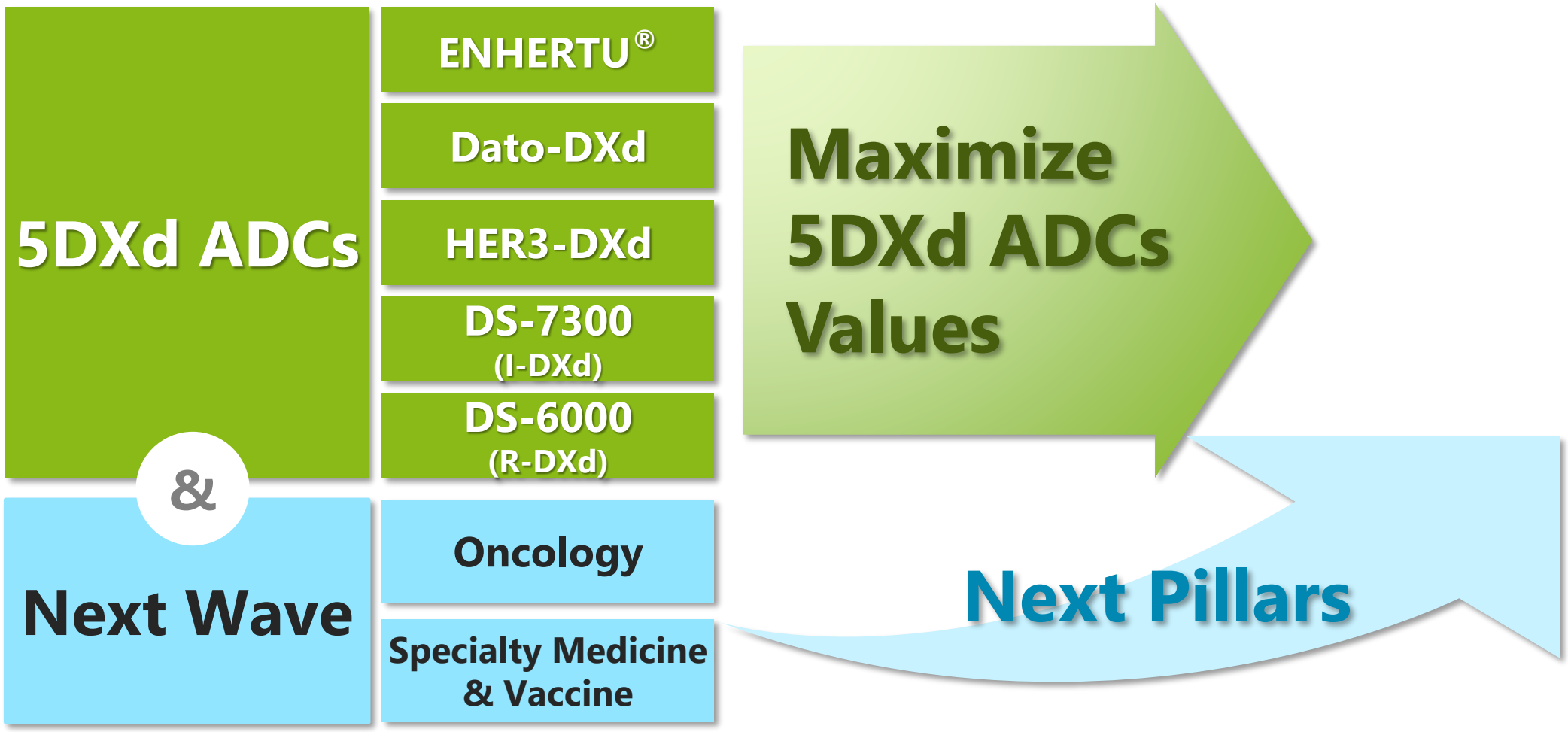
→ **DXd ADCs**
**+"Beyond DXd ADC" drugs**

**Several inventors of ENHERTU® have been involved in other launched products**

- They have long tenure at DS, leveraged their expertise and are now research leaders growing our future talent

ADC: antibody-drug conjugate, DDS: drug delivery system, DS: Daiichi Sankyo, mAb: monoclonal antibody

# 5DXd ADCs and Next Wave



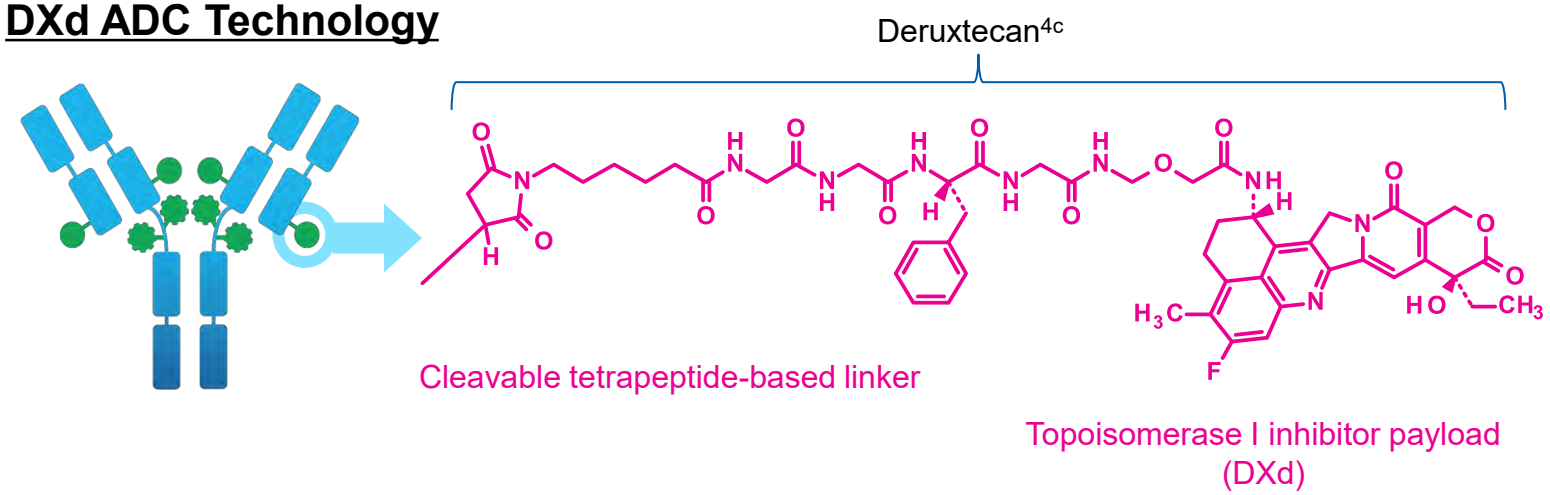

**ENHERTU®**: trastuzumab deruxtecan (International Nonproprietary Name: INN), T-DXd, DS-8201 (HER2-directed ADC), **Dato-DXd**: datopotamab deruxtecan (INN), DS-1062 (TROP2-directed ADC), **HER3-DXd**: patritumab deruxtecan (INN), U3-1402 (HER3-directed ADC), **DS-7300**: ifinatamab deruxtecan, I-DXd (B7-H3-directed ADC), **DS-6000**: raludotatug deruxtecan, R-DXd（CDH6-directed ADC）

# DXd ADCs Were Designed With 7 Key Attributes

## DXd ADCs are composed of 3 parts[1,2]:

- A monoclonal antibody for a tumor-selective antigen
- A tetrapeptide-based cleavable linker that covalently bonds the other 2 components
- A topoisomerase I inhibitor payload (an exatecan derivative, DXd)

## DXd ADC Technology




The **monoclonal antibody** directs the DXd ADC to the tumor cell.

1. Optimized drug-to-antibody ratio[1-4,a]

The **linker** binds the monoclonal antibody to the payload.

2. Plasma stable linker-payload[2,3,5,a]
3. Tumor-selective cleavable linker[2-6,a]

The **payload** induces cell death when delivered to the tumor.

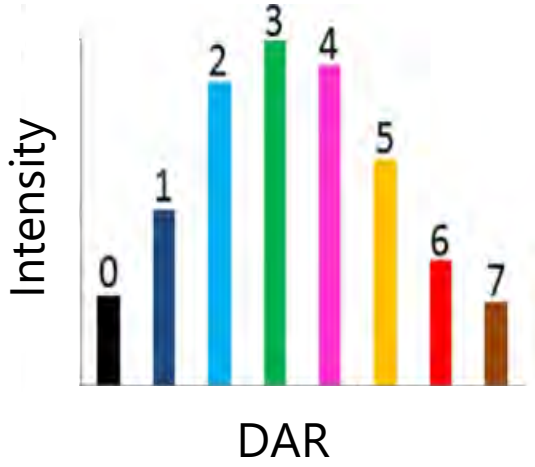
4. Topoisomerase I inhibitor[1-5,a]
5. High potency[2-5,a]
6. Short systemic half-life[2,3,a,c]
7. Bystander antitumor effect[2,7,a]

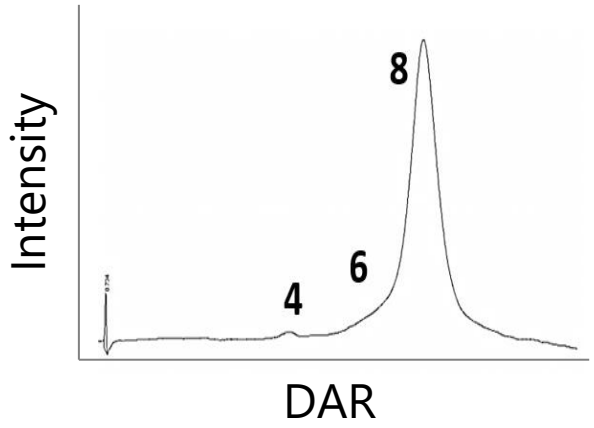
. [a]The clinical relevance of these features is under investigation. [c]Approximately 1.4 hours based on animal data.. **1.** Okajima D, et al. *Mol Cancer Ther*. 2021;20(12):2329-2340. **2.** Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67(3):173-185. **3.** Ogitani Y, et al. *Clin Cancer Res*. 2016;22(20):5097-5108. **4.** Hashimoto Y, et al. *Clin Cancer Res.* 2019;25:7151-7161. **5.** Koganemaru S, et al. *Mol Cancer Ther.* 2019;18:2043-2050. **6.** Haratani K, et al. *J Clin Invest.* 2020;130(1):374-388. **7.** Ogitani Y, et al. *Cancer Sci*. 2016;107(7):1039-1046.

# 1: Optimized drug to antibody ratio

## High drug-to-antibody ratio (DAR)

| | T-DM1 | Enhertu |
|---|---|---|
| **Antibody** | Trastuzumab | Anti-HER2 Ab |
| **Payload** | Tubulin inhibitor (DM1) | DNA Topoisomerase I inhibitor (DXd) |
| **DAR** | 3.5 | 7-8 |



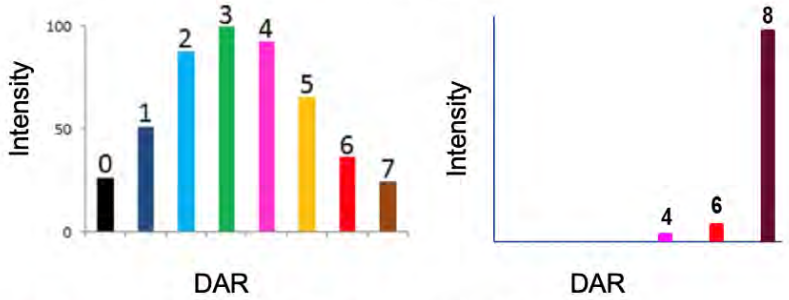

Source: Ogitani-Y *et al.*, Clin. Cancer Res. 2016; 22:5097-5108, Marcoux-J *et al.*, Protein Science 2015; 24:1210-1223

# 1: Optimized drug to antibody ratio

## DAR8: DS-8201, U3-1402, DS-6000

High Drug Antibody Ratio
Compared to T-DM1

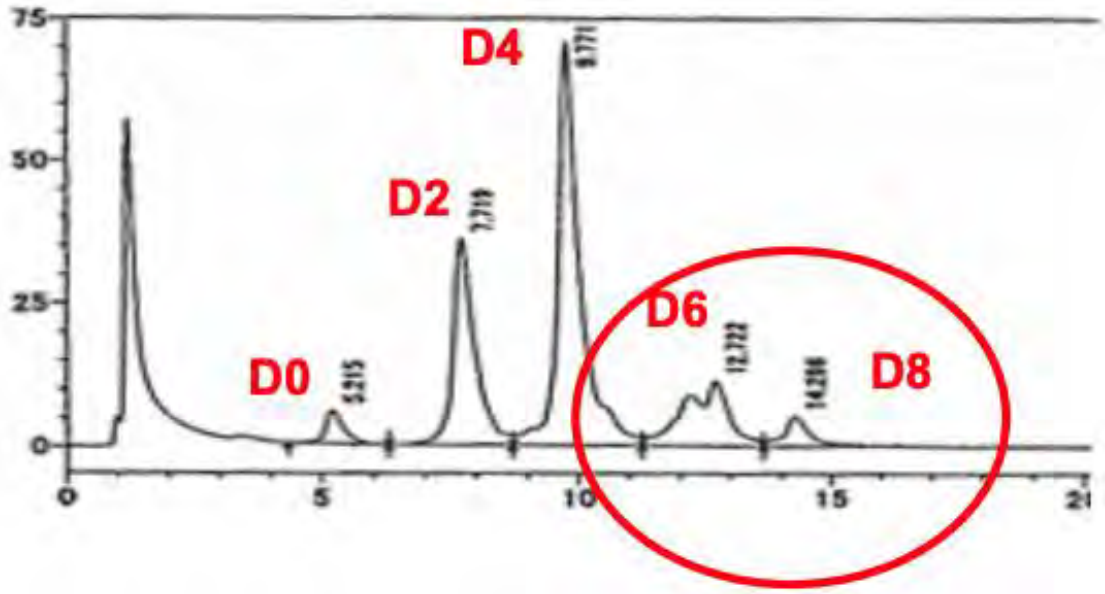
| | T-DM1 | DS-8201 |
|---|---|---|
| **Antibody** | Trastuzumab | Anti-HER2 Ab |
| **Payload** | Tubulin inhibitor (DM1) | DNA Topoisomerase I inhibitor (DXd) |
| **DAR** | 3.5 | 7-8 |




Source: Ogitani Y *et al.*, Clin. Cancer Res. 2016; 22:5097-5108, Marcoux J *et al.*, Protein Science 2015; 24:1210-1223

## DAR4: DS-1062, DS-7300

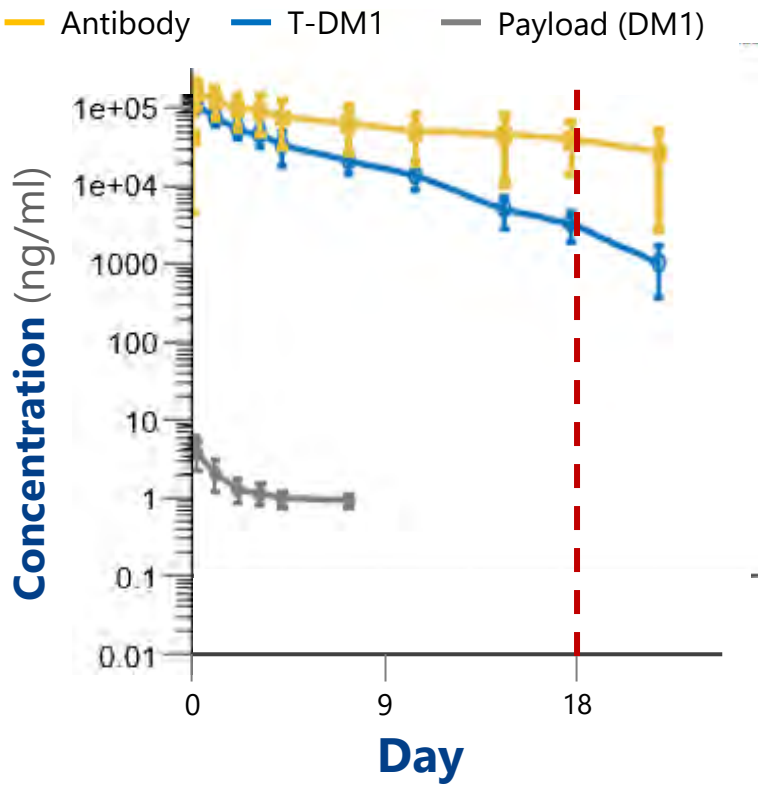
D4-enriched DAR4



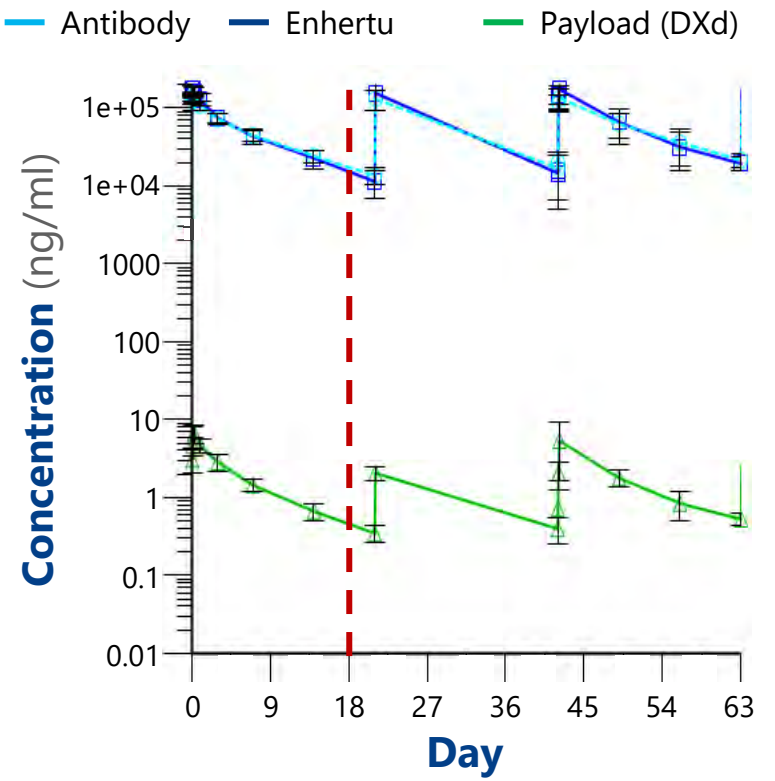
# 2: Plasma stable linker-payload

## Pharmacokinetics profile

### T-DM1, 3.6 mg/kg (Phase 1)




### Enhertu, 6.4 mg/kg (Phase 1)



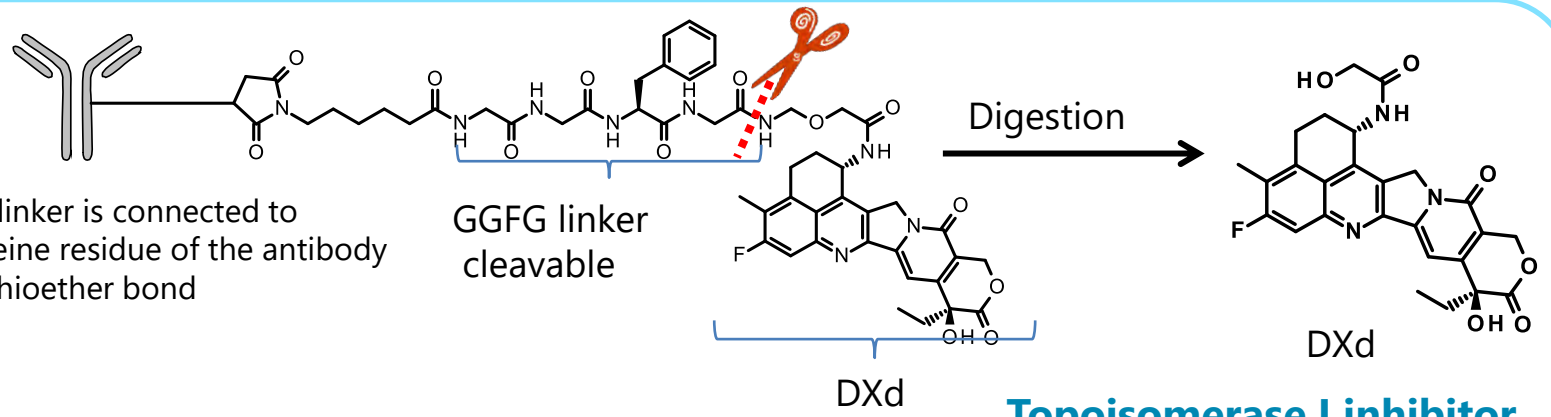

**Enhertu: High linker stability and low free payload concentration**

Source: Krop-I et al., J. Clin. Oncol. 2010; 28:2698-2704, Tamura-K *et al.*, abstract 4585 (LBA17), ESMO 2016

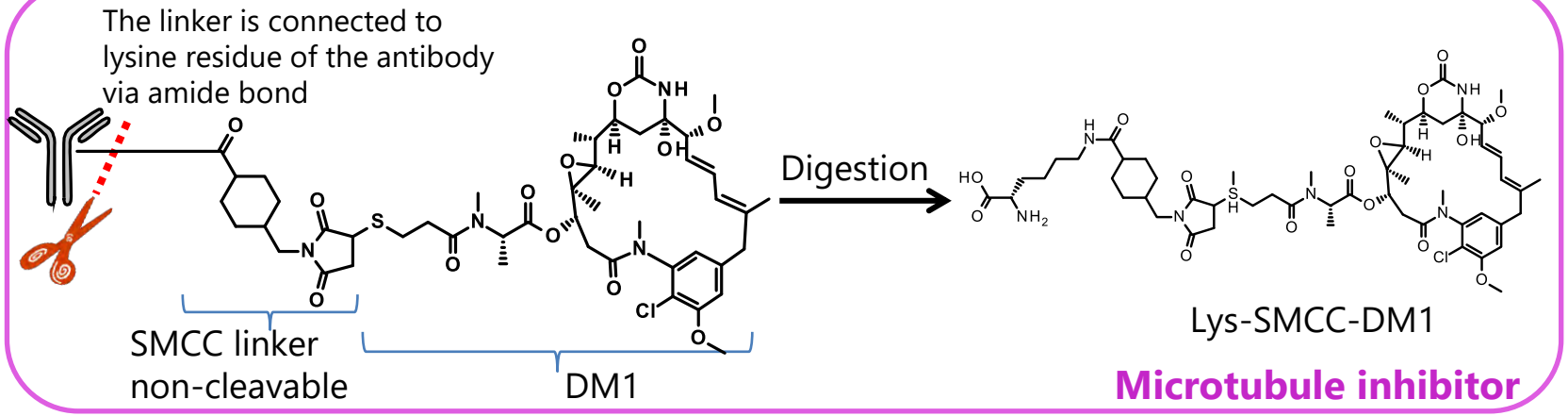
# 3: Tumor-selective cleavable linker

**Enhertu**

Cleaved by cathepsin highly expressed on tumors




**Topoisomerase I inhibitor**




**Microtubule inhibitor**

**T-DM1**

Cleaved by protease in lysosome

# 4: Topoisomerase I inhibitor

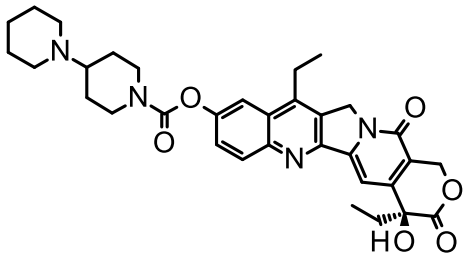
| | T-DM1 | Enhertu | SYD-985 | XMT-1522 | MEDI4276 |
|---|---|---|---|---|---|
| Company | Genentech | Daiichi Sankyo | Synthon | Mersana | Medimmune |
| Payload | DM1 | DXd | Duocarmicine | AF-HPA | Tubulysin |
| MOA | Microtubule inhibitor | **Topoisomerase I inhibitor** | DNA alkylator | Microtubule inhibitor | Microtubule inhibitor |
| Linker | Undissociated | Dissociated | Dissociated | Dissociated | Dissociated |
| Attachment site | Lysine residue | Cysteine residue | Cysteine residue | Cysteine residue | Engineered cysteine |
| Drug-to-antibody ratio （average） | 3.5 | 7-8 | 2 | 12-15 | 4 |
| Human Dose (Ph1） | 3.6mg/kg* | 6.4mg/kg | 1.2mg/kg** | 0.765mg/kg*** | NA |

*Yamamoto-H, Jpn J Clin Oncol. 2015 Jan;45(1):12-8
**Aftimos-PG, SABCS, 2016
***Buris-HA, Mersana homepage TPS2606

# 5: High potency

**From an extensive in-house compound library, candidate payloads were selected and screened, leading to the discovery of DXd**

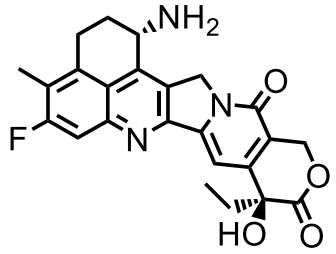
## Irinotecan (CPT-11)



Prodrug of SN-38

**Approved for refractory tumors in 1994.**

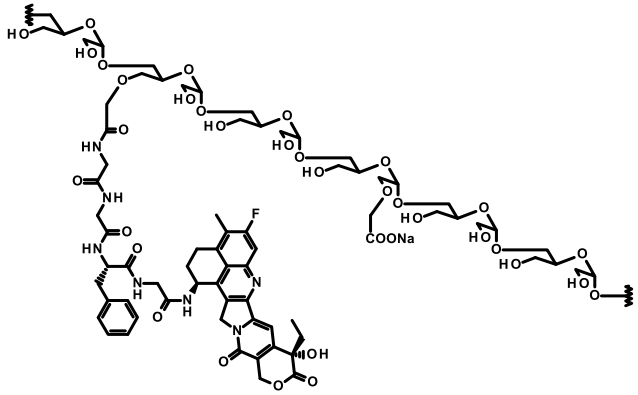
## Exatecan (DX-8951)



10-fold more potent than SN-38

**Discontinued (Ph3 study)**

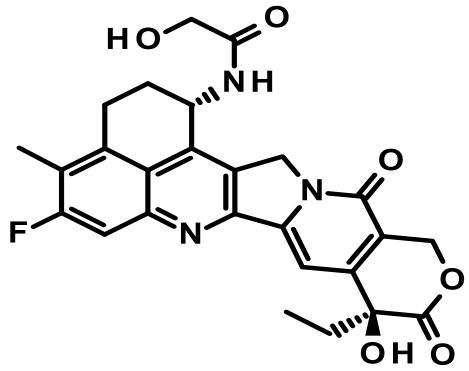
## DE-310



Polymer-conjugate of exatecan

**Discontinued (Ph1 study)**

## DXd (Exatecan derivative)



Novel topoisomerase I inhibitor

DXd has 10 times more potent effect than irinotecan

Source: *R De Jager et al., Ann N Y Acad Sci. 922:260-273 (2000), Soepenberg O et al., Clin Cancer Res 11:703-711 (2005)*

# 6: Short systemic half-life

High concentration of free payload in blood is one of the reason of adverse events

Released payload is designed to be excreted immediately which results in lowering occurrence of adverse events

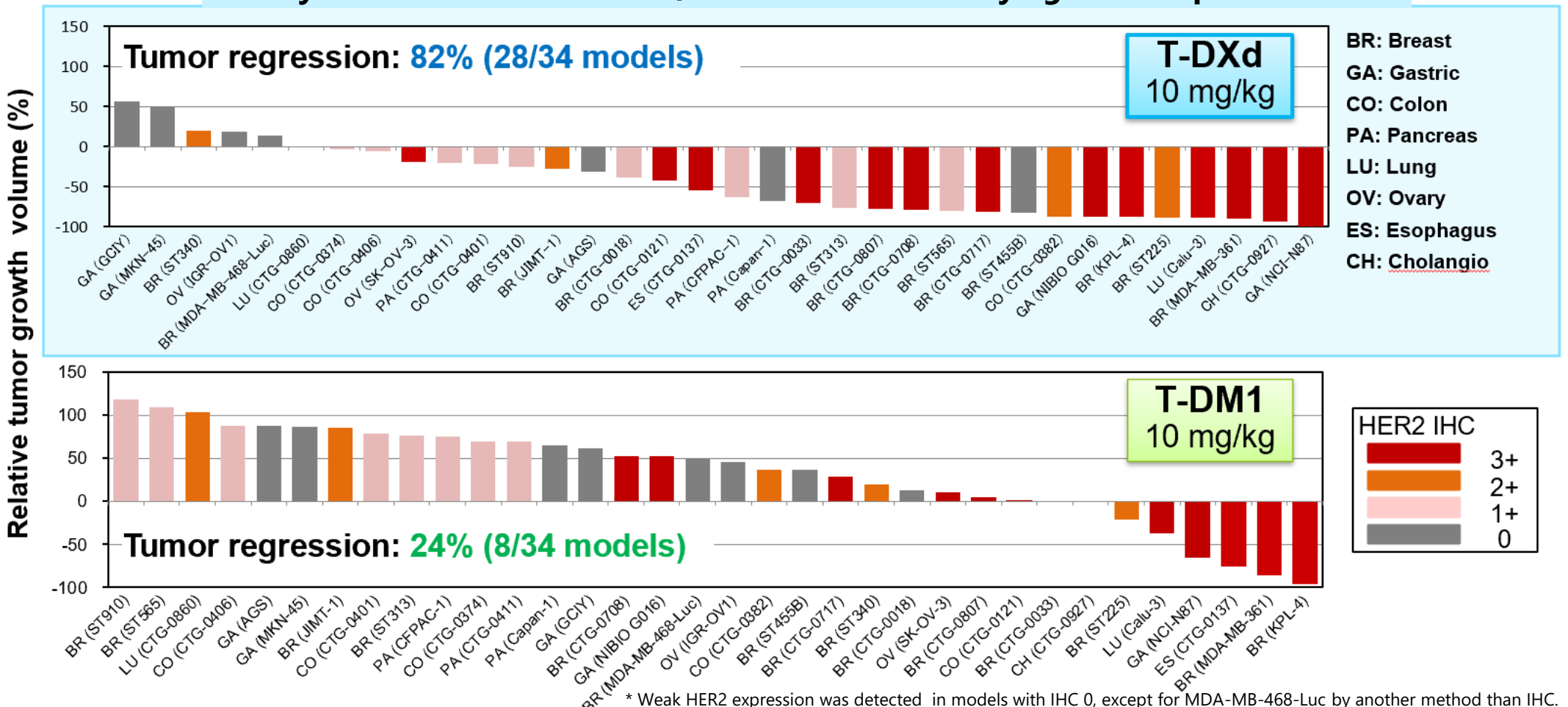
| Payload | $T_{1/2}$ in Rat (hour) |
|---|---|
| DXd* (payload of DXd-ADC) | 0.9 |
| DM1** (payload of T-DM1) | 3.3-10 |
| MMAE*** (payload of Adcetris) | 5.7-11 |

** In-house report*
*** KADCYLA BLA*
**** ADCETRIS BLA*

# 7: Bystander antitumor effect

## Thorough drug screening utilizing a diverse range of animal models was conducted to confirm the potential of the drugs

### Efficacy of ENHERTU® in 34 CDX/PDX models with varying HER2 expression level

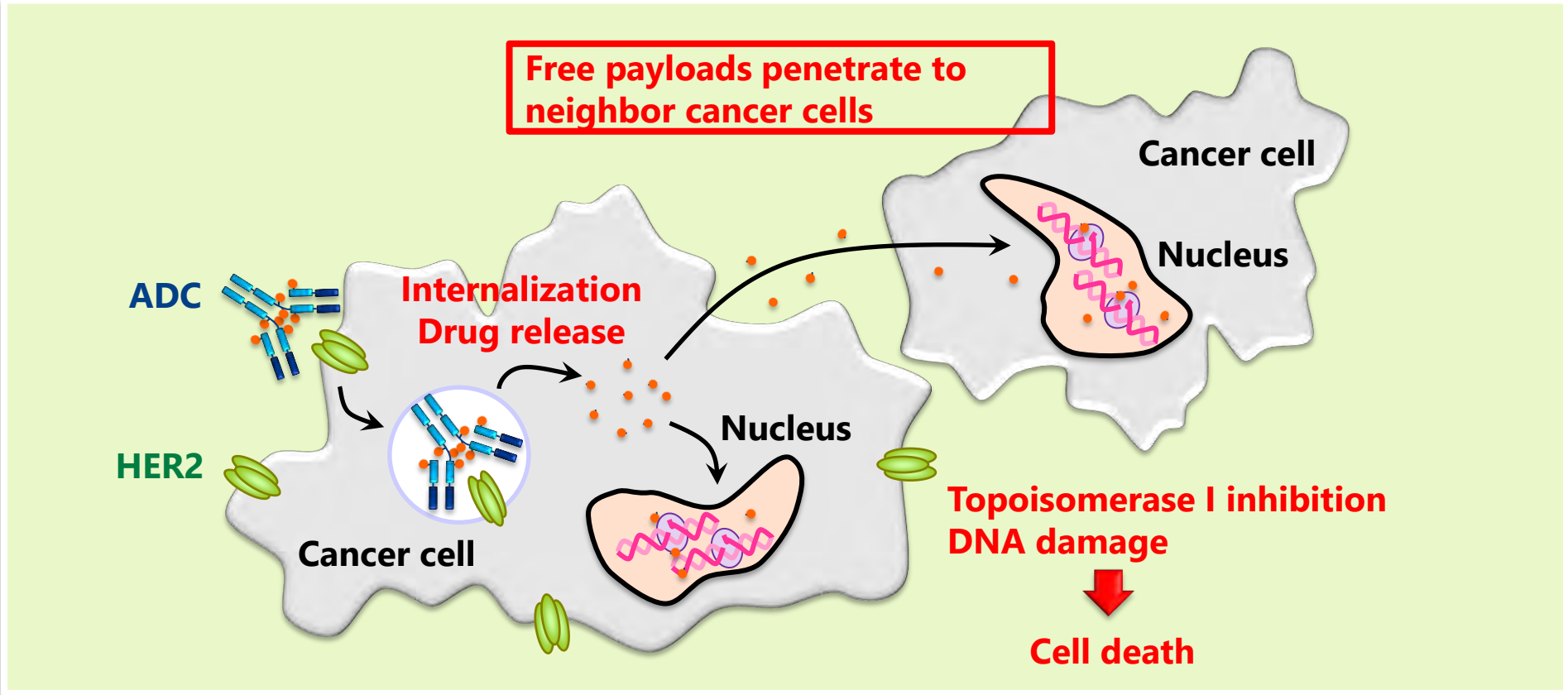



Source: *Yuki Abe et al., Bioconjugate 2016*

* Weak HER2 expression was detected in models with IHC 0, except for MDA-MB-468-Luc by another method than IHC.
CDX: cell line derived xenograft, IHC: immunohistochemistry, PDX: patient derived xenograft, T-DXd, trastuzumab deruxtecan (ENHERTU®)

# 7: Bystander antitumor effect

Bystander effect of ADC:
- ◆ Released payloads in cancer cells penetrate the cell membrane and show activity on neighboring dividing cancer cells.
- ◆ Through this effect, activity against target antigen-negative cancer cells, in other words, activity against tumors with antigen heterogeneity is observed



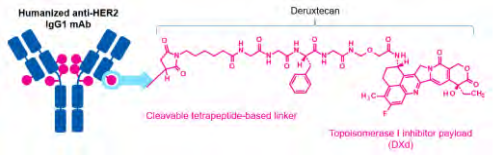
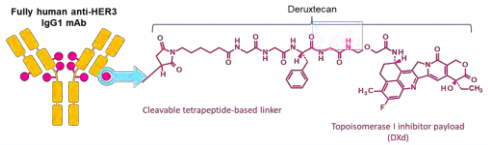
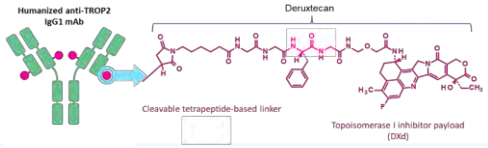
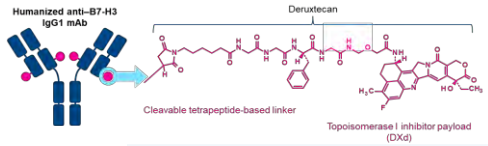
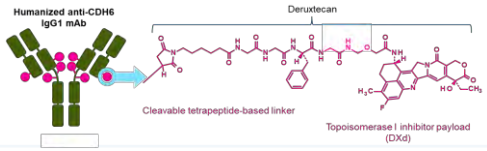
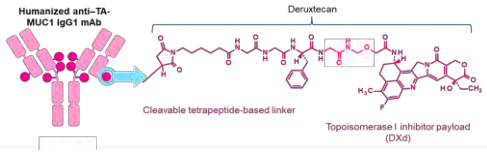
# DXd ADC Franchise

| | Project (Target) | Target indications | Discovery | Pre-Clinical | Ph1 | Ph2 | Ph3 | Filed | Launched |
|---|---|---|---|---|---|---|---|---|---|
| 1 | ENHERTU® (HER2) | Breast, Gastric, NSCLC, CRC, etc. | | | | | | | |
| 2 | DATROWAY® (TROP2) | NSCLC, Breast, etc. | | | | | | | |
| 3 | HER3-DXd (HER3) | NSCLC, Breast | | | | | | | |
| 4 | I-DXd (B7-H3) | ESCC, CRPC, sq-NSCLC, SCLC, etc. | | | | | | | |
| 5 | R-DXd (CDH6) | Renal, Ovarian | | | | | | | |
| 6 | DS-3939 (TA-MUC1) | Solid tumors | | | | | | | |
| 7 | DS-XXXX (Undisclosed) | Undisclosed | | | | | | | |

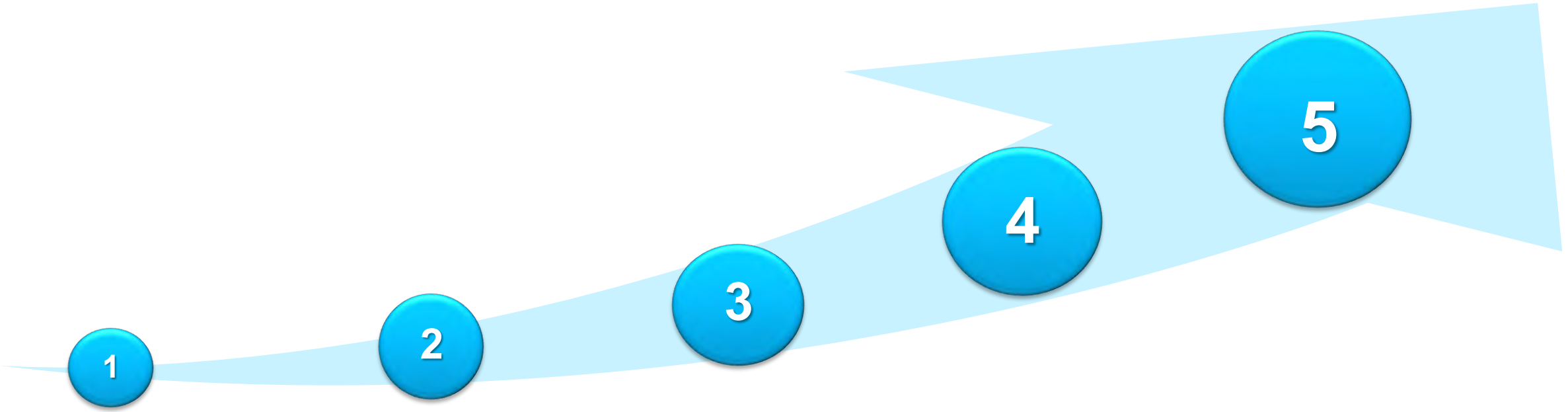
Timeline indicates the most advanced stage of each project

CRC: colorectal cancer, CRPC: castration-resistant prostate cancer, ESCC: esophageal squamous cell carcinoma, GIST: gastrointestinal stromal tumor, NSCLC: non small cell lung cancer,. SCLC: small cell lung cancer

# Daiichi Sankyo DXd ADC Overview

| ADC | Structure | Target | DAR | Major Areas of Study |
|---|---|---|---|---|
| **T-DXd** |  | HER2 | ≈8 | Breast cancer<br>Gastric cancer<br>NSCLC<br>CRC<br>Gynecologic cancer<br>HER2+ cancers (tumor agnostic) |
| **HER3-DXd** |  | HER3 | ≈8 | Breast cancer<br>NSCLC |
| **Dato-DXd** |  | TROP2 | ≈4 | Breast cancer<br>NSCLC |
| **I-DXd (DS-7300)** |  | B7-H3 | ≈4 | ES-SCLC<br>ESCC<br>mCRPC<br>Sq NSCLC |
| **R-DXd (DS-6000)** |  | CDH6 | ≈8 | Ovarian cancer |
| **DS-3939** |  | TA-MUC1 | ≈8 | Solid tumors |

# Sustainable ADC Development




## DXd ADC

**ENHERTU®**
**Dato-DXd**
**HER3-DXd**
**DS-7300 (I-DXd)**
**DS-6000 (R-DXd)**
**DS-3939**
**DS-XXXX**

## Next Generation ADC

- **DS-9606**
- Multiple projects in IND enabling & discovery stage

## New Concept ADC 1

Multiple projects in IND enabling stage

## New Concept ADC 2

Multiple projects in discovery stage

## New Concept ADC 3

Multiple projects in discovery stage

cept 4

cept 5

ADC: antibody-drug conjugate, IND: investigational new drug application

# Combinations to expand DXd ADCs' opportunity

Daiichi-Sankyo

**DXd ADC** +

**Combinations in on-going clinical trials** (examples, not exhaustive)

| | | Ph1 or Ph2 | Ph3 |
|---|---|---|---|
| **Checkpoint Inhibitor** | pembrolizumab | DS8201-A-U106 | TROPION-Lung02 |
| | | TROPION-Lung08 | TROPION-Lung07 |
| | durvalumab | DESTINY-Breast07 | DESTINY-Breast08 |
| | | TROPION-Breast03 | BEGONIA |
| | | DESTINY-Lung03 | TROPION-Lung04 |
| | | | HUDSON |
| | AZD2936 or MEDI5752 | TROPION-Lung04 | |
| **Targeted Therapy** | pertuzumab | DESTINY-Breast09 | |
| | tucatinib | DESTINY-Breast07 | |
| | capivasertib | DESTINY-Breast08 | |
| | osimertinib | ORCHARD | U31402-A-U103 |

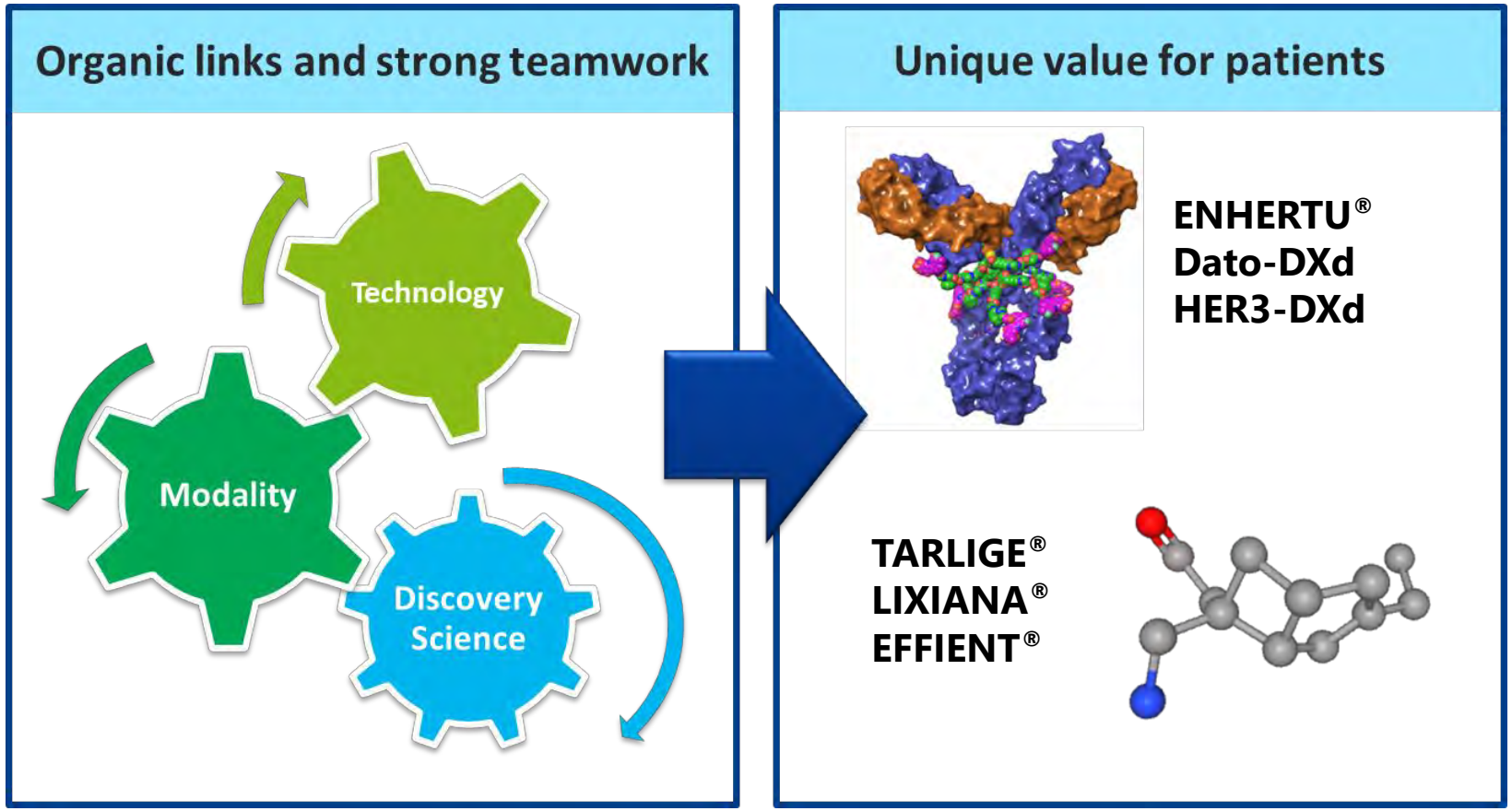
+ **Internal Assets**

- **ENHERTU® + EZHARMIA® (EZH1/2 inhibitor) in HER2 low mBC** (Ongoing in collaboration with MDACC)
- **ENHERTU® + DS-1103 (anti-SIRPα antibody)** (FSD in H1 FY2023)
- More potential combo partners in preclinical pipeline

FSD, first subject dosed; mBC, metastatic breast cancer; MDACC, MD Anderson Cancer Center

Key success factors of Daiichi Sankyo drug discovery:

# Science & Technology through Craftspersonship




## At DS, we

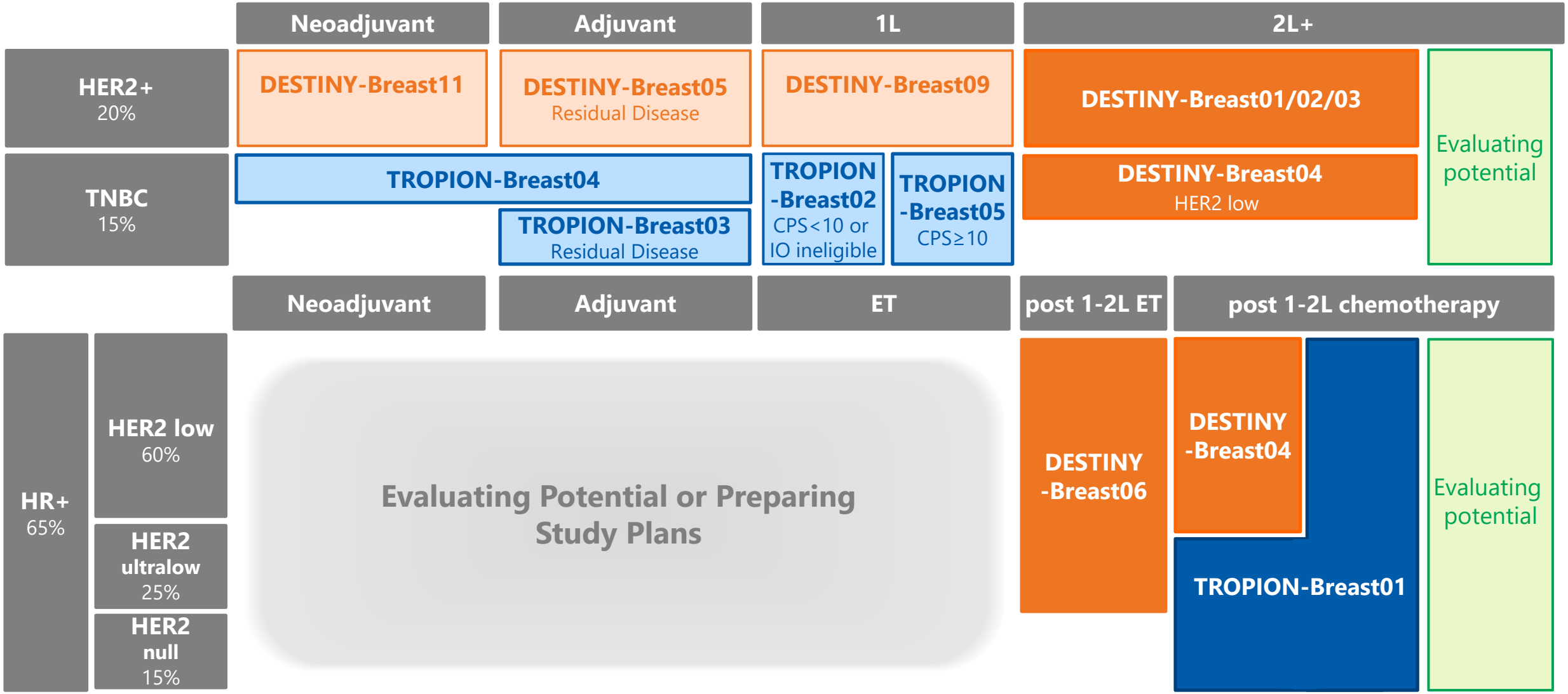
- Have an insatiable passion to pursue new science & technology
- Apply exceptional craftspersonship aiming for perfection
- Deliver unique value for patients

5DXd ADCs

# Establish and Expand DXd ADCs to Address the Broader Spectrum of Breast Cancer

As of Feb 2025

Daiichi-Sankyo




Launched | On-going | ENHERTU® | DATROWAY® | HER3-DXd, 1103, Valemetostat

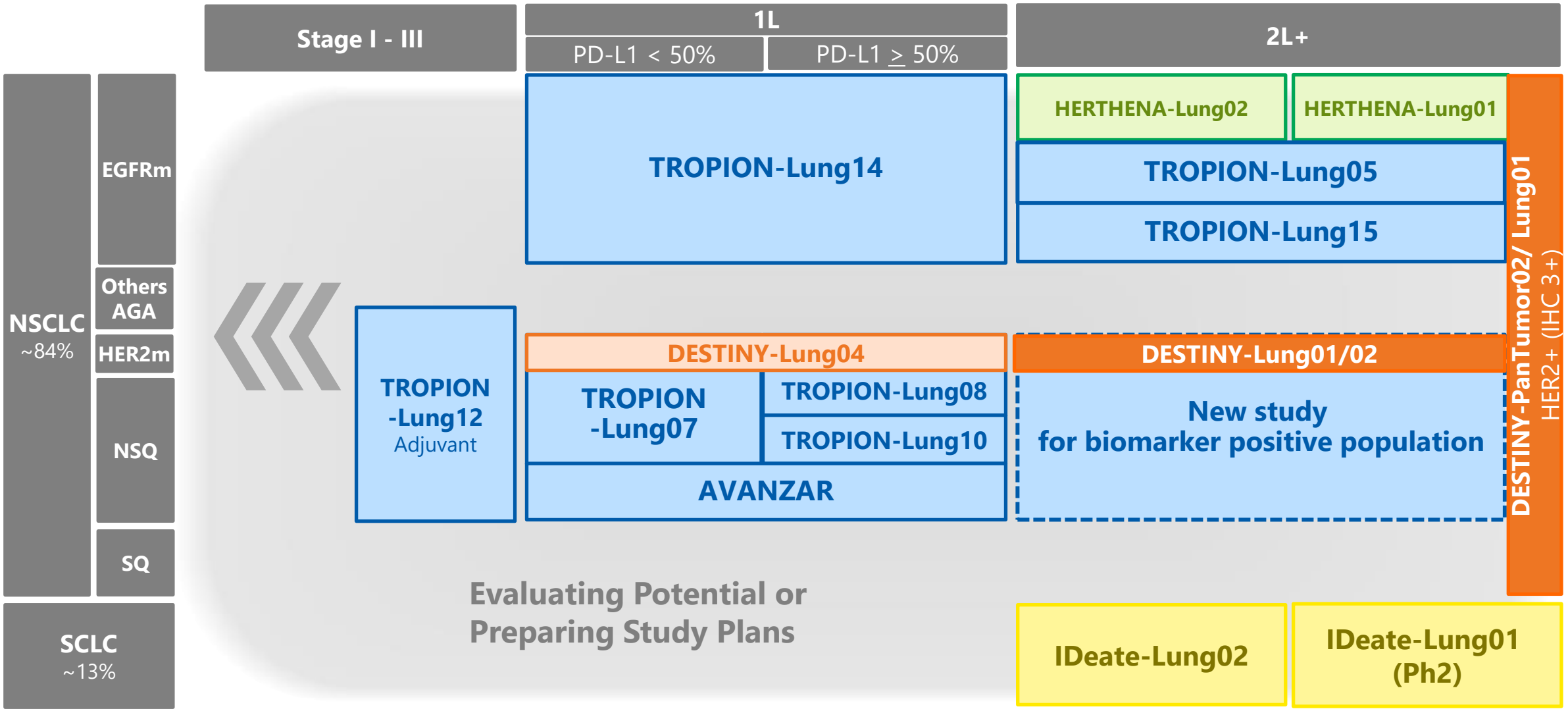
- Pivotal studies only, not exhaustive
- Box size does not reflect the patient population
- Box indicates current potential target segment

CPS: combined positive score; ET: endocrine therapy; HR: hormone receptor; IHC: immunohistochemistry, IO: immune oncology, TNBC: triple-negative breast cancer

5DXd ADCs

# Establish and Expand DXd ADCs to Address the Broad Spectrum of Lung Cancer

As of Feb 2025




Launched | On-going | Planning | ENHERTU® | DATROWAY® | HER3-DXd | I-DXd

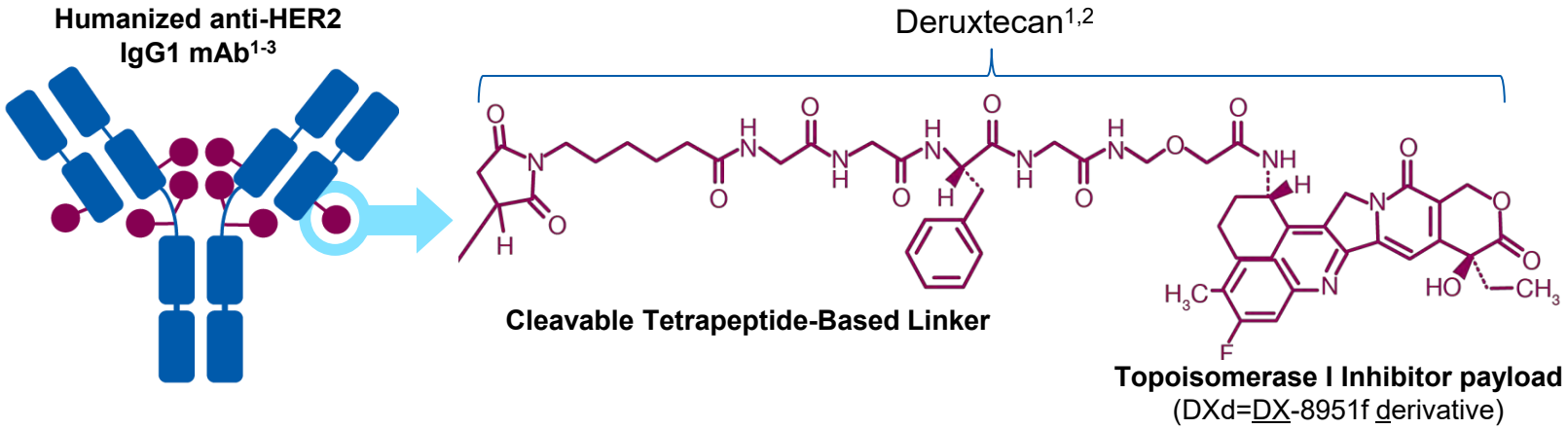
- Pivotal studies and major Ph2 only, not exhaustive
- Box size does not reflect the patient population
- Box indicates current potential target segment

AGA: actionable genomic alteration, IHC: immunohistochemistry, NSQ: non- squamous, NSCLC: non-small cell lung cancer, SCLC: small cell lung cancer, SQ: squamous

# Enhertu

## Enhertu is an ADC composed of 3 components[1,2]:

- A humanized anti-HER2 IgG1 mAb with the same amino acid sequence as trastuzumab, covalently linked to:
- A topoisomerase I inhibitor payload, an exatecan derivative, via
- A tetrapeptide-based cleavable linker




[a]The clinical relevance of these features is under investigation.

**1.** Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67(3):173-185. **2.** Ogitani Y, et al. *Clin Cancer Res*. 2016;22(20):5097-5108. **3.** Trail PA, et al. *Pharmacol Ther.* 2018;181:126-142. **4.** Ogitani Y, et al. *Cancer Sci*. 2016;107(7):1039-1046.

# HER2 status epidemiology in Breast Cancer


*Lower confidence due to limited data

1. All prevalence estimated from: THYME AZD8931 study data (not published); Owens et al, Clinical Breast Cancer 2004; Lambein et al; American Journal of Clinical Pathology 2013 and Decision Resources , inclusive of US, EU5, and Japan (Breast Cancer, Last updated, December 2017, CAncerMPACT (2017)); AZ unpublished data including real world image analysis dataset (n=3000); Schettini et al, ESMO BC 2020; REGISTEM registry SABCS 2020; Mattos Brazil, SABCS 2020


145

# DESTINY-Breast04: First Randomized Phase 3 Study of T-DXd for HER2-low mBC

DESTINY-Breast04

Daiichi-Sankyo

## An open-label, multicenter study (NCT03734029)

**Patients[a]**
- HER2-low (IHC 1+ vs IHC 2+/ISH−), unresectable, and/or mBC treated with 1-2 prior lines of chemotherapy in the metastatic setting
- HR+ disease considered endocrine refractory

R 2:1

**T-DXd**
5.4 mg/kg Q3W
(n = 373)

HR+ ≈ 480
HR− ≈ 60

**TPC**
Capecitabine, eribulin, gemcitabine, paclitaxel, nab-paclitaxel[c]
(n = 184)

**Primary endpoint**
- PFS by BICR (HR+)

**Key secondary endpoints[b]**
- PFS by BICR (all patients)
- OS (HR+ and all patients)

**Stratification factors**
- Centrally assessed HER2 status[d] (IHC 1+ vs IHC 2+/ISH−)
- 1 versus 2 prior lines of chemotherapy
- HR+ (with vs without prior treatment with CDK4/6 inhibitor) versus HR−

ASCO/CAP, American Society of Clinical Oncology/College of American Pathologists; BICR, blinded independent central review; CDK, cyclin-dependent kinase; DOR, duration of response; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; mBC, metastatic breast cancer; OS, overall survival; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

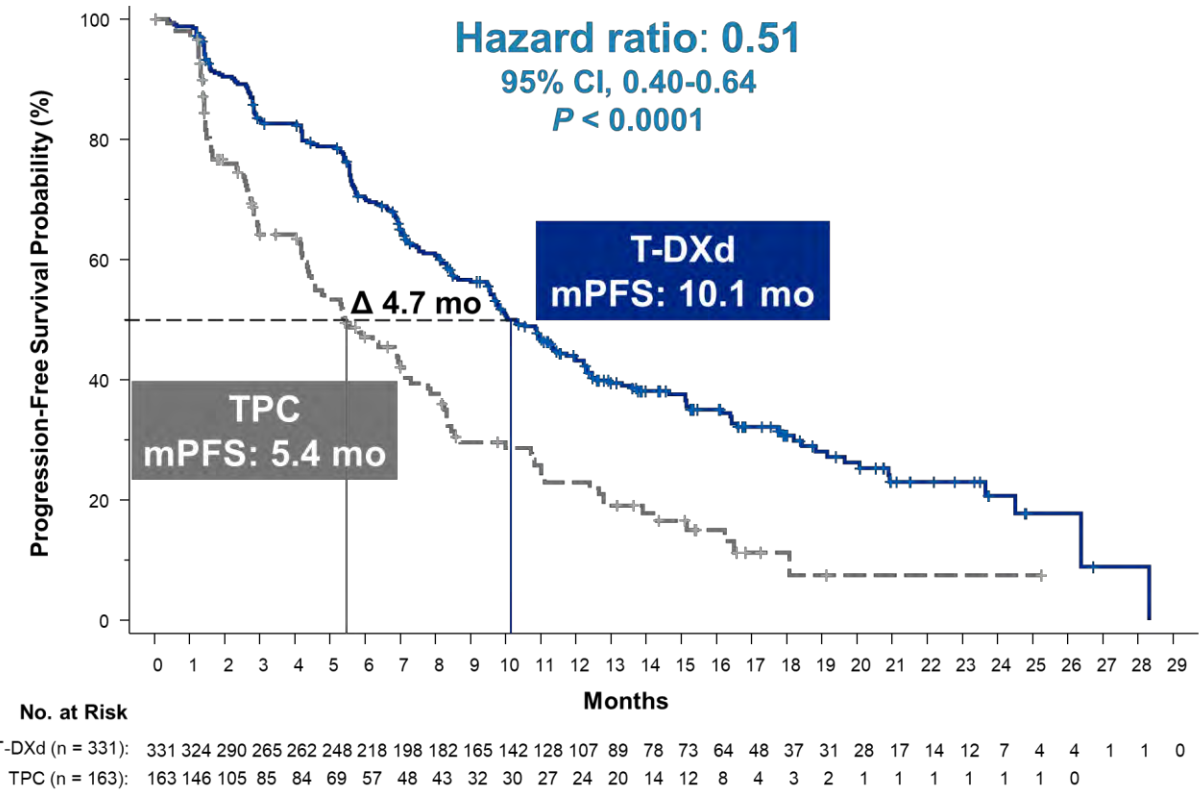
[a]If patients had HR+ mBC, prior endocrine therapy was required. [b]Other secondary endpoints included ORR (BICR and investigator), DOR (BICR), PFS (investigator), and safety; efficacy in the HR− cohort was an exploratory endpoint. [c]TPC was administered accordingly to the label. [d]Performed on adequate archived or recent tumor biopsy per ASCO/CAP guidelines using the VENTANA HER2/neu (4B5) investigational use only [IUO] Assay system.

# PFS in HR+ and All Patients

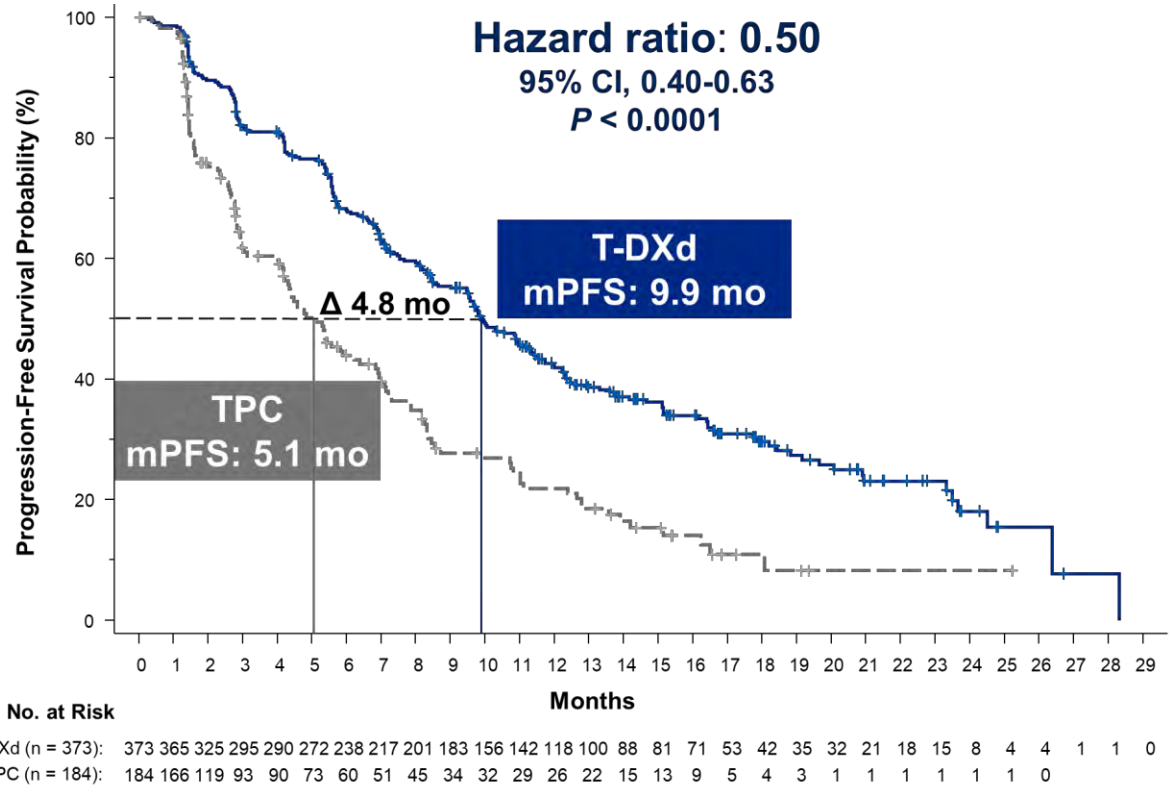




## Hormone receptor–positive




## All patients




**PFS by blinded independent central review.**

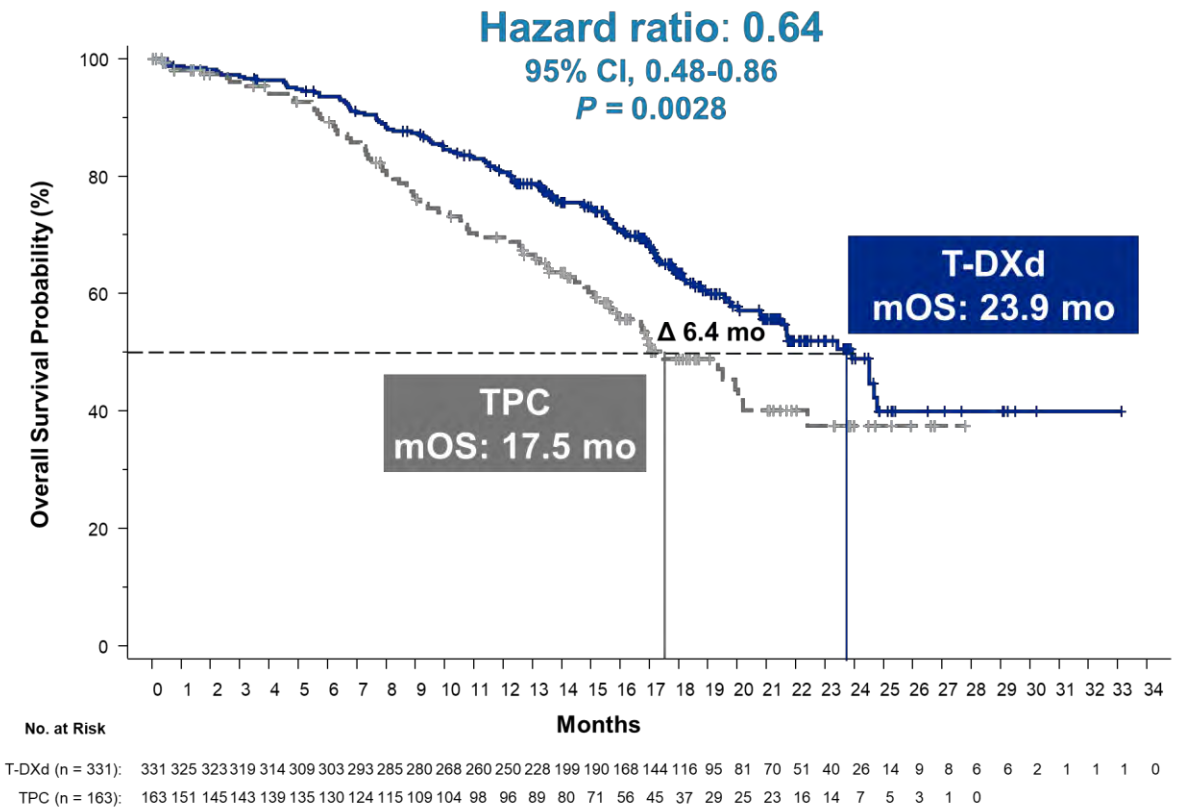
HR, hormone receptor; mPFS, median progression-free survival; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

# OS in HR+ and All Patients

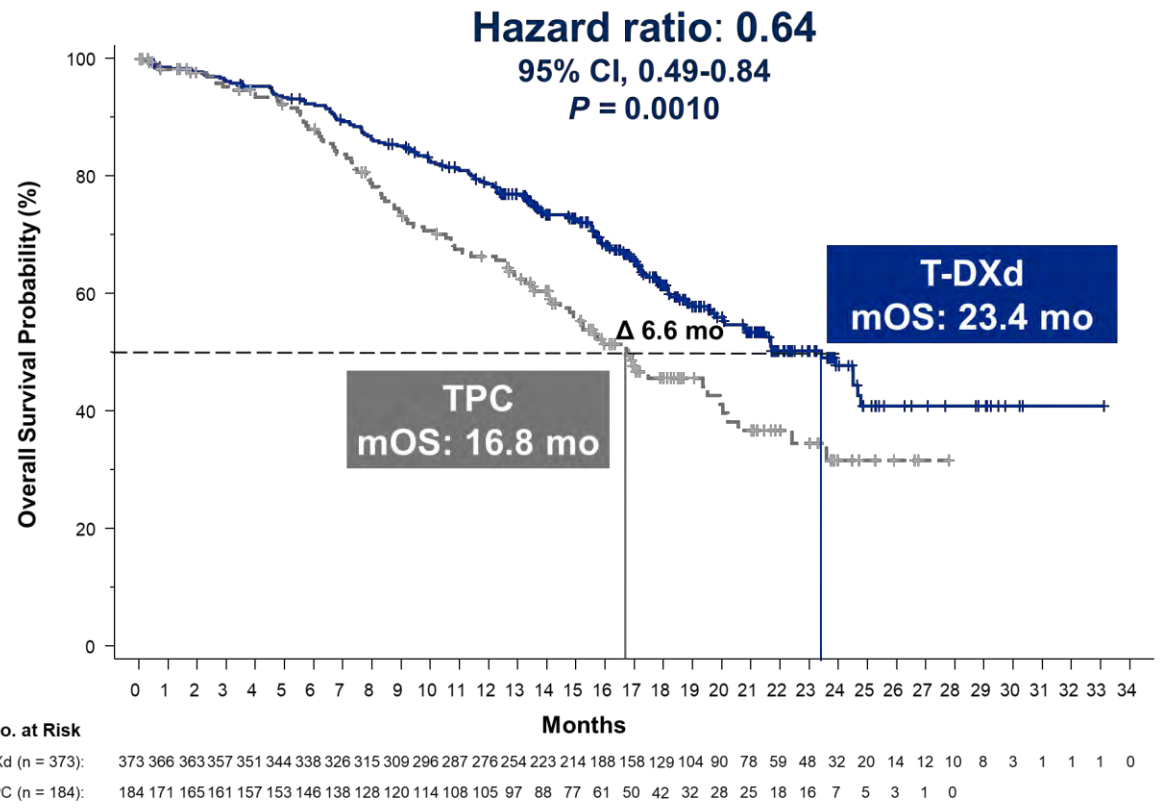




## Hormone receptor–positive




## All patients




HR, hormone receptor; mOS, median overall survival; OS, overall survival; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

# Adverse Events of Special Interest

## Adjudicated as drug-related ILD/pneumonitis[a]

| n (%) | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 | Any Grade |
|---|---|---|---|---|---|---|
| T-DXd (n = 371) | 13 (3.5) | 24 (6.5) | 5 (1.3) | 0 | 3 (0.8) | 45 (12.1) |
| TPC (n = 172) | 1 (0.6) | 0 | 0 | 0 | 0 | 1 (0.6) |

## Left ventricular dysfunction[b]

| n (%) | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 | Any Grade |
|---|---|---|---|---|---|---|
| **Ejection fraction decreased** | | | | | | |
| T-DXd (n = 371) | 1 (0.3) | 14 (3.8) | 1 (0.3) | 0 | 0 | 16 (4.3) |
| TPC (n = 172) | 0 | 0 | 0 | 0 | 0 | 0 |
| **Cardiac failure[c]** | | | | | | |
| T-DXd (n = 371) | 0 | 1 (0.3) | 1 (0.3) | 0 | 0 | 2 (0.5) |
| TPC (n = 172) | 0 | 0 | 0 | 0 | 0 | 0 |

ILD, interstitial lung disease; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.
[a]Median time to onset of ILD/pneumonitis for patients with T-DXd was 129.0 days (range, 26-710). [b]Left ventricular dysfunction was reported in a total of 17 (4.6%) patients in the T-DXd arm. One patient initially experienced ejection fraction decrease, then later developed cardiac failure. [c]Both patients with cardiac failure were reported to have recovered.

# Study design

DESTINY-Breast06

Daiichi-Sankyo

## DESTINY-Breast06: a Phase 3, randomized, multicenter, open-label study (NCT04494425)

### PATIENT POPULATION

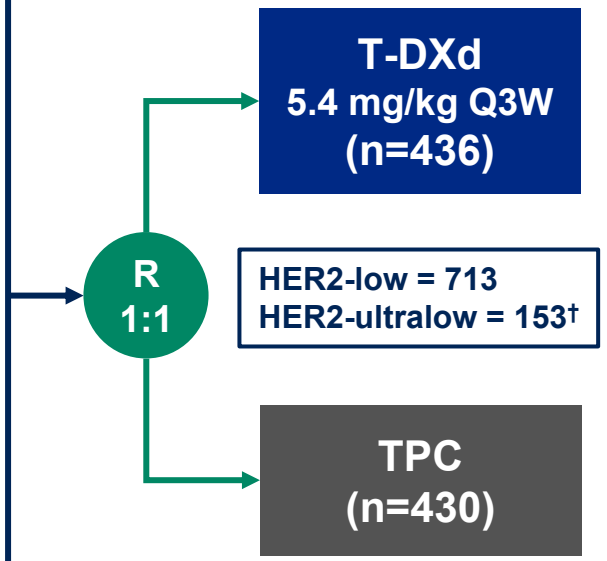
- HR+ mBC
- HER2-low (IHC 1+ or IHC 2+/ISH−) or HER2-ultralow (IHC 0 with membrane staining)*
- **Chemotherapy naïve in the mBC setting**

**Prior lines of therapy**

- ≥2 lines of ET ± targeted therapy for mBC
  **OR**
- 1 line for mBC **AND**
  - Progression ≤6 months of starting first-line ET + CDK4/6i
    **OR**
  - Recurrence ≤24 months of starting adjuvant ET

**Stratification factors**

- Prior CDK4/6i use (yes vs no)
- HER2 expression (IHC 1+ vs IHC 2+/ISH− vs IHC 0 with membrane staining)
- Prior taxane in the non-metastatic setting (yes vs no)




### ENDPOINTS

**Primary**

- PFS (BICR) in HER2-low

**Key secondary**

- PFS (BICR) in ITT (HER2-low + ultralow)
- OS in HER2-low
- OS in ITT (HER2-low + ultralow)

**Other secondary**

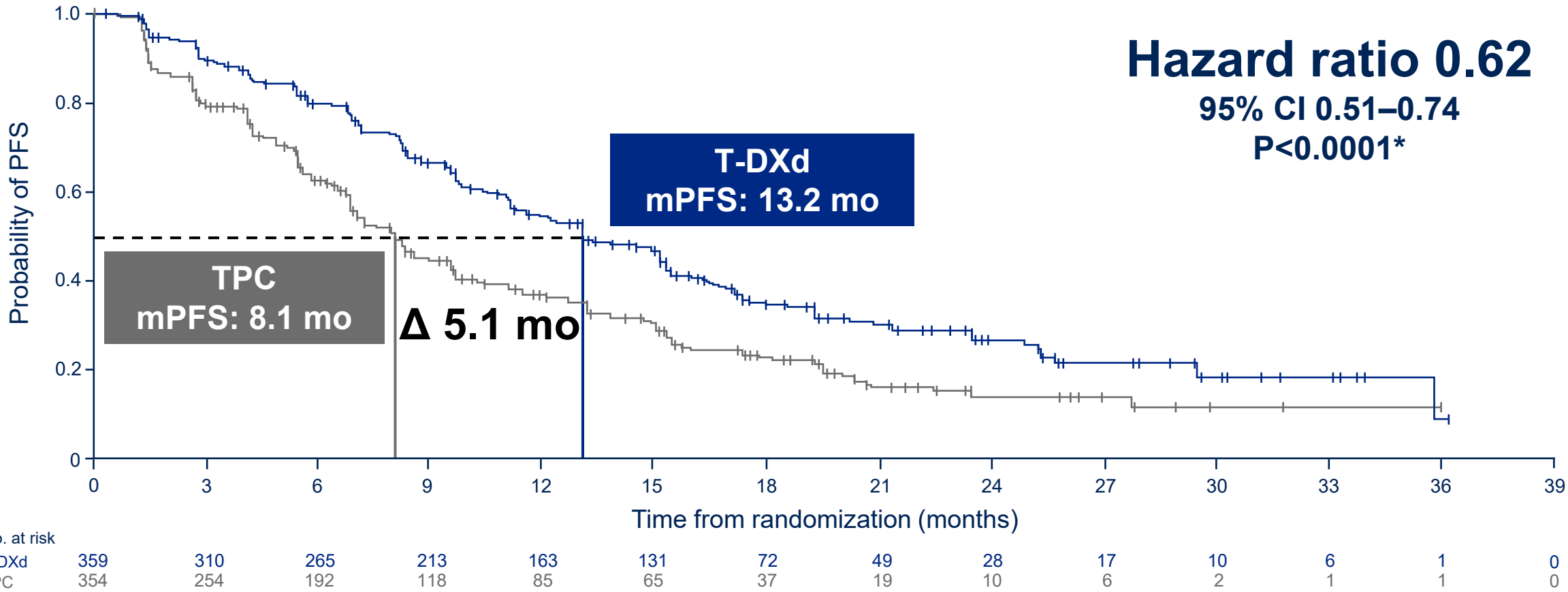
- PFS (INV) in HER2-low
- ORR (BICR/INV) and DOR (BICR/INV) in HER2-low and ITT (HER2-low + ultralow)
- Safety and tolerability
- Patient-reported outcomes‡

*Study enrollment was based on central HER2 testing. HER2 status was determined based on the most recent evaluable HER2 IHC sample prior to randomization. HER2-ultralow was defined as faint, partial membrane staining in ≤10% of tumor cells (also known as IHC >0<1+); †HER2-ultralow status as determined per IRT data (note: efficacy analyses in the HER2-ultralow subgroup were based on n=152 as determined per central laboratory testing data); ‡to be presented separately
BICR, blinded independent central review; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DOR, duration of response; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR+, hormone receptor–positive; IHC, immunohistochemistry; INV, investigator assessed; IRT, interactive response technology; ISH, in situ hybridization; ITT, intent-to-treat; mBC, metastatic breast cancer; ORR, objective response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice
NCT04494425. Updated. April 12, 2024. Available from: https://clinicaltrials.gov/study/NCT04494425 (Accessed May 13, 2024)

# PFS (BICR) in HER2-low: primary endpoint

DESTINY-Breast06

Daiichi-Sankyo




**T-DXd demonstrated a statistically significant and clinically meaningful improvement in PFS compared with standard-of-care chemotherapy in HER2-low**

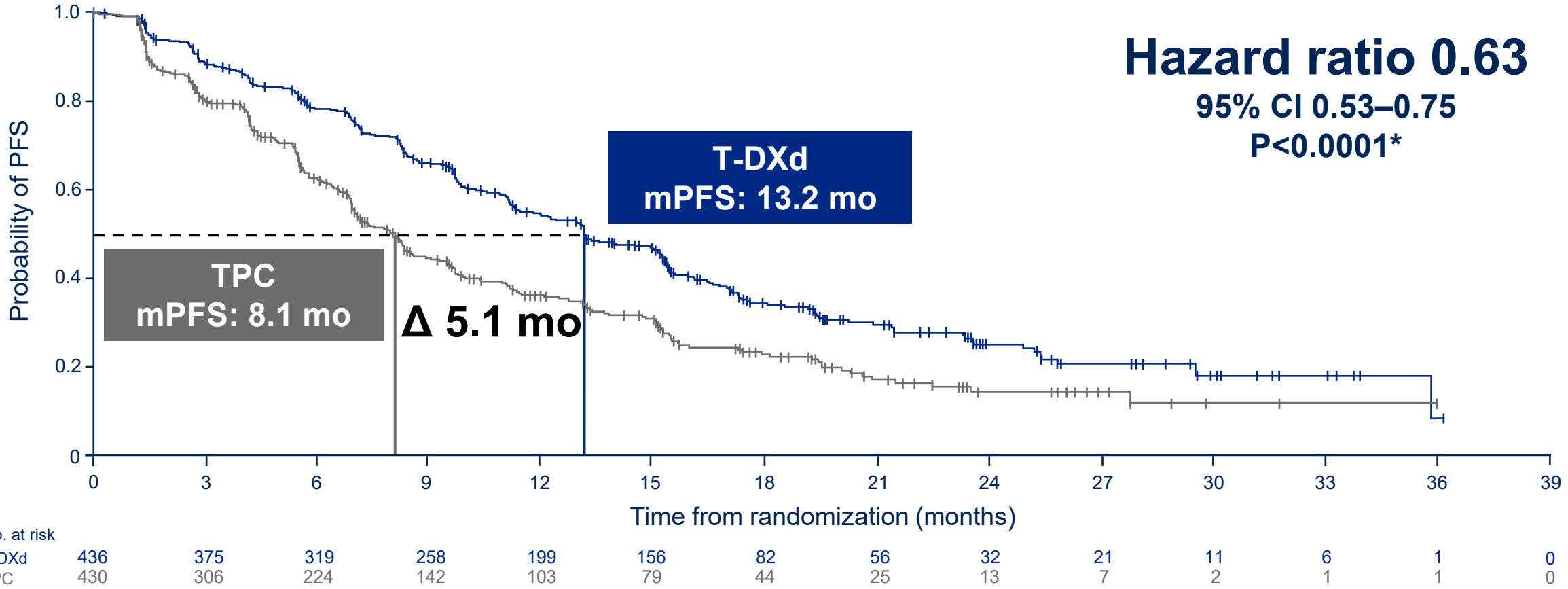
*P-value of <0.05 required for statistical significance

BICR, blinded independent central review; CI, confidence interval; HER2, human epidermal growth factor receptor 2; mo, months; (m)PFS, (median) progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

# PFS (BICR) in ITT: key secondary endpoint

DESTINY-Breast06

Daiichi-Sankyo




**T-DXd demonstrated a statistically significant and clinically meaningful improvement in PFS compared with standard-of-care chemotherapy in ITT**

*P-value of <0.015 required for statistical significance
BICR, blinded independent central review; CI, confidence interval; ITT, intent-to-treat; mo, months; (m)PFS, (median) progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

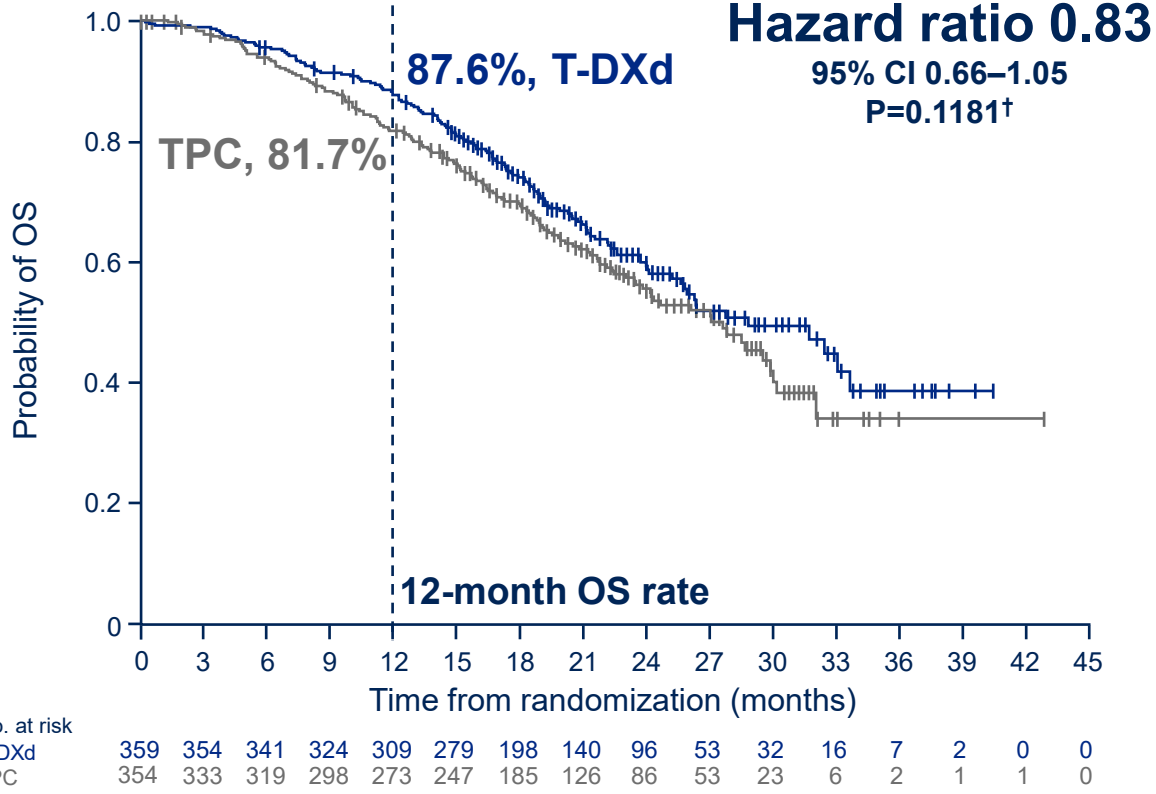
# OS in HER2-low and ITT: key secondary endpoints (~40% maturity)

DESTINY-Breast06

Daiichi-Sankyo

## HER2-low*

n=713



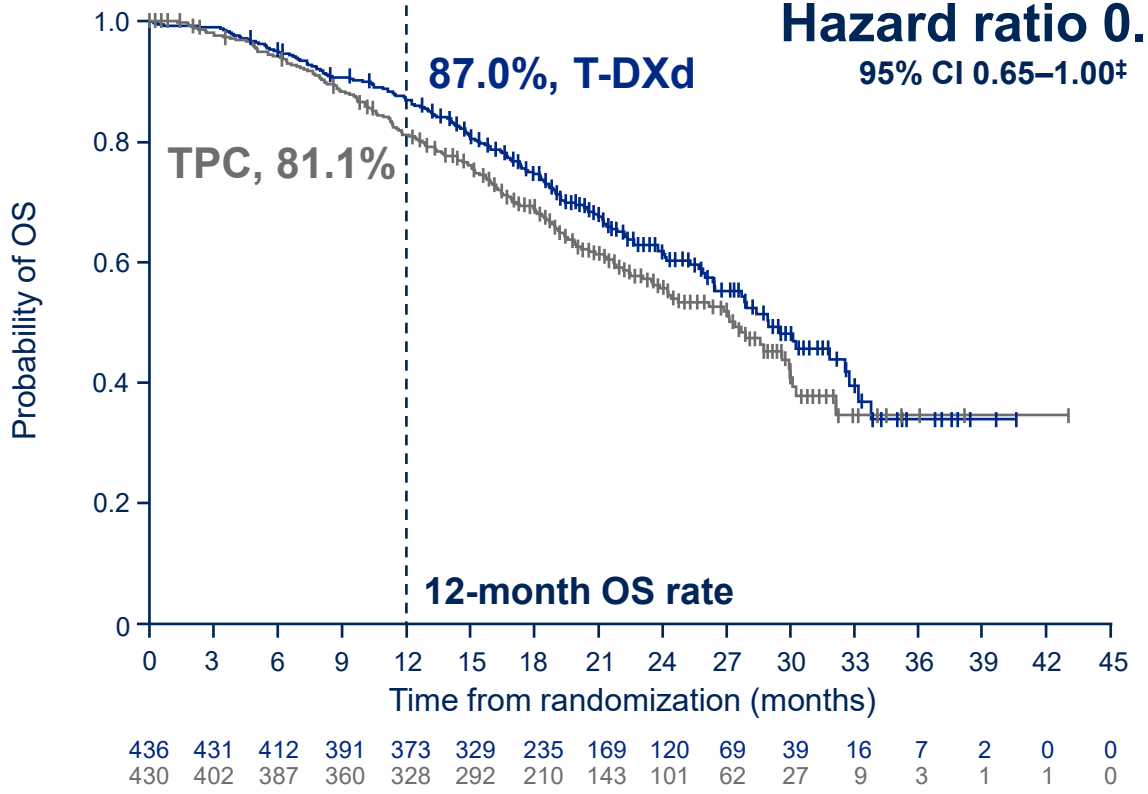

No. at risk

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| T-DXd | 359 | 354 | 341 | 324 | 309 | 279 | 198 | 140 | 96 | 53 | 32 | 16 | 7 | 2 | 0 | 0 |
| TPC | 354 | 333 | 319 | 298 | 273 | 247 | 185 | 126 | 86 | 53 | 23 | 6 | 2 | 1 | 1 | 0 |

**20.1% of patients in the TPC group received T-DXd post treatment discontinuation (HER2-low)**

## ITT (HER2-low + HER2-ultralow)

N=866




| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| T-DXd | 436 | 431 | 412 | 391 | 373 | 329 | 235 | 169 | 120 | 69 | 39 | 16 | 7 | 2 | 0 | 0 |
| TPC | 430 | 402 | 387 | 360 | 328 | 292 | 210 | 143 | 101 | 62 | 27 | 9 | 3 | 1 | 1 | 0 |

**17.9% of patients in the TPC group received T-DXd post treatment discontinuation (ITT)**

*39.6% maturity (of total N for population) at this first interim analysis; median duration of follow up was 18.6 months (HER2-low); †P-value of <0.0046 required for statistical significance; ‡no test of significance was performed in line with the multiple testing procedure; median duration of follow up was 18.2 months (ITT)

CI, confidence interval; HER2, human epidermal growth factor receptor 2; ITT, intent-to-treat; OS, overall survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

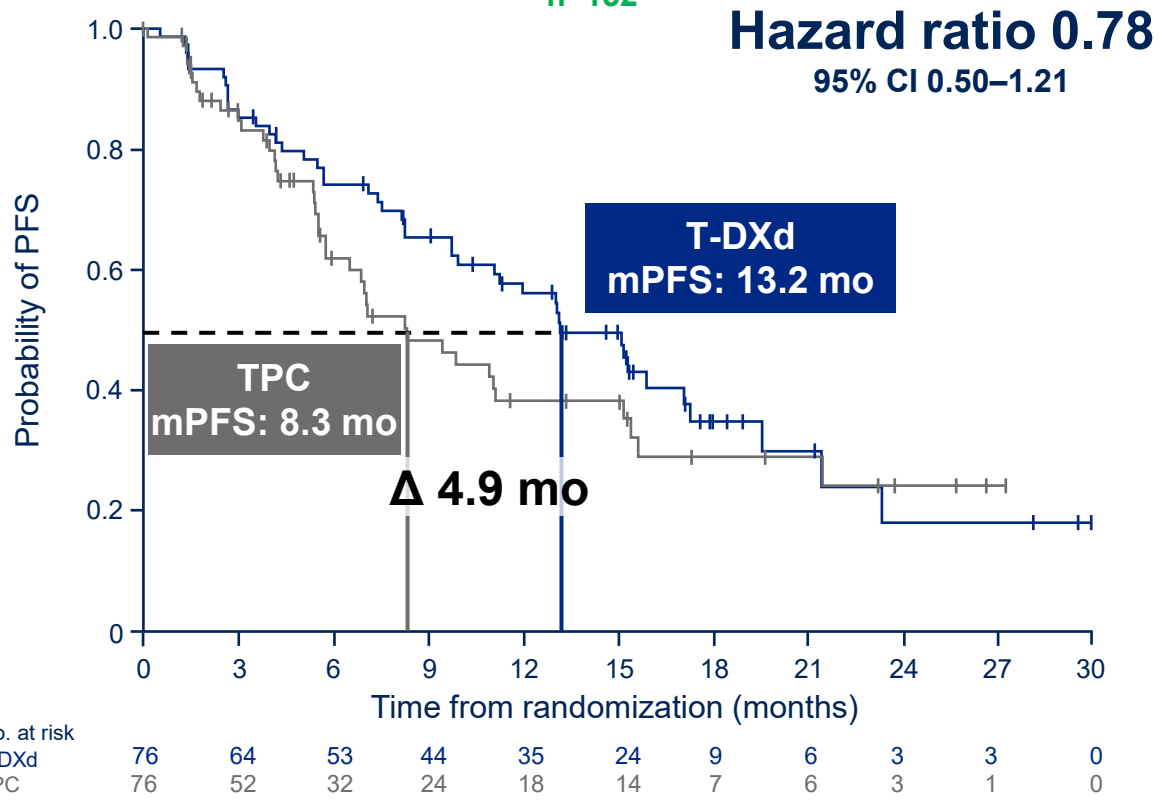
# PFS and OS in HER2-ultralow: prespecified exploratory analyses

DESTINY-Breast06

Daiichi-Sankyo

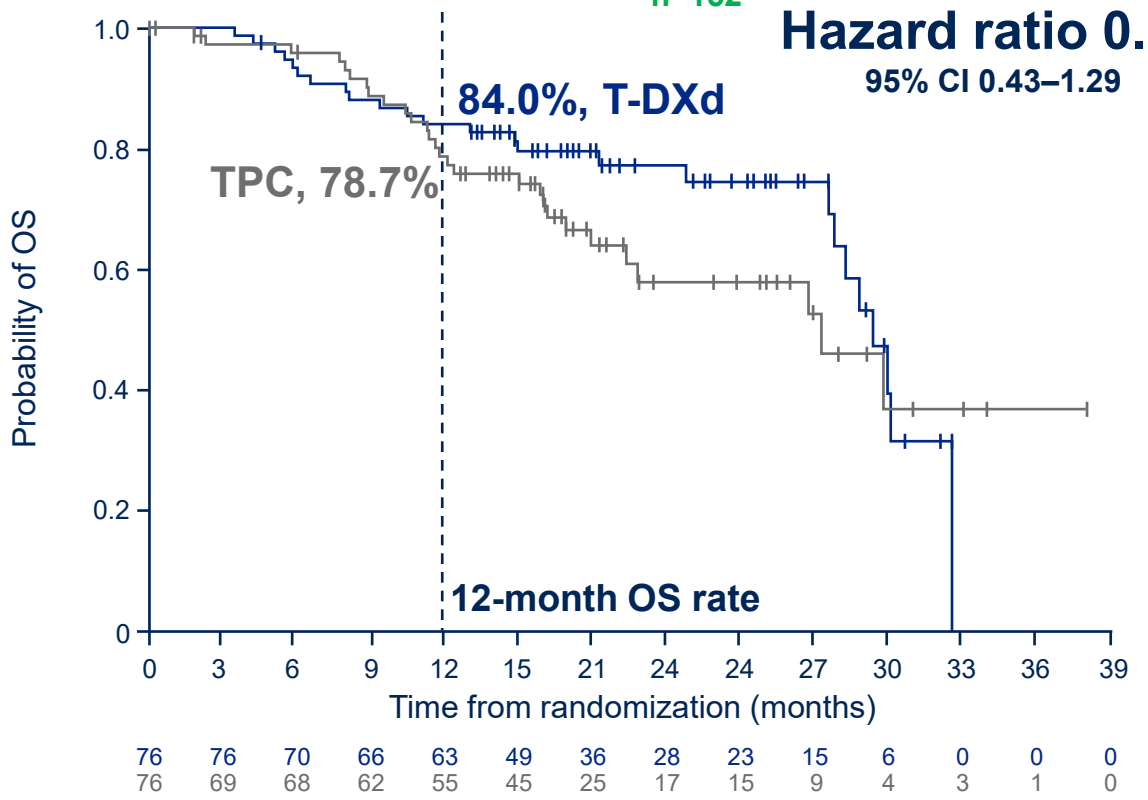
## PFS (BICR)

n=152




## OS*

n=152




**PFS improvement with T-DXd vs TPC in HER2-ultralow was consistent with results in HER2-low**

*34.9% maturity (of total N for population) at this first interim analysis; median duration of follow up was 16.8 months
BICR, blinded independent central review; CI, confidence interval; HER2, human epidermal growth factor receptor 2; OS, overall survival; mo, months; (m)PFS, (median) progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

# Study design

DESTINY-Breast07

Daiichi-Sankyo

## DESTINY-Breast07: a Phase 1b/2, multicenter, open-label, two-part, modular study (NCT04538742)

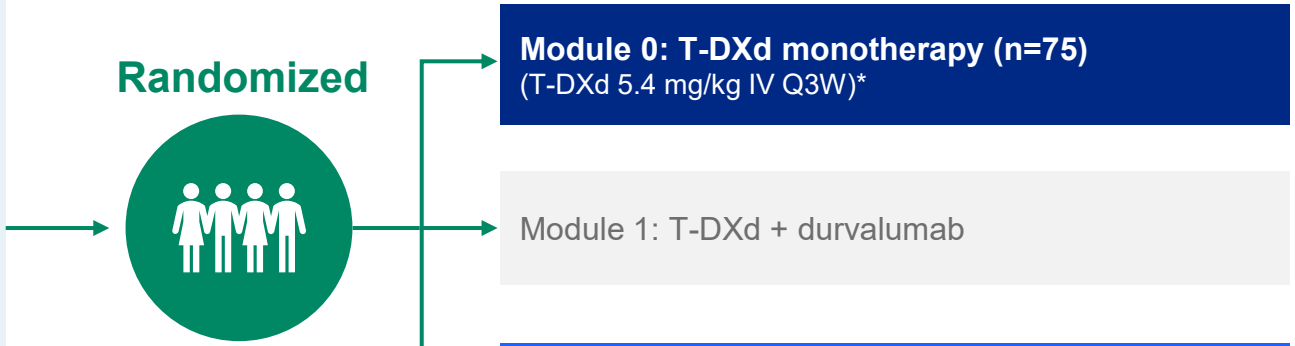
### PATIENT POPULATION

- Locally assessed HER2+ (IHC 3+, IHC 2+/ISH+) advanced/mBC, with measurable disease per RECIST 1.1
- Either no brain metastases or previously treated stable brain metastases
- ECOG PS of 0 or 1

**Prior lines of therapy**

- No prior therapy for mBC was allowed
- A disease-free interval of ≥12 months from adjuvant HER2-directed therapy or chemotherapy was required
- Prior taxane, trastuzumab, and pertuzumab exposure was allowed in the (neo)adjuvant setting

**This is the first dataset of T-DXd monotherapy and T-DXd + pertuzumab as first-line treatment for HER2+ mBC**




**Stratification factors**

- HR status
- Disease status
- PD-L1 status

**Endpoints for the Part 2 dose-expansion phase**

**Primary**
Safety and tolerability, including AEs and SAEs

**Key secondary**
ORR, PFS (evaluated by investigator per RECIST 1.1), and DOR

**DCO: December 22, 2023‡**

**Results reported here are from an interim analysis of the Part 2 dose-expansion phase for Modules 0 and 2 only; the Part 1 dose-finding phase of the study has been described previously[1]**

*Patients in Module 0 received the approved T-DXd dose for HER2+ breast cancer; †patients received the RP2D from the study's dose-finding phase; ‡the corresponding abstract reported data from the August 1, 2023, DCO
AE, adverse event; DCO, data cutoff; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; HER2+, human epidermal growth factor receptor 2–positive; HR, hormone receptor; IHC, immunohistochemistry; ISH+, in situ hybridization–positive; IV, intravenous; mBC, metastatic breast cancer; ORR, objective response rate; PD-L1, programmed cell death ligand 1; PFS, progression-free survival; Q3W, every 3 weeks; RECIST 1.1, Response Evaluation Criteria in Solid Tumours version 1.1; RP2D, recommended Phase 2 dose; SAE, serious adverse event; T-DXd, trastuzumab deruxtecan

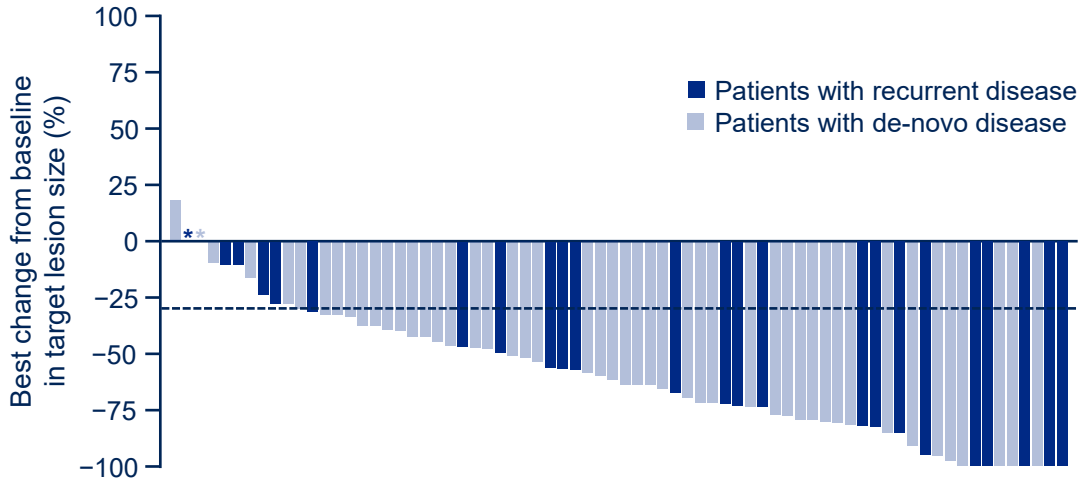
1. André F, et al. Poster presented at ASCO 2022 (Abstract 3025)

# Response to treatment per RECIST 1.1 by investigator

DESTINY-Breast07

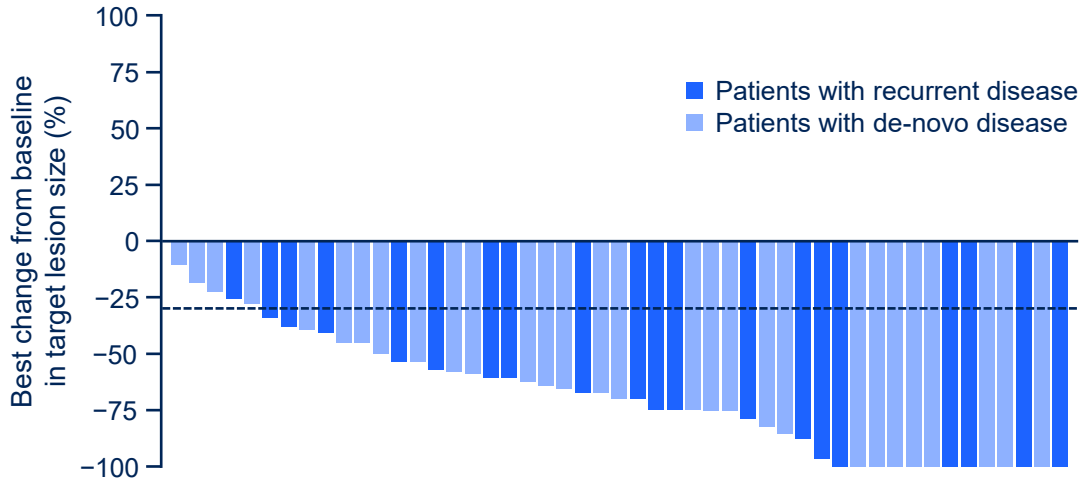
Daiichi-Sankyo

## T-DXd monotherapy (n=75)




| Confirmed ORR, % (80% CI) | 76.0 (68.5–82.4) |
|---|---|
| Complete response, n (%) | 6 (8.0) |
| Partial response, n (%) | 51 (68.0) |
| **Median DOR, months (range)** | NE (2.1–28.5) |

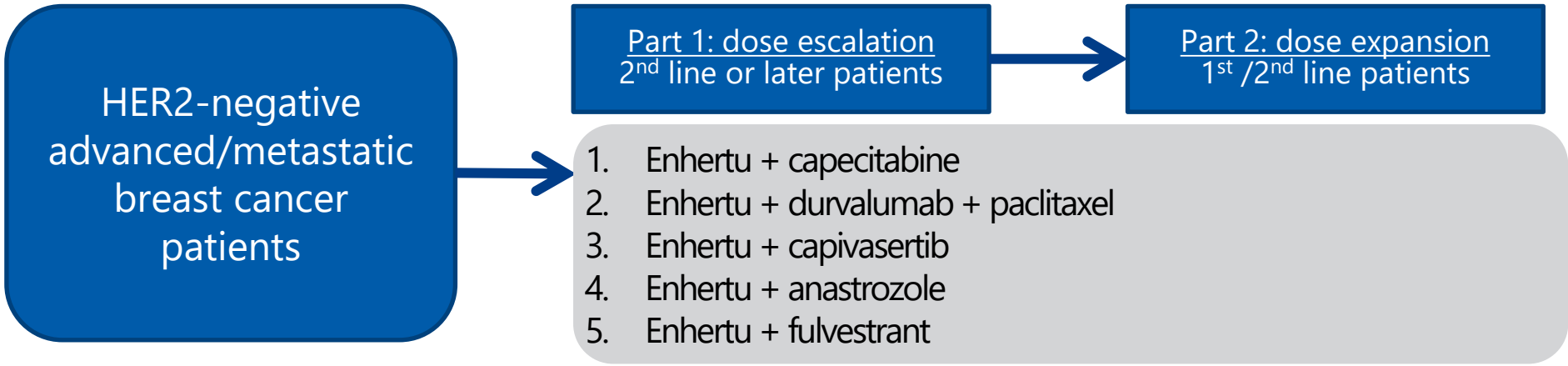
## T-DXd + pertuzumab (n=50)




| Confirmed ORR, % (80% CI) | 84.0 (75.3–90.5) |
|---|---|
| Complete response, n (%) | 10 (20.0) |
| Partial response, n (%) | 32 (64.0) |
| **Median DOR, months (range)** | NE (4.5–28.3) |

Dashed reference line at −30% indicates the threshold for partial response
Responses are captured for patients with baseline data and at least one follow-up assessment
DCO was December 22, 2023. Median duration of follow up was 23.9 months for T-DXd monotherapy and 25.3 months for T-DXd + pertuzumab
*Patients had 0% change from baseline
CI, confidence interval; DCO, data cutoff; DOR, duration of response; NE, not evaluable; ORR, objective response rate; RECIST 1.1, Response Evaluation Criteria in Solid Tumours version 1.1; T-DXd, trastuzumab deruxtecan

# DESTINY-Breast08: Study Design




| | |
|---|---|
| Summary | A Phase 1b Multicentre, Open-label, Modular, Dose-finding and Dose-expansion Study to Explore the Safety, Tolerability, Pharmacokinetics and Anti-tumour Activity of Trastuzumab Deruxtecan (T-DXd) in Combination With Other Anti-cancer Agents in Patients With Metastatic HER2-low Breast Cancer |
| Estimated enrollment | 185 patients |
| Primary Endpoint | Safety |
| Secondary endpoint | ORR, PFS, DOR, OS, PK |
| JAPIC/CT.gov | NCT04556773 |

ENHERTU®

# DESTINY-Breast08

SABCS 2023

Daiichi-Sankyo

## ENHERTU® +Endocrine Therapy is tolerable and active in chemotherapy-naïve patients with HER2 low mBC, potentially supporting further investigation

### DESTINY-Breast08 Study

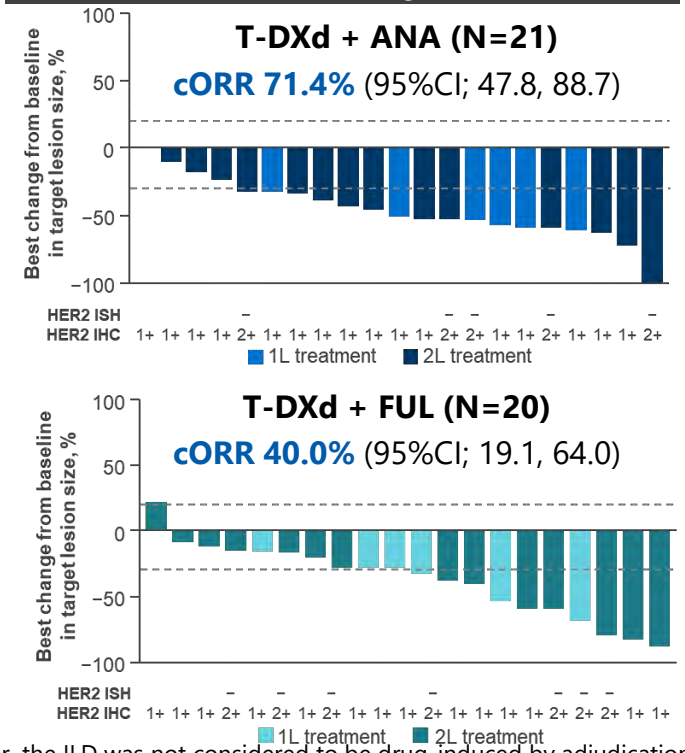
A Ph1b study to investigate safety, tolerability, PK and preliminary anti-tumor activity of ENHERTU® in combination with other therapeutics in patients with HER2 low mBC

### Safety

| | T-DXd + ANA (N=21) | T-DXd + FUL (N=20) |
|---|---|---|
| **Any-grade AEs** | 20 (95.2) | 20 (100) |
| **Any AEs ≥Grade 3** | 10 (47.6) | 11 (55.0) |
| **Any AEs ≥Grade 3 possibly related to either drug** | 7 (33.3) | 10 (50.0) |
| **AEs leading to dose interruptions/delays of T-DXd** | 12 (57.1) | 9 (45.0) |
| **AEs leading to dose reduction of T-DXd** | 6 (28.6) | 4 (20.0) |
| **AEs leading to discontinuation of T-DXd** | 4 (19.0) | 6 (30.0) |
| **Any SAEs** | 4 (19.0) | 4 (20.0) |
| **AEs leading to death†** | 1 (4.8) | 0 |
| **AESIs**<br>Ejection fraction decreased‡<br>Pneumonitis (adjudicated as ILD related to any study drug) | 1 (4.8)<br>0 | 1 (5.0)<br>5 (25.0), all grade 2 |

Data cutoff: Aug 16, 2023

### Efficacy




- For T-DXd+ ANA and T-DXd + FUL arms, 66.7% and 70.0% of patients received a prior line of treatment for mBC, respectively
- Safety profiles were generally consistent or comparable to the known safety profile
- No ILD in T-DXd + ANA arm, while 5 Grade 2 ILD/pneumonitis events in T-DXd + FUL arm
- Confirmed ORR was 71.4% in T-DXd + ANA arm and 40.0% in T-DXd + FUL arm
- mPFS was 13.4 months (95% CI; 8.5, 19.4) in T-DXd + ANA arm and NE (95% CI; 5.6, NE) in T-DXd + FUL arm
- Small datasets limit the interpretation of the efficacy results; need further research

† Reported by investigator as related to disease and drug-induced pneumonitis; however, the ILD was not considered to be drug-induced by adjudication. ‡Both cases Grade 2 and resolved at DCO.*NE signifies that DOR or PFS was not reached for these patients at the time of data cutoff.

AE: adverse event, AESI: adverse event of special interest, ANA: anastrozole, CI: confidence interval, cORR: confirmed overall response rate, DOR: duration of response, ET: endocrine therapy, FUL: fulvestrant, IHC: immunohistochemistry, ISH: *in situ* hybridization, mBC: metastatic breast cancer, mPFS: median progression-free survival, NE: not evaluable, ORR: objective response rate, SAE: serious adverse event, T-DXd: trastuzumab deruxtecan (ENHERTU®)

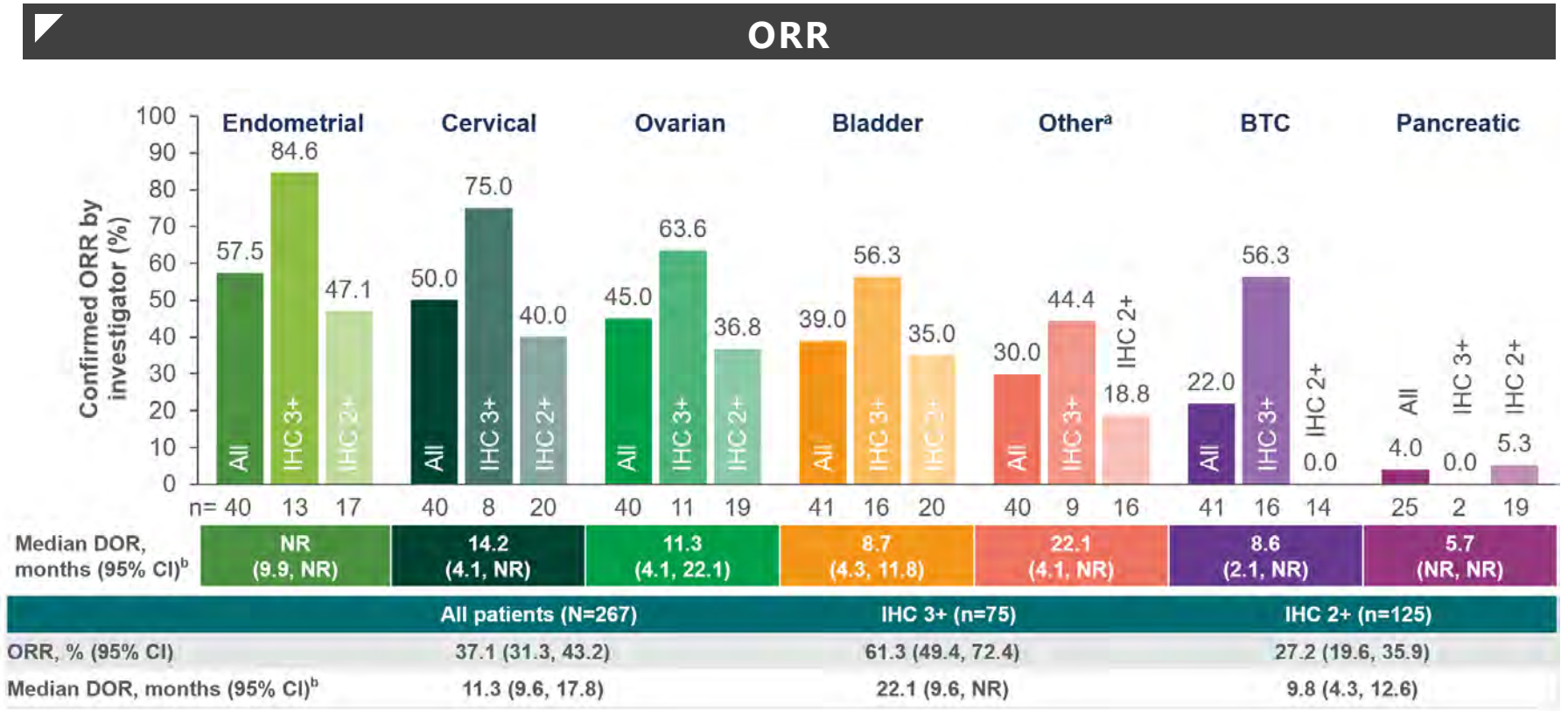
ENHERTU®

# DESTINY-PanTumor02

ESMO 2023

Daiichi-Sankyo

## DESTINY-PanTumor02 demonstrated clinically meaningful and durable responses across a broad range of HER2 expressing advanced solid tumors



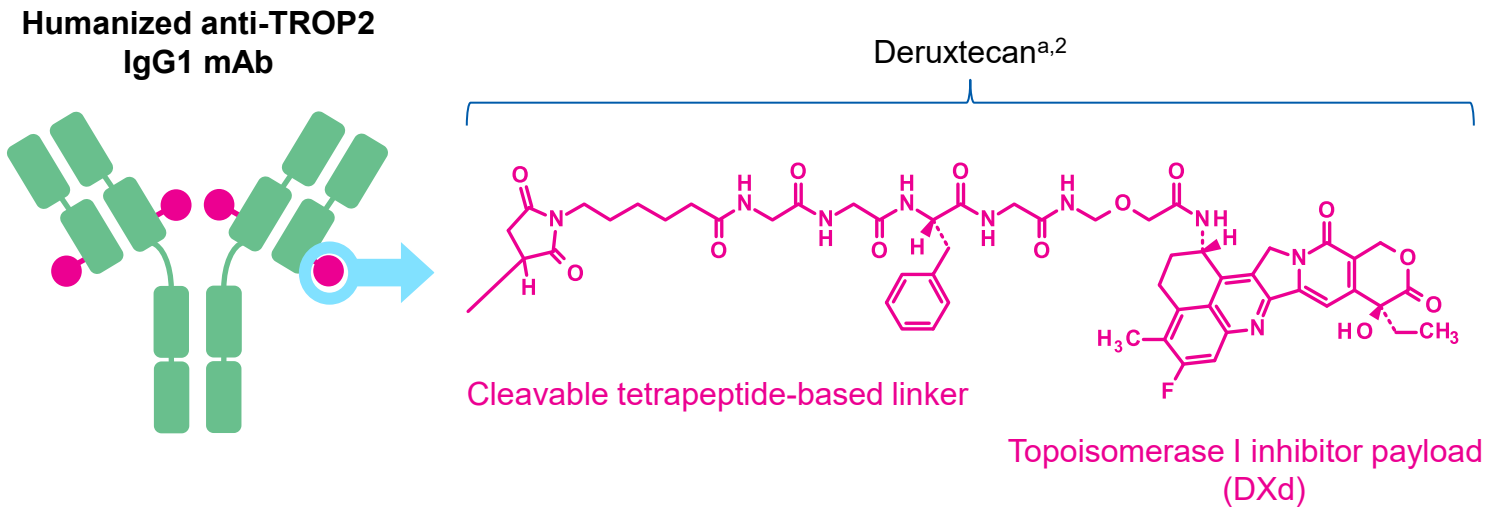

| | All patients (N=267) | IHC 3+ (n=75) | IHC 2+ (n=125) |
|---|---|---|---|
| ORR, % (95% CI) | 37.1 (31.3, 43.2) | 61.3 (49.4, 72.4) | 27.2 (19.6, 35.9) |
| Median DOR, months (95% CI)[b] | 11.3 (9.6, 17.8) | 22.1 (9.6, NR) | 9.8 (4.3, 12.6) |

- All patients: ORR 37.1% and median DOR 11.3months
- Patients with IHC 3+: ORR 61.3% and median DOR 22.1months
- Durable responses led to clinically meaningful PFS & OS
- The safety profile was consistent with the known profile with grade 5 ILD 1.1%
- **Plan to file** with DESTINY-PanTumor02 study data **within FY2023** for a potential **tumor agnostic therapy** in previously treated patients with HER2 expressing solid tumors in the US

Analysis of ORR by investigator was performed in patients who received ≥1 dose of T-DXd; all patients (n=267; including 67 patients with IHC 1+ [n=25], IHC 0 [n=30], or unknown IHC status [n=12] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=75) or IHC 2+ (n=125) status. Analysis of DOR was performed in patients with objective response who received ≥1 dose of T-DXd; all patients (n=99; including 19 patients with IHC 1+ [n=6], IHC 0 [n=9], or unknown IHC status [n=4] by central testing) and patients with centrally confirmed HER2 IHC 3+ (n=46) or IHC 2+ (n=34) status. [a] Responses in extramammary Paget's disease, head and neck cancer, oropharyngeal neoplasm, and salivary gland cancer; [b] includes patients with a confirmed objective response only,
BTC: biliary tract cancer, CI: confidence interval, DOR: duration of response, IHC: immunohistochemistry, ILD: interstitial lung disease, NR: not reached, ORR: objective response rate, OS: overall survival, PFS: progression-free survival, T-DXd: trastuzumab deruxtecan (ENHERTU®)

# Dato-DXd

- A humanized anti-TROP2 IgG1[1] monoclonal antibody attached to:
- A topoisomerase I inhibitor payload, an exatecan derivative, via
- A tetrapeptide-based cleavable linker



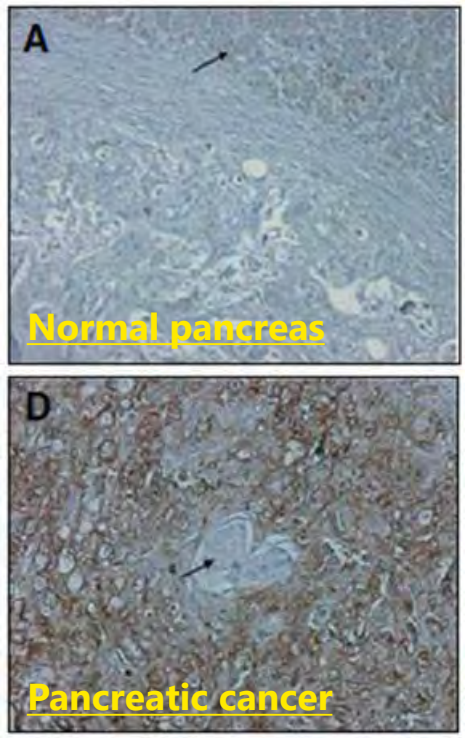

[a] Image is for illustrative purposes only; actual drug positions may vary.
[b] The clinical relevance of these features is under investigation.
[c] Based on animal data.


1. Daiichi Sankyo Co. Ltd. DS-1062. Daiichi Sankyo.com. Accessed October 6, 2020. https://www.daiichisankyo.com/media_investors/investor_relations/ir_calendar/files/005438/DS-1062%20Seminar%20Slides_EN.pdf
2. Krop I, et al. Oral presentation at: SABCS Symposium; December 10-14, 2019; San Antonio, TX [abstract GS1-03].

# TROP2 as ADC Target

- A 36-kDa single pass transmembrane glycoprotein
- TROP2 is overexpressed in a variety of human carcinomas including lung, breast, pancreatic, cervical, ovarian, colorectal and gastric cancers
  - ✓ Some overlap with Irinotecan indications
  - ✓ TROP2 correlates with poor prognosis

    (Clin. Cancer Res. 2006, Br. J. Cancer 2008)
- TROP2 is effectively internalized with binding antibody
- TROP2 is expressed in the epithelium of normal tissues including skin, esophagus and lung
  - ✓ Normal cell turnover is slower than tumor cells
  - ✓ High expression in non-target tissues requires careful determination of risk/benefit profile

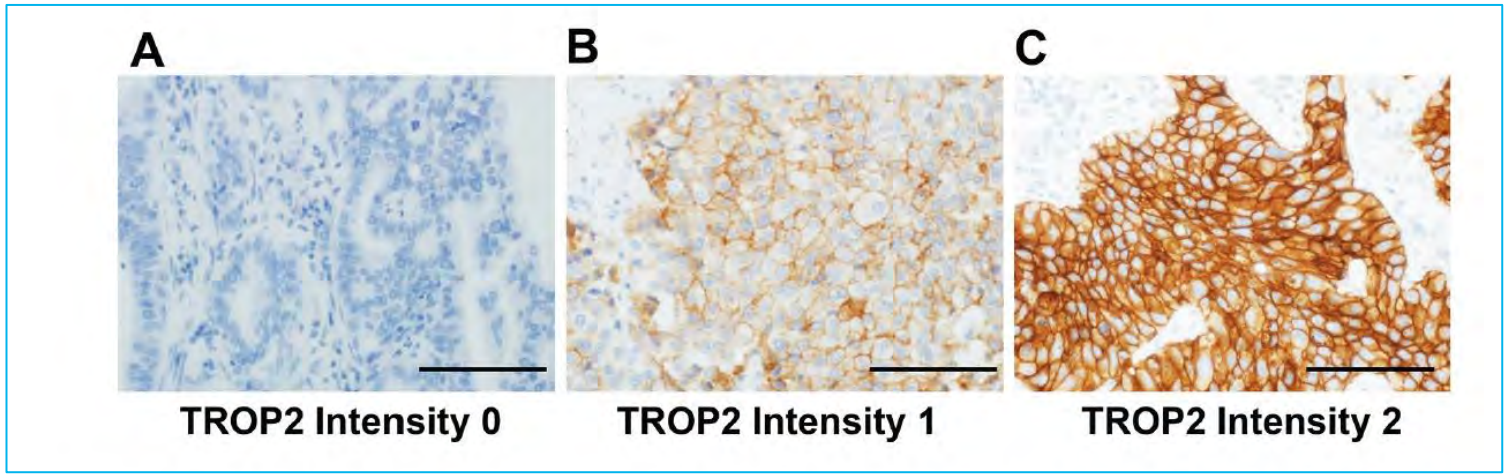


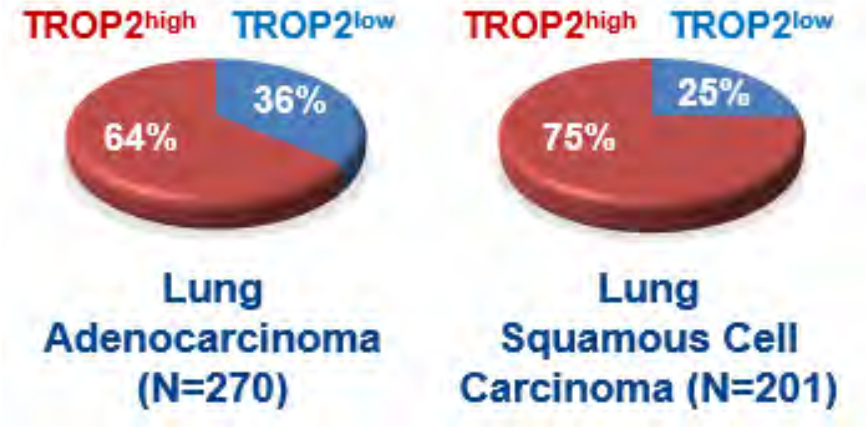

**TROP2 immunostaining in pancreatic cancer**

**(Br. J. Cancer 2008)**

**TROP2 is an attractive target for ADC therapy**

# TROP2 Expression in Lung

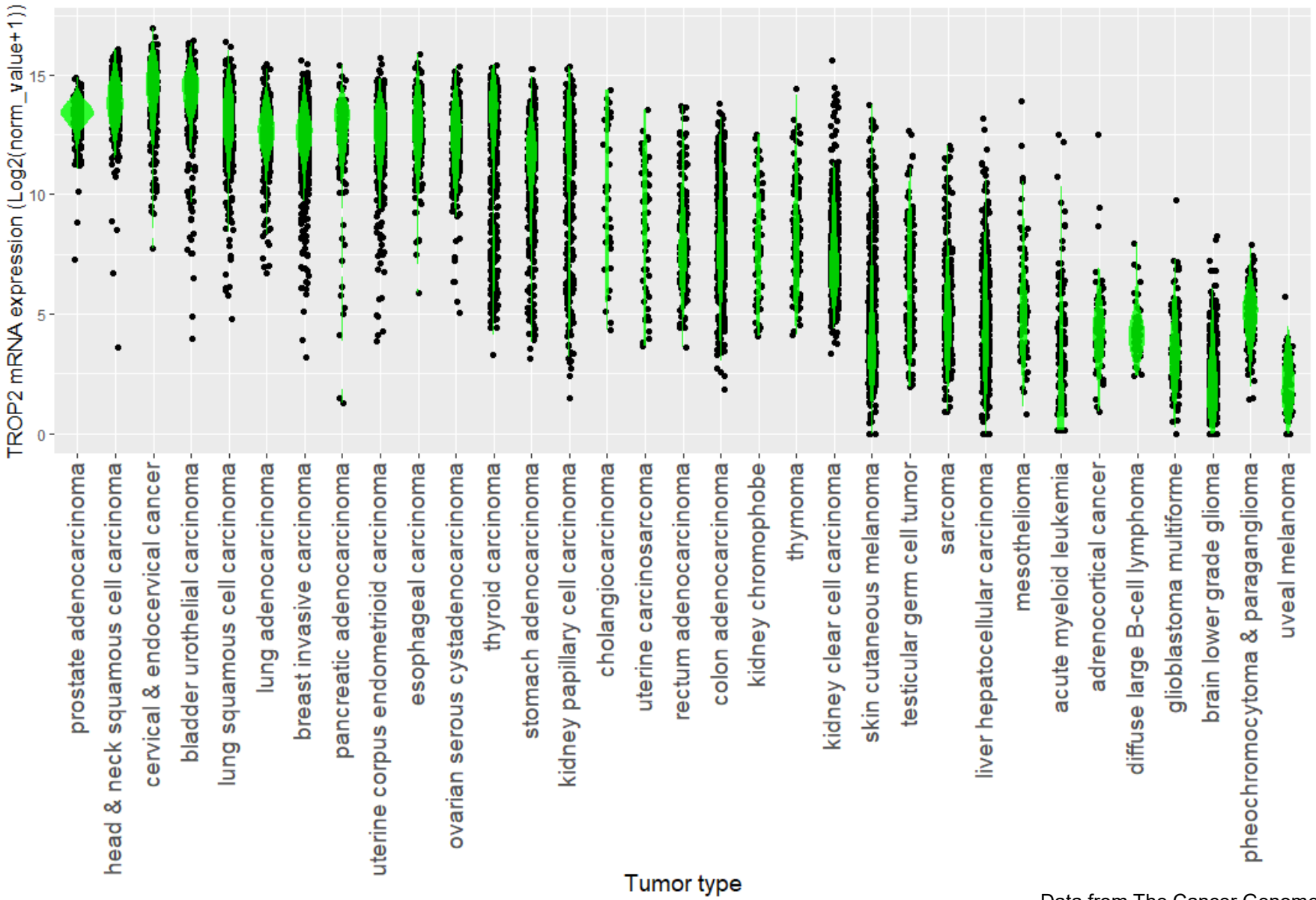



NSCLC is a good indication for DS-1062 because of its high TROP2 expression in both adeno and squamous cell carcinoma

Source: Inamura K et al., *Oncotarget* 2017; 8:28725-28735

# TROP2 Expression in Various Cancers




Data from The Cancer Genome Atlas

# TROPION-Lung01: Study design

## TROPION-Lung01 Study Design

Randomized, Phase 3, Open-Label, Global Study (NCT04656652)

### Key Eligibility Criteria

- NSCLC (stage IIIB, IIIC, or IV)
- ECOG PS of 0 or 1
- No prior docetaxel

**Without actionable genomic alterations[a]**

- 1 or 2 prior lines, including platinum CT and anti–PD-(L)1 mAb therapy

**With actionable genomic alterations**

- Positive for *EGFR*, *ALK*, *NTRK*, *BRAF*, *ROS1*, *MET* exon 14 skipping, or *RET*
- 1 or 2 prior approved targeted therapies + platinum-based CT, and ≤1 anti–PD-(L)1 mAb

R 1:1

**Dato-DXd**
6 mg/kg Q3W
(N=299)

**Docetaxel**
75 mg/m$^2$ Q3W
(N=305)

### Dual Primary Endpoints

- PFS by BICR
- OS

### Secondary Endpoints

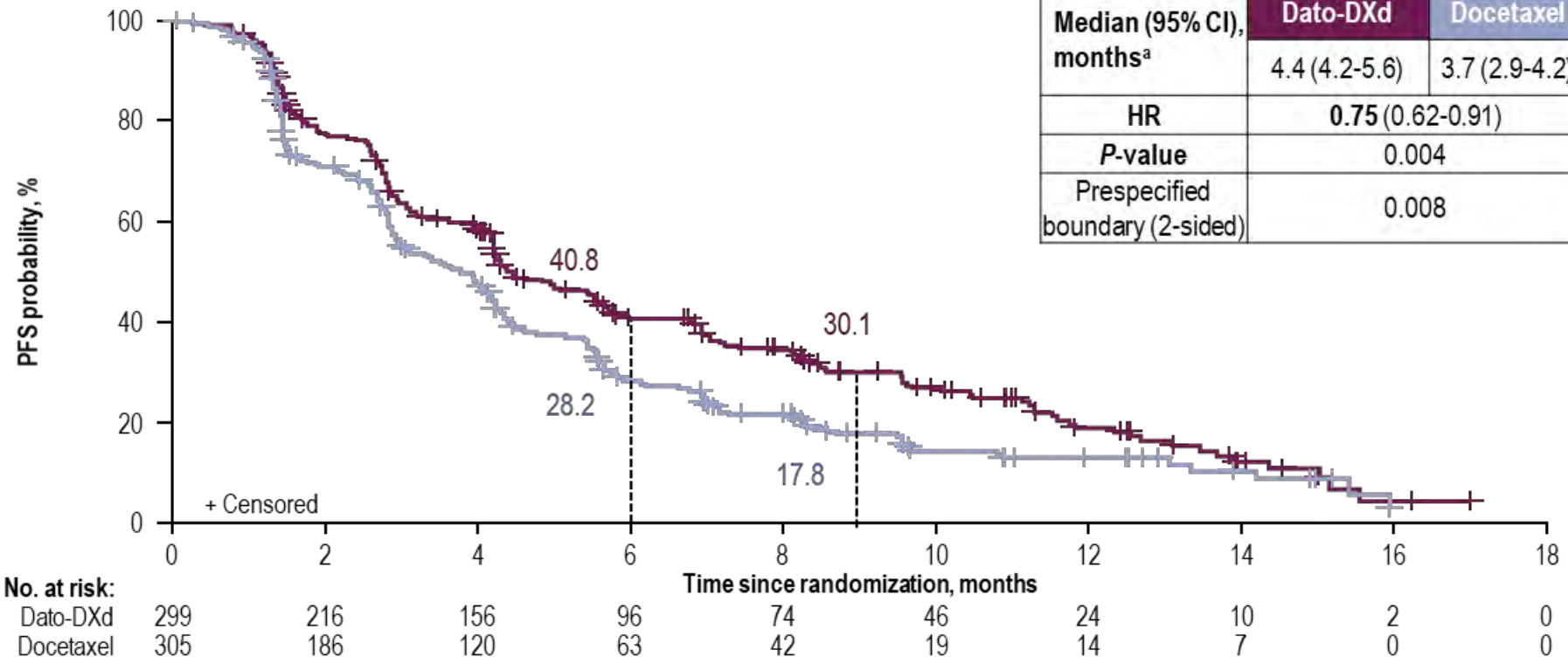
- ORR by BICR
- DOR by BICR
- Safety

**Stratified by:** histology,[b] actionable genomic alteration,[c] anti–PD-(L)1 mAb included in most recent prior therapy, geography[d]

Enrollment period: 19 February 2021 to 7 November 2022.
BICR, blinded independent central review; CT, chemotherapy; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PD-(L)1, programmed cell death 1 (ligand 1); PFS, progression-free survival; Q3W, every 3 weeks; R, randomized.
[a]Patients with *KRAS* mutations in the absence of known actionable genomic alterations are eligible; must meet prior therapy requirements for patients without actionable genomic alterations. [b]Squamous vs non-squamous. [c]Presence vs absence. [d]United States/Japan/Western Europe vs rest of world.

# TROPION-Lung01: PFS (ITT)

## Progression-Free Survival: ITT




| Median (95% CI), months[a] | Dato-DXd | Docetaxel |
|---|---|---|
| | 4.4 (4.2-5.6) | 3.7 (2.9-4.2) |
| HR | **0.75** (0.62-0.91) | |
| *P*-value | 0.004 | |
| Prespecified boundary (2-sided) | 0.008 | |

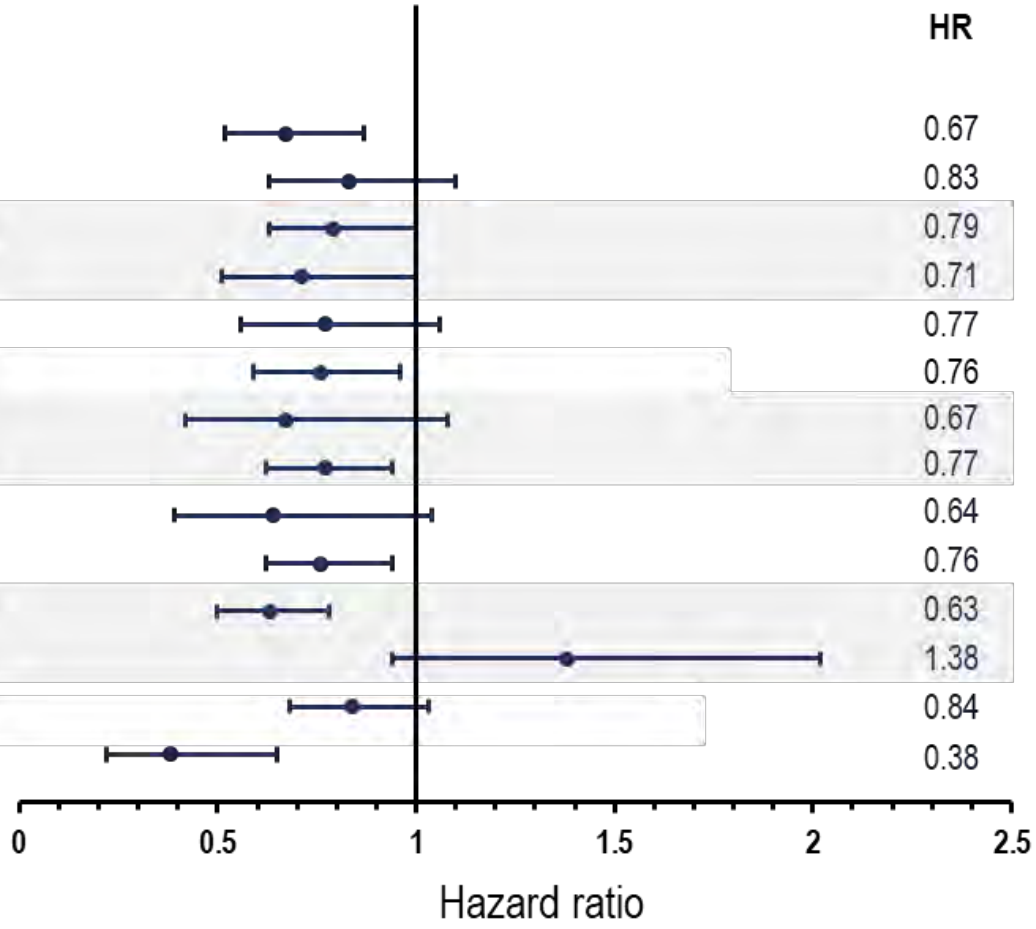
| | Dato-DXd | Docetaxel |
|---|---|---|
| **ORR** (95% CI), %[b] | **26.4** (21.5-31.8) | **12.8** (9.3-17.1) |
| **DOR** (95% CI), mo | **7.1** (5.6-10.9) | **5.6** (5.4-8.1) |

CR, complete response; DOR, duration of response; HR, hazard ratio; ITT, intention to treat; ORR, objective response rate; PFS, progression-free survival; PR, partial response.
[a]Median PFS follow-up was 10.9 (95% CI, 9.8-12.5) and 9.6 (95% CI, 8.2-11.9) months for Dato-DXd and docetaxel, respectively. [b]Included 4 CRs and 75 PRs for Dato-DXd and 39 PRs for docetaxel.

# TROPION-Lung01: PFS in key subgroups

## PFS in Key Subgroups

| | | Events/n | | HR |
|---|---|---|---|---|
| | | Dato-DXd | Docetaxel | |
| Age at randomization | <65 years | 118/162 | 115/155 | 0.67 |
| | ≥65 years | 95/137 | 103/150 | 0.83 |
| Sex | Male | 136/183 | 158/210 | 0.79 |
| | Female | 77/116 | 60/95 | 0.71 |
| Race | Asian | 76/119 | 82/120 | 0.77 |
| | Non-Asian | 131/172 | 129/177 | 0.76 |
| Smoking status | Never | 36/61 | 33/52 | 0.67 |
| | Former/current | 177/238 | 184/251 | 0.77 |
| Brain metastasis at baseline | With | 33/50 | 31/47 | 0.64 |
| | Without | 180/249 | 187/258 | 0.76 |
| Histology | Non-squamous | 156/229 | 168/232 | 0.63 |
| | Squamous | 57/70 | 50/73 | 1.38 |
| Actionable genomic alterations[a] | Absent | 189/252 | 184/255 | 0.84 |
| | Present | 24/47 | 34/50 | 0.38 |



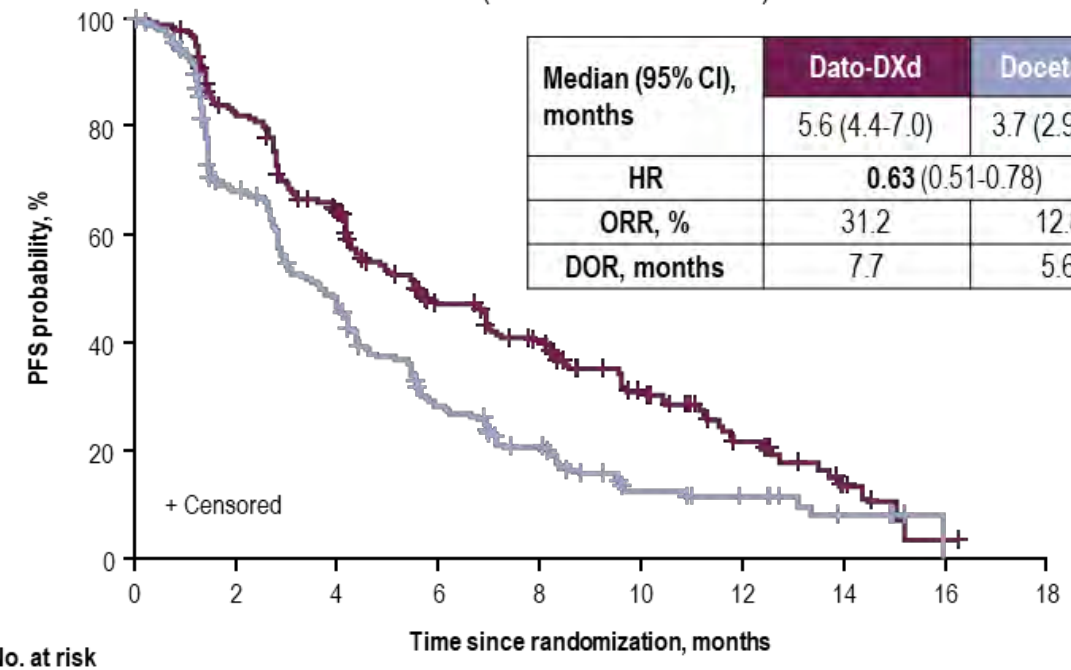

[a]Regardless of histology.

# TROPION-Lung01: PFS by histology

## PFS by Histology

### Non-squamous
(with and without AGAs)

| Median (95% CI), months | Dato-DXd | Docetaxel |
|---|---|---|
| | 5.6 (4.4-7.0) | 3.7 (2.9-4.2) |
| HR | **0.63** (0.51-0.78) | |
| ORR, % | 31.2 | 12.8 |
| DOR, months | 7.7 | 5.6 |

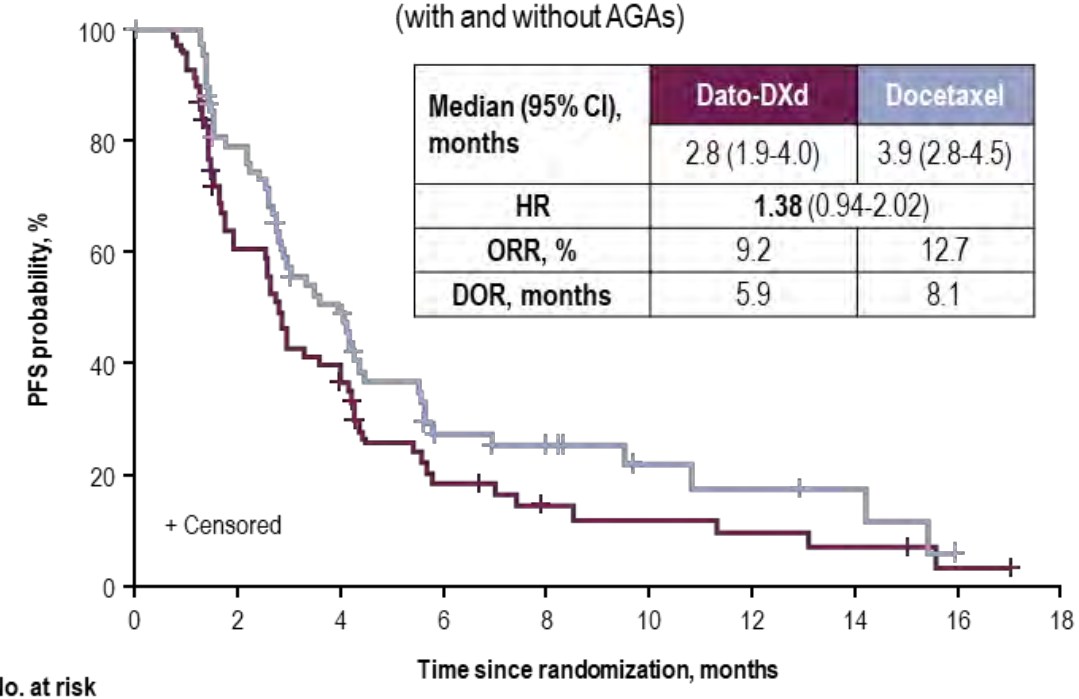



No. at risk

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Dato-DXd | 229 | 178 | 134 | 86 | 68 | 41 | 20 | 7 | 1 | 0 |
| Docetaxel | 232 | 135 | 90 | 50 | 32 | 14 | 10 | 4 | 0 | 0 |

### Squamous
(with and without AGAs)

| Median (95% CI), months | Dato-DXd | Docetaxel |
|---|---|---|
| | 2.8 (1.9-4.0) | 3.9 (2.8-4.5) |
| HR | **1.38** (0.94-2.02) | |
| ORR, % | 9.2 | 12.7 |
| DOR, months | 5.9 | 8.1 |




No. at risk

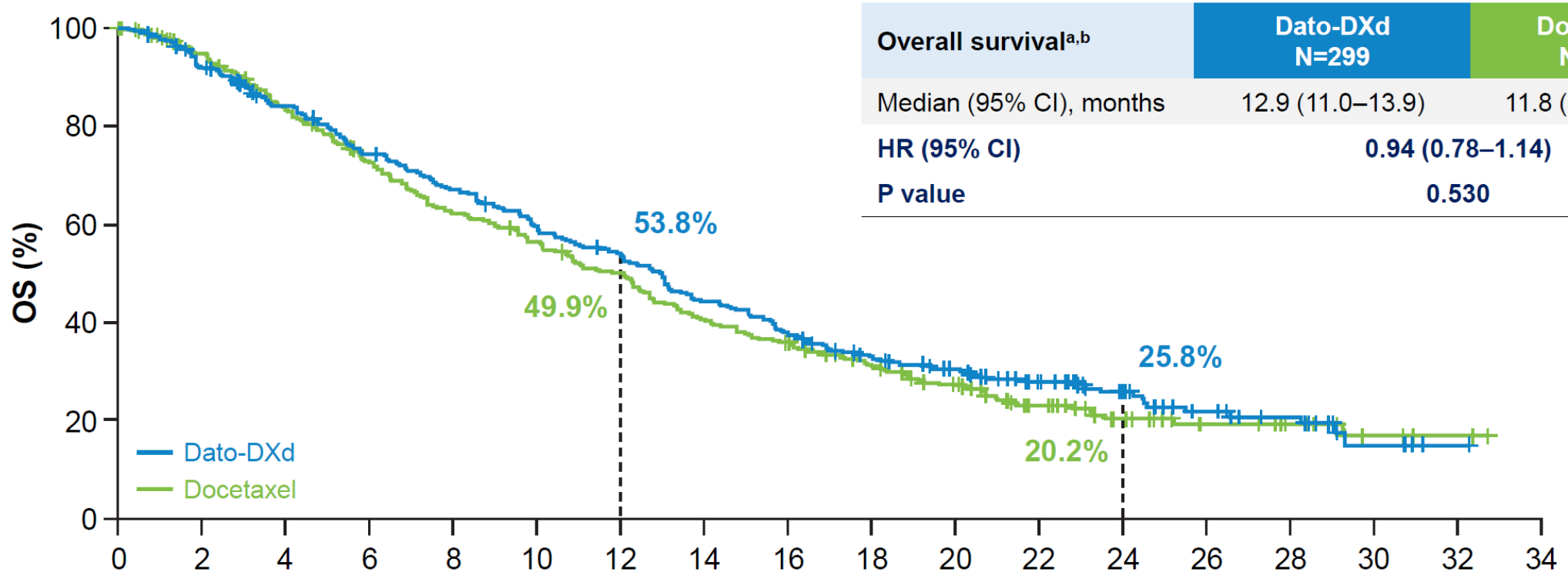
| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Dato-DXd | 70 | 38 | 22 | 10 | 6 | 5 | 4 | 3 | 1 | 0 |
| Docetaxel | 73 | 51 | 30 | 13 | 10 | 5 | 4 | 3 | 0 | 0 |

**PFS HR for non-squamous without AGAs: 0.71 (0.56, 0.91)**

AGA, actionable genomic alteration; DOR, duration of response; HR, hazard ratio; ORR, objective response ratel PFS, progression-free survival.
Squamous subset included 3 patients with AGAs

# TROPION-Lung01: Overall Survival: ITT

| Overall survival[a,b] | Dato-DXd N=299 | Docetaxel N=305 |
|---|---|---|
| Median (95% CI), months | 12.9 (11.0–13.9) | 11.8 (10.0–12.8) |
| **HR (95% CI)** | **0.94 (0.78–1.14)** | |
| **P value** | **0.530** | |

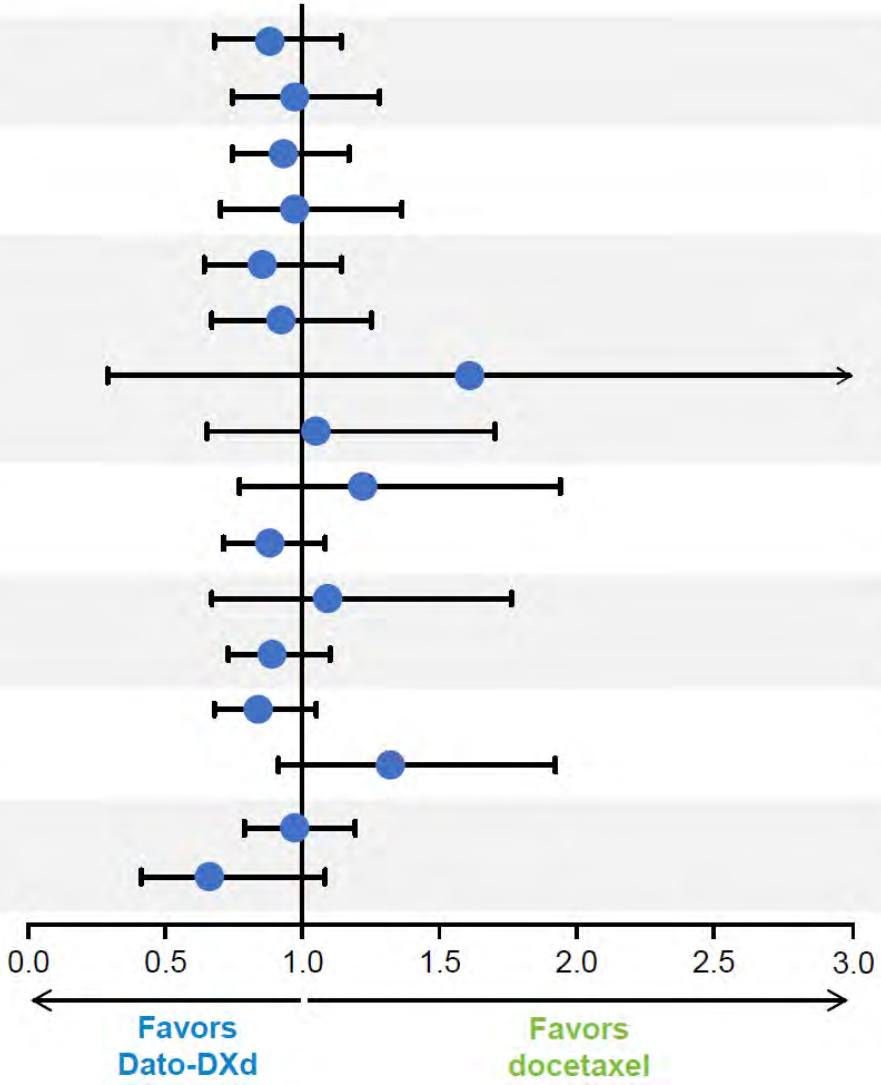



| No. at risk: | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dato-DXd | 299 | 272 | 242 | 213 | 190 | 168 | 151 | 124 | 106 | 84 | 71 | 51 | 35 | 22 | 16 | 5 | 1 | 0 |
| Docetaxel | 305 | 273 | 239 | 205 | 175 | 157 | 138 | 112 | 98 | 81 | 63 | 41 | 26 | 15 | 11 | 4 | 2 | 0 |

[a]Median (95% CI) OS follow-up was 23.1 (22.0, 24.8) months for Dato-DXd and 23.1 (21.7, 24.2) months for docetaxel. [b]At primary OS analysis (data cutoff: March 1, 2024), 433 OS events (IF) were observed.
IF, information fraction.

# TROPION-Lung01: Overall Survival: Subgroup Analyses

| | | No. of events/No. of patients | | HR |
|---|---|---|---|---|
| | | Dato-DXd | Docetaxel | |
| **Age at randomization** | <65 years | 117/162 | 112/155 | 0.88 |
| | ≥65 years | 98/137 | 106/150 | 0.97 |
| **Sex** | Male | 136/183 | 156/210 | 0.93 |
| | Female | 79/116 | 62/95 | 0.97 |
| **Race** | White | 90/123 | 95/126 | 0.85 |
| | Asian | 83/121 | 79/120 | 0.92 |
| | Black/African American | 4/6 | 2/4 | 1.61 |
| | Other | 33/43 | 35/47 | 1.05 |
| **Smoking status** | Never | 43/60 | 31/52 | 1.22 |
| | Former/current | 172/239 | 186/251 | 0.88 |
| **Brain metastases at baseline** | With | 37/50 | 31/47 | 1.09 |
| | Without | 178/249 | 187/258 | 0.89 |
| **Histology** | Nonsquamous | 160/234 | 163/234 | 0.84 |
| | Squamous | 55/65 | 55/71 | 1.32 |
| **Actionable genomic alterations[a]** | Absent | 182/249 | 185/254 | 0.97 |
| | Present | 33/50 | 33/51 | 0.66 |

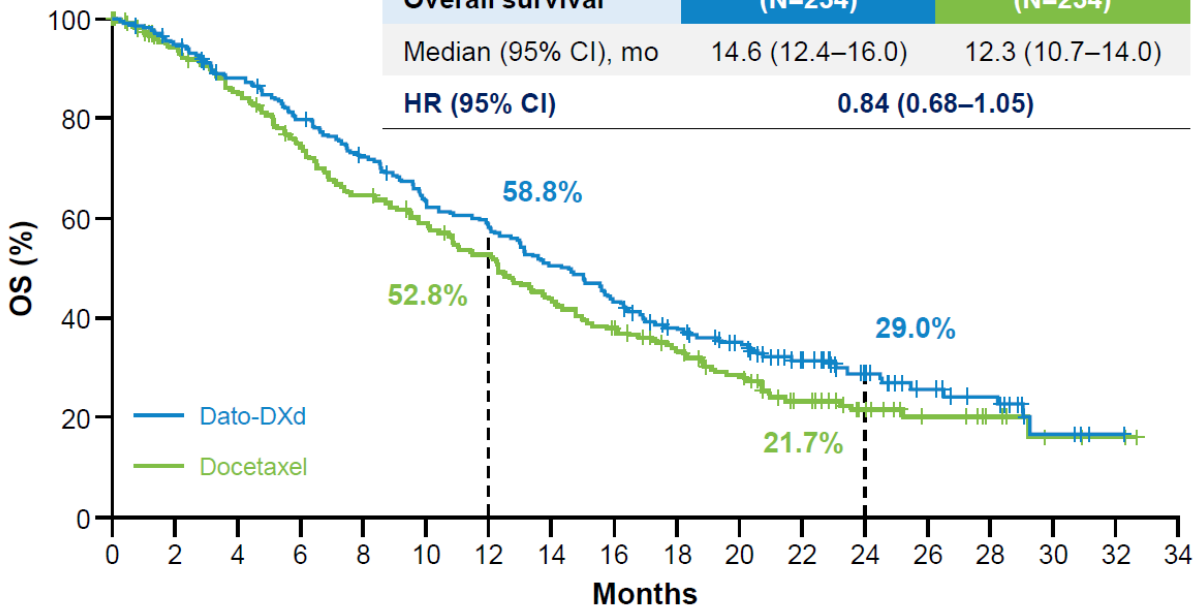



Data cutoff: March 1, 2024.
[a]Regardless of histology.

# TROPION-Lung01: Overall Survival by Histology

## Nonsquamous

| Overall survival | Dato-DXd (N=234) | Docetaxel (N=234) |
|---|---|---|
| Median (95% CI), mo | 14.6 (12.4–16.0) | 12.3 (10.7–14.0) |
| HR (95% CI) | 0.84 (0.68–1.05) | |

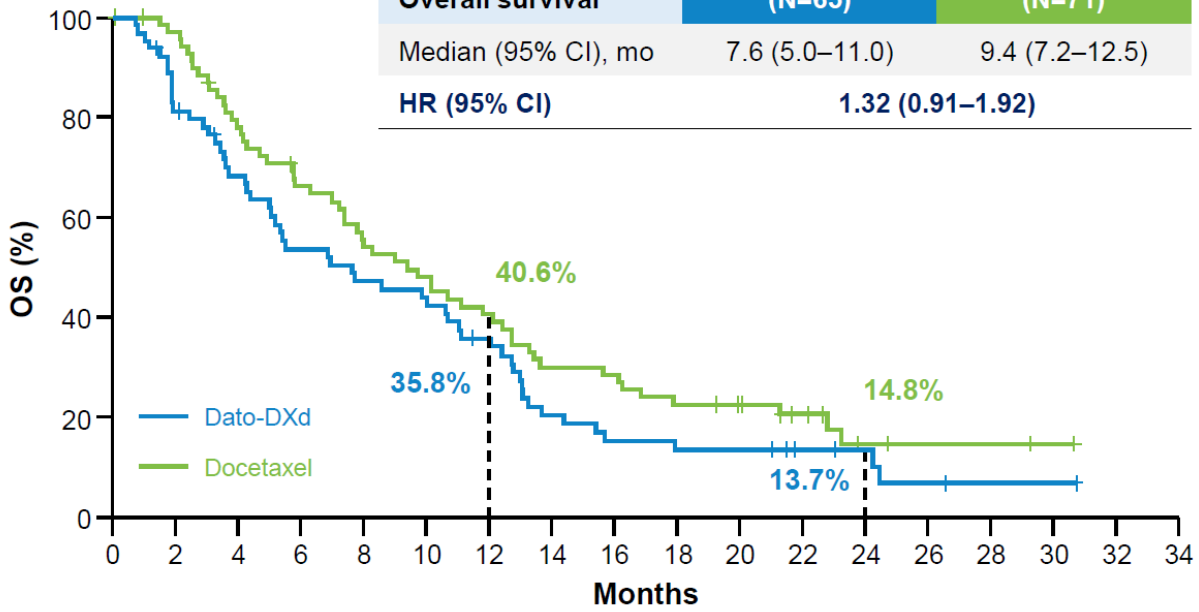



No. at risk:

| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Dato-DXd | 234 | 220 | 200 | 180 | 161 | 141 | 130 | 112 | 97 | 76 | 63 | 46 | 31 | 20 | 15 | 4 | 1 | 0 |
| Docetaxel | 234 | 206 | 186 | 161 | 139 | 125 | 111 | 92 | 79 | 66 | 50 | 32 | 22 | 12 | 8 | 3 | 2 | 0 |

## Squamous

| Overall survival | Dato-DXd (N=65) | Docetaxel (N=71) |
|---|---|---|
| Median (95% CI), mo | 7.6 (5.0–11.0) | 9.4 (7.2–12.5) |
| HR (95% CI) | 1.32 (0.91–1.92) | |




| | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 65 | 52 | 42 | 33 | 29 | 27 | 21 | 12 | 9 | 8 | 8 | 5 | 4 | 2 | 1 | 1 | 0 | 0 |
| | 71 | 67 | 53 | 44 | 36 | 32 | 27 | 20 | 19 | 15 | 13 | 9 | 4 | 3 | 3 | 1 | 0 | 0 |

- In patients with NSQ histology, 16% risk reduction for death and 2.3-month improvement in median OS with Dato-DXd
- OS improvements in the NSQ subset were seen regardless of actionable genomic alteration status[a]:
  - **Present**: 15.6 vs 9.8 months (HR [95% CI], 0.65 [0.40–1.08]); **Absent:** 13.6 vs 12.3 months (HR [95% CI], 0.89 [0.70–1.13])

Data cutoff: March 1, 2024.
[a]Based on the number of patients in the respective actionable genomic alteration subsets. Values were calculated based on patient data in the electronic case report forms.

# TROPION-Lung01: TRAEs ≥15% and Adjudicated Drug-Related ILD

| TRAEs,[a] n (%) | Dato-DXd (N=297) | | Docetaxel (N=290) | |
|---|---|---|---|---|
| | Any grade | Grade ≥3 | Any grade | Grade ≥3 |
| **Stomatitis** | 141 (47)[b] | 20 (7) | 45 (16) | 3 (1) |
| **Nausea** | 101 (34) | 7 (2) | 48 (17) | 3 (1) |
| **Alopecia** | 95 (32) | 0 | 101 (35) | 1 (<1)[c] |
| **Decreased appetite** | 68 (23) | 1 (<1) | 46 (16) | 1 (<1) |
| **Asthenia** | 56 (19) | 8 (3) | 56 (19) | 5 (2) |
| **Anemia**[d] | 44 (15) | 12 (4) | 60 (21) | 12 (4) |
| **Diarrhea** | 30 (10) | 1 (<1) | 55 (19) | 4 (1) |
| **Neutropenia**[e] | 14 (5) | 2 (1) | 76 (26) | 68 (23) |
| **Leukopenia**[f] | 9 (3) | 0 | 45 (16) | 38 (13) |
| **Adjudicated drug-related ILD or pneumonitis** | 26 (9)[g] | 11 (4) | 12 (4) | 4 (1) |

- Stomatitis events, the most common TRAE with Dato-DXd, were primarily grade 1 (23%) or grade 2 (18%)
- Hematologic toxicities, including neutropenia and febrile neutropenia[h], were more common with docetaxel
- No new adjudicated drug-related ILD events or deaths occurred since the PFS database lock
- Similar safety profiles were seen for the full safety analysis set and the NSQ subgroup

Data cutoff: March 1, 2024.
[a]Occurring in ≥15% of patients in either treatment group, plus all events of adjudicated drug-related ILD or pneumonitis. [b]Due to rounding, summed rates may not reflect total percentage of TRAEs. [c]Includes an event incorrectly reported as grade 3. [d]Grouped preferred terms of anemia, hemoglobin decreased, and red blood cell count decreased. [e]Grouped preferred terms of neutropenia and neutrophil count decreased. [f]Grouped preferred terms of leukopenia and white blood cell count decreased. [g]Includes one patient in the Dato-DXd group who experienced a grade 2 event that was adjudicated to be drug-related ILD by the adjudication committee. The investigator attributed the event to disease progression and removed the patient from the clinical database. [h]0.3% vs 6.9% for Dato-DXd and docetaxel, respectively.

Dato-DXd

# TROPION-Lung05

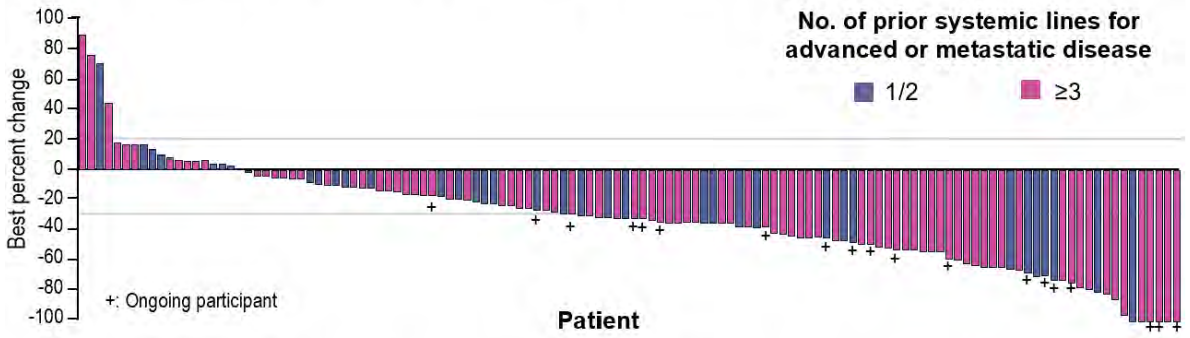
ESMO 2023

Daiichi-Sankyo

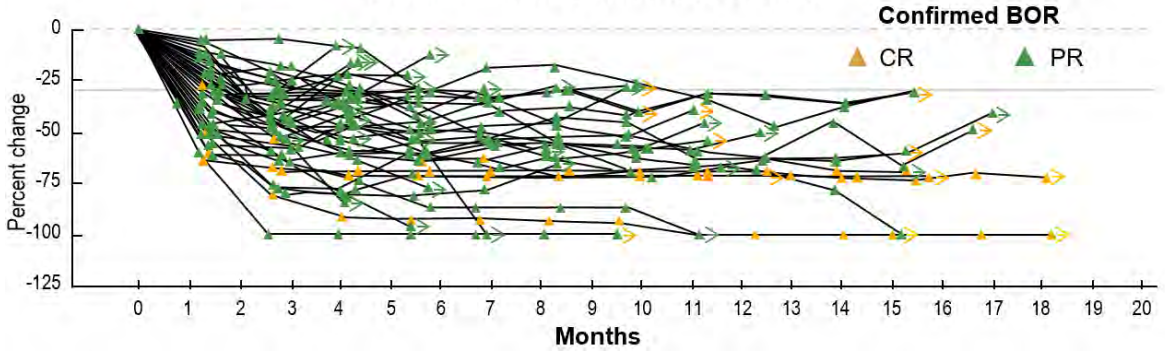
## Encouraging antitumor activity was observed with Dato-DXd treatment in a heavily pretreated NSCLC population with AGAs

### Efficacy

**Best Percent Change From Baseline in Sum of Diameters of Target Lesions**




**Percent Change From Baseline in Sum of Diameters of Target Lesions in Patients With Confirmed CR/PR[c]**




### TROPION-Lung05 Study

Ph2, single-arm study evaluating Dato-DXd in patients with advanced or metastatic NSCLC with AGAs that progressed on or after targeted therapy and platinum-based chemotherapy

| Response per BICR | All treated patients (N=137) | Patients with *EGFR* mutations (N=78) | Patients with *ALK* rearrangement (N=34) |
|---|---|---|---|
| **ORR confirmed,** n (%) [95% CI][a] | 49 (35.8) [27.8-44.4] | 34 (43.6) [32.4-55.3] | 8 (23.5) [10.7-41.2] |
| **Median DOR** (95% CI), months | 7.0 (4.2-9.8) | 7.0 (4.2-10.2) | 7.0 (2.8-8.4) |
| **DCR confirmed,** n (%) [95% CI][a] | 108 (78.8) [71.0-85.3] | 64 (82.1) [71.7-89.8] | 25 (73.5) [55.6-87.1] |
| **Median PFS,** (95% CI), months[b] | 5.4 (4.7-7.0) | 5.8 (5.4-8.3) | 4.3 (2.6-6.9) |

Data cutoff: Dec 2022

- Confirmed ORR and median PFS in all treated patients were **35.8% and 5.4 months**, respectively
- Dato-DXd had a manageable safety profile, characterized by a low incidence of hematologic or drug-related grade ≥3 toxicities
- Adjudicated drug related ILD was 5 (4%) in total and 1 (1%) for grade ≥3 (as a grade 5 event)

[a] The 2-sided 95% Cis are based on the Clopper-Pearson exact binomial method. [b] Median PFS and PFS probabilities are based on the Kaplan-Meier method. [c] Per BICR

AGA: actionable genomic alterations, BICR: blinded independent central review, BOR: best overall response, CI: confidence interval, CR: complete response, DCR: disease control rate, DOR: duration of response, ILD: interstitial lung disease, NSCLC: non-small cell lung cancer, ORR: objective response rate, PFS: progression-free survival, PR: partial response

Dato-DXd

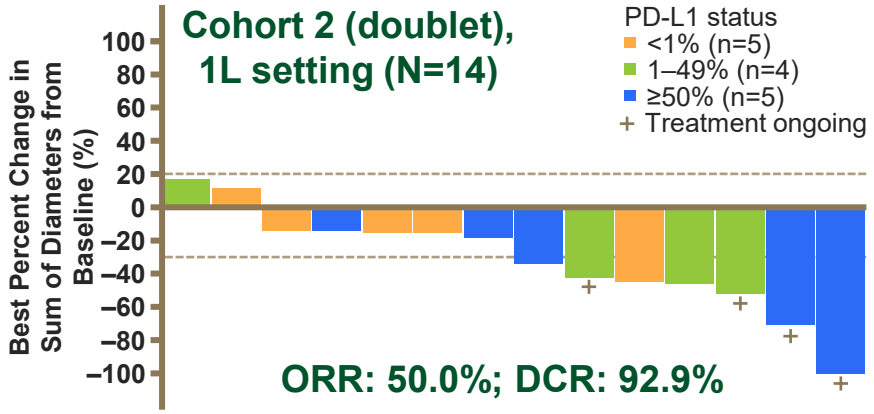
# TROPION-Lung04

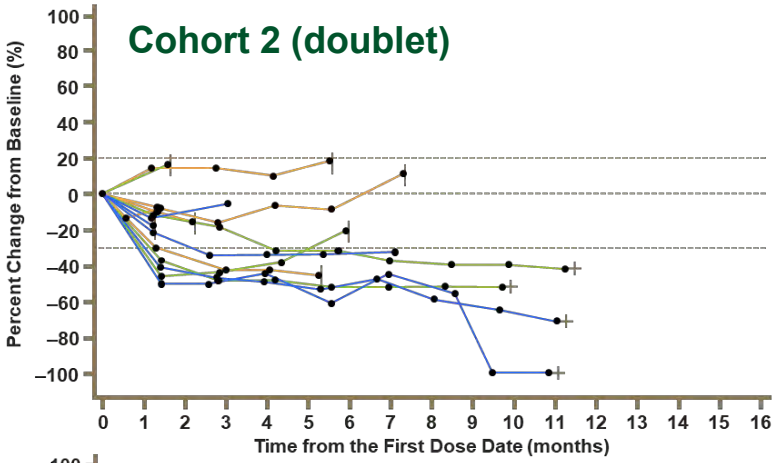
WCLC 2023

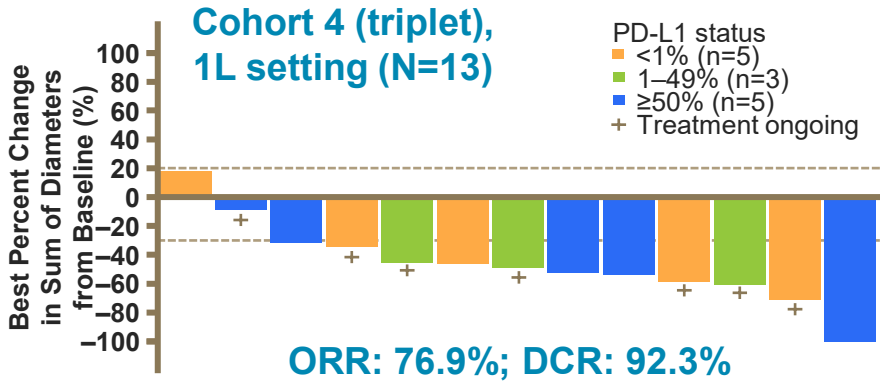
Daiichi-Sankyo

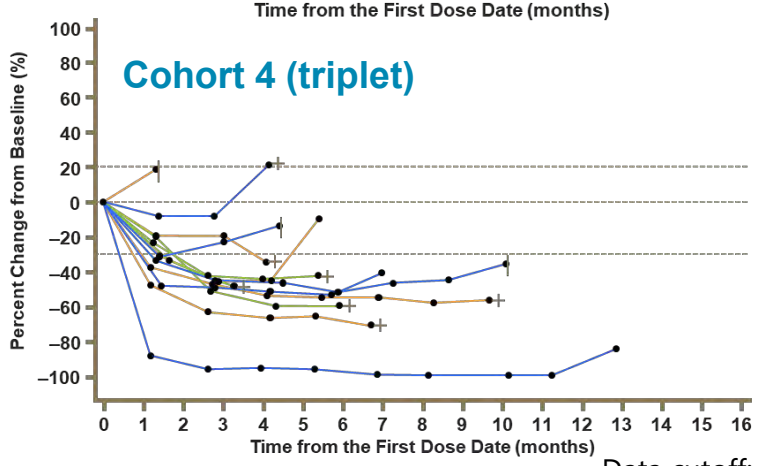
## The interim analysis data demonstrated promising ORRs with durable responses in NSCLC for both the doublet and triplet combination

### Efficacy




### TROPION-Lung04 Study

Ph1b study in NSCLC to investigate Dato-DXd in combination with immunotherapy agents ± carboplatin

- Interim analysis data of combination with durvalumab (cohort 2) and durvalumab + carboplatin (cohort 4) were reported in WCLC 2023

- In the overall population, confirmed ORR were 47.4% for cohort 2 (n=19) and 71.4% for cohort 4 (n=14). **In the 1st line setting, cORR were 50.0% for cohort 2 (n=14) and 76.9% for cohort 4 (n=13)**
- No new safety signals were observed. There were four cases of ILD; 3 cases were grade 1 or 2 and one grade 4 in cohort 2. None were grade 5.

Data cutoff: Mar 2023

DCR: disease control rate, ILD: interstitial lung disease, NSCLC: non-small cell lung cancer, ORR: objective response rate, WCLC: World Conference on Lung Cancer

Dato-DXd

# TROPION-Lung07: Study Design

## Planning to initiate new Ph3 study for PD-L1 <50% non-squamous NSCLC

### Patient Population (N≈975)

- Advanced or metastatic non-squamous NSCLC without actionable genomic alterations
- No prior systemic therapy for advanced non-squamous NSCLC
- PD-L1 <50%

R 1:1:1

Randomization

**Arm A**: Dato-DXd (6 mg/kg) + pembrolizumab+ platinum chemotherapy

**Arm B**: Dato-DXd (6 mg/kg) + pembrolizumab

**Arm C**: pembrolizumab + pemetrexed + platinum chemotherapy

| Dato-DXd NSCLC (Ph3) | Advanced 1L | Advanced 2L | Advanced 3L |
|---|---|---|---|
| NSCLC without actionable genomic alterations | **TROPION-Lung07** (PD-L1 <50%) To be initiated in FY2022 H2 | **TROPION-Lung01** (includes actionable genomic alterations) | |
| | **TROPION-Lung08** (PD-L1 ≥50%) | | |

### TROPION-Lung07 study

- Global study, open label
- Primary endpoint: PFS, OS
  Secondary endpoint: ORR, DoR, TTR, DCR, ADA, etc.

ADA: anti-drug antibody, DCR: disease control rate, DoR: duration of response, NSCLC: non-small cell lung cancer, ORR: objective response rate, OS: overall survival, PFS: progression-free survival, TTR: time to response

# TROPION-Lung08: Study Design

## Study Design and Population

**Patient population (N≈740)**

- Stage IIIB, IIIC, or IV NSCLC
- No actionable genomic alterations (documented *EGFR/ALK/ROS1* negative)
- No previous systemic therapy for adv/met NSCLC[a]
- ECOG PS 0 or 1
- Central PD-L1 TPS ≥50%

**Stratified by:**

- Histology (squamous vs non-squamous)
- Geography (East Asia vs rest of world)
- Smoking status (former/current vs never)
- ECOG PS (0 vs 1)

R 1:1

Dato-DXd 6 mg/kg IV Q3W
+
Pembrolizumab 200 mg IV Q3W

Pembrolizumab 200 mg IV Q3W

**Treatment until:**

- Occurrence of progressive disease by BICR, unacceptable toxicity, or other discontinuation criteria
- Completion of 35 cycles of pembrolizumab (no maximum limit for Dato-DXd)

adv/met, advanced/metastatic; ALK, anaplastic lymphoma kinase; BICR, blinded independent central review; Dato-DXd, datopotamab deruxtecan; ECOG PS, Eastern Cooperative Oncology Group performance status; EGFR, epidermal growth factor receptor; IV, intravenous, PD-L1, programmed cell death 1 ligand 1; Q3W, every 3 weeks; ROS1, ROS proto-oncogene 1; TPS, tumor proportion score; R, randomization.

[a] Patients who previously received neoadjuvant/adjuvant therapy without immune checkpoint inhibitors may be considered for enrollment if therapy was completed ≥6 months prior to the diagnosis of adv/met disease.

# TROPION-Lung10 study

## New Ph3 combination study of Dato-DXd and Rilvegostomig* for 1L locally-advanced or metastatic nonsquamous NSCLC

### TROPION-Lung10 study design

**Key Eligibility**

- Stage IIIB-IV nonsquamous NSCLC
- No prior treatment for advanced/ metastatic disease
- No AGA
- High PD-L1 expression (TC ≥ 50%)


■ Compare Dato-DXd in combination with Rilvegostomig or Rilvegostomig monotherapy with Pembrolizumab monotherapy

■ **Plan to start in 2024 H1**

Primary endpoint: PFS and OS in TROP2 BM+
Secondary endpoint: PFS and OS in ITT, ORR, DOR etc.

* Rilvegostomig is a PD-1/TIGIT bispecific antibody in a clinical development by AstraZeneca

AGA: actionable genetic alterations, BM: biomarker, DOR: duration of response, ITT: intention-to-treat, NSCLC: non small cell lung cancer, ORR: objective response rate, OS: overall survival, PFS: progression-free survival, q3w: every 3 weeks, TC: tumor cells

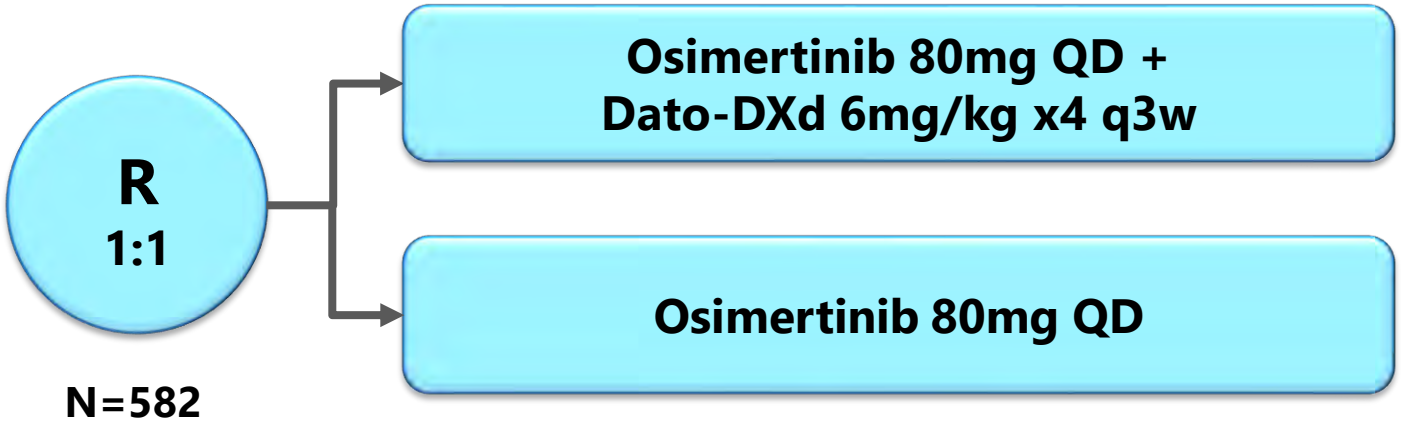
# TROPION-Lung14 study

## Started a new Ph3 study for 1L EGFR mutated, locally advanced or metastatic nonsquamous NSCLC in Apr 2024

### TROPION-Lung14 study design

**Key Eligibility**

- EGFR mutation (Ex19Del or L858R)
- Locally advanced/metastatic nonsquamous NSCLC
- No prior therapy for advanced disease




N=582

Primary endpoint: PFS by BICR
Secondary endpoint: OS, ORR, DOR, DCR, Safety, PK and Immunogenicity etc.

- Ph3 study comparing the efficacy and safety of Osimertinib mono therapy and combination of Osimertinib and Dato-DXd for 1L of **nonsquamous NSCLC with at least one EGFR mutation, Ex19Del or L858R**.

BICR: blinded independent central review, DCR: disease control ratio, DOR: duration of response, NSCLC: small cell lung cancer, ORR: objective response rate, OS: overall survival, PFS: progression-free survival, PK: pharmacokinetics , q3w: quaque 3 weeks, QD: quaque die,

Dato-DXd

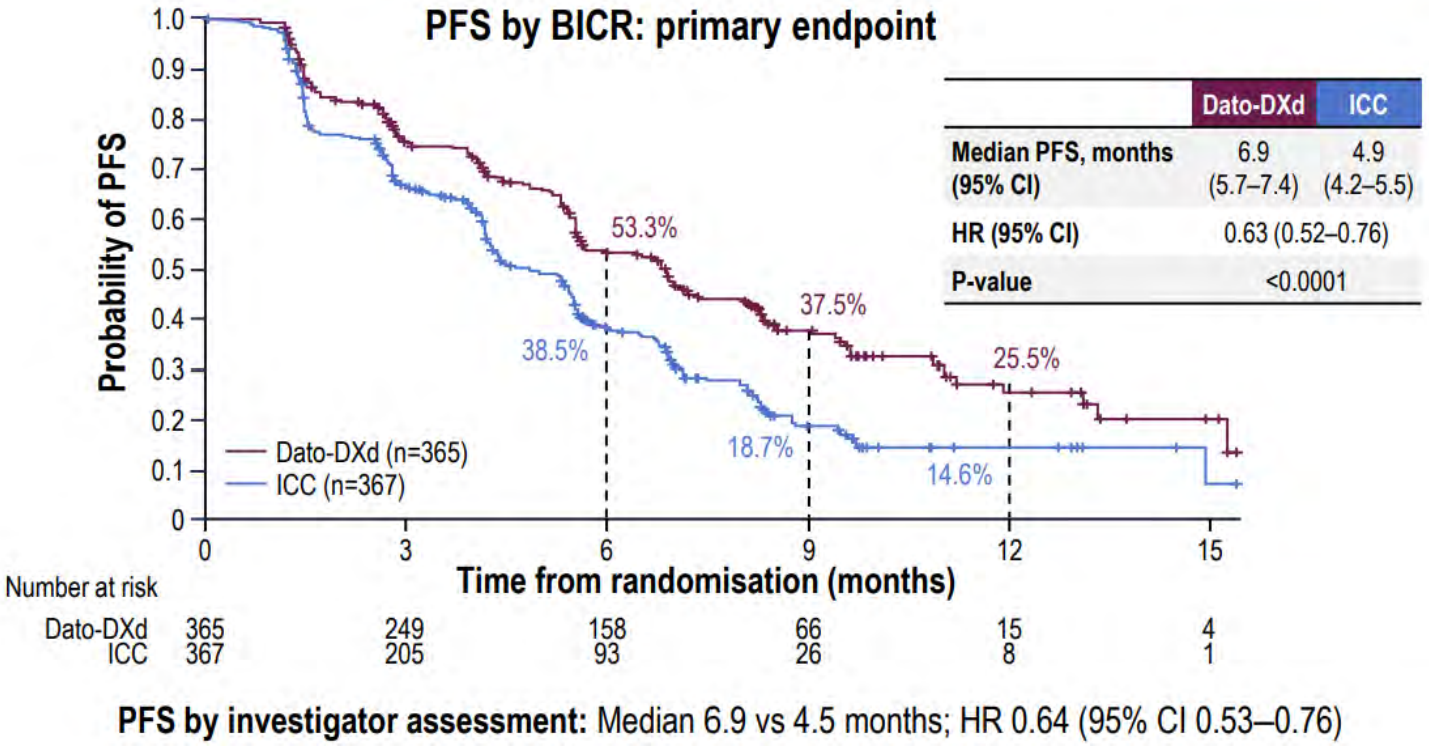
# TROPION-Breast01

ESMO 2023

Daiichi-Sankyo

## TROPION-Breast01 enables Dato-DXd to aim to set a new standard for TROP2 ADCs in HR+/HER2 low or negative BC

**PFS**




**PFS by investigator assessment:** Median 6.9 vs 4.5 months; HR 0.64 (95% CI 0.53–0.76)

Data cutoff: Jul 2023

### TROPION-Breast01 Study

- The dual primary endpoints are PFS and OS
- TLR was obtained in Sep 2023

- 63% of the patients received 1L and 37% received 2L chemotherapy prior to Dato-DXd
- **Median PFS by BICR: 6.9 months** for Dato-DXd (n=365) and 4.9 months for ICC (n=367). OS data was not mature at the point of analysis
- **Confirmed ORR: 36.4%** for Dato-DXd and 22.9% for ICC.
- Rate of grade≥3 TRAEs in the Dato-DXd group (21%) was **less than half** that in the ICC group (45%)
- **ILD rate was low; mainly grade 1/2 events**. There were one grade 3 and one grade 5 adjudicated ILD event
- **Plan to file** in the US with TROPION-Breat01 study data **within FY2023**

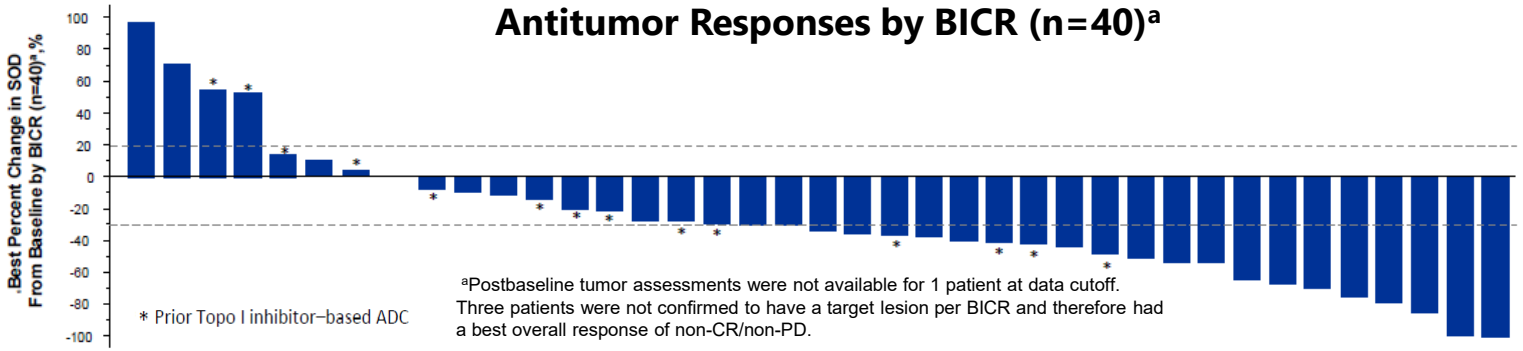
ADC: antibody-drug conjugate, BC: breast cancer, BICR: blinded independent central revie, CI: confidence interval, HR: hazard ratio, HR: hormone receptor, ICC: investigator's choice of chemotherapy, ILD: interstitial lung disease, ORR: objective response rate, PFS: progression-free survival, OS: overall survival, TLR: top line results, TRAE: treatment related adverse events

# TROPION-PanTumor01 TNBC

## SABCS 2022

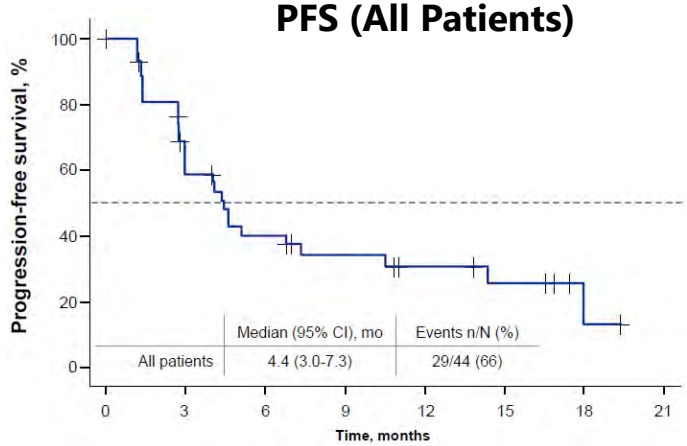
## Efficacy

### Antitumor Responses by BICR (n=40)[a]

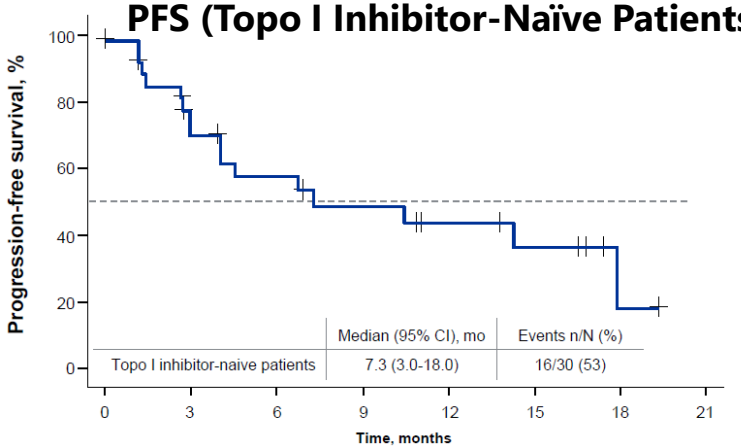



[a]Postbaseline tumor assessments were not available for 1 patient at data cutoff. Three patients were not confirmed to have a target lesion per BICR and therefore had a best overall response of non-CR/non-PD.

### PFS (All Patients)




### PFS (Topo I Inhibitor-Naïve Patients)




**Dato-DXd continues to demonstrate manageable safety profile and encouraging efficacy, that support on-going Ph3 study TROPION-Breast02 in 1L TNBC**

- ORR was 32% in all patients (n=44) and 44% in Topo I inhibitor-naïve patients (n=27) with measurable disease; mDOR was 16.8 months in both groups
- mPFS was 4.4 months in all patients and 7.3 months in Topo I inhibitor-naïve patients
- mOS was 13.5 months in all patients and 14.3 months in Topo I inhibitor-naïve patients

## Safety

- Among 44 patients, grade ≥3 TEAEs were observed in 52% of patients
- The most common TEAEs (any grade, grade ≥3) were stomatitis (73%, 11%), nausea (66%, 2%), and vomiting (39%, 5%)
- One patient experienced grade 3 decreased neutrophil count
- No cases of ILD, febrile neutropenia, or grade ≥3 diarrhea were reported
- No treatment-related deaths were observed

Data cutoff: July 22, 2022

BICR: blinded independent central review, CI: confidence interval, ILD: interstitial lung disease, mDOR: median duration of response, mOS: median overall survival, mPFS: median progression-free survival, ORR: objective response rate, PFS: progression-free survival, SABCS: San Antonio Breast Cancer Symposium, TEAEs: treatment emergent adverse events, TNBC: triple-negative breast cancer

Dato-DXd

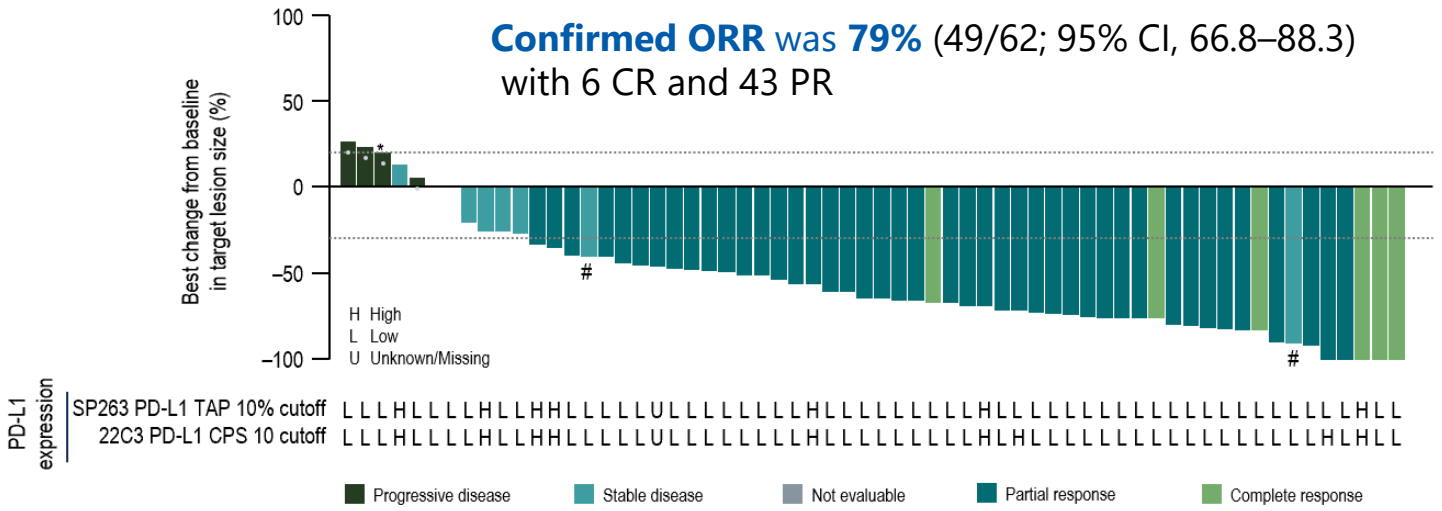
# BEGONIA Data Update

ESMO 2023

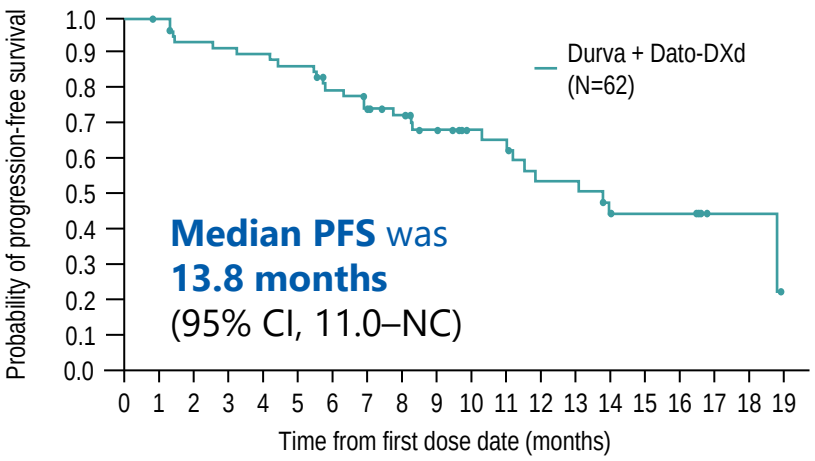
Daiichi-Sankyo

## Dato-DXd + durvalumab continues to demonstrate robust, durable responses in 1L TNBC in a biomarker-unselected population

### Objective Response




### PFS




Data Cutoff: Feb 2023

**BEGONIA (Arm 7)**

BEGONIA is open-label platform study to evaluate safety and efficacy of durvalumab combined with other novel therapies in 1L advanced/ metastatic TNBC. Combination of durvalumab and Dato-DXd is evaluated in Arm 7 and Arm 8 (PD-L1 high)

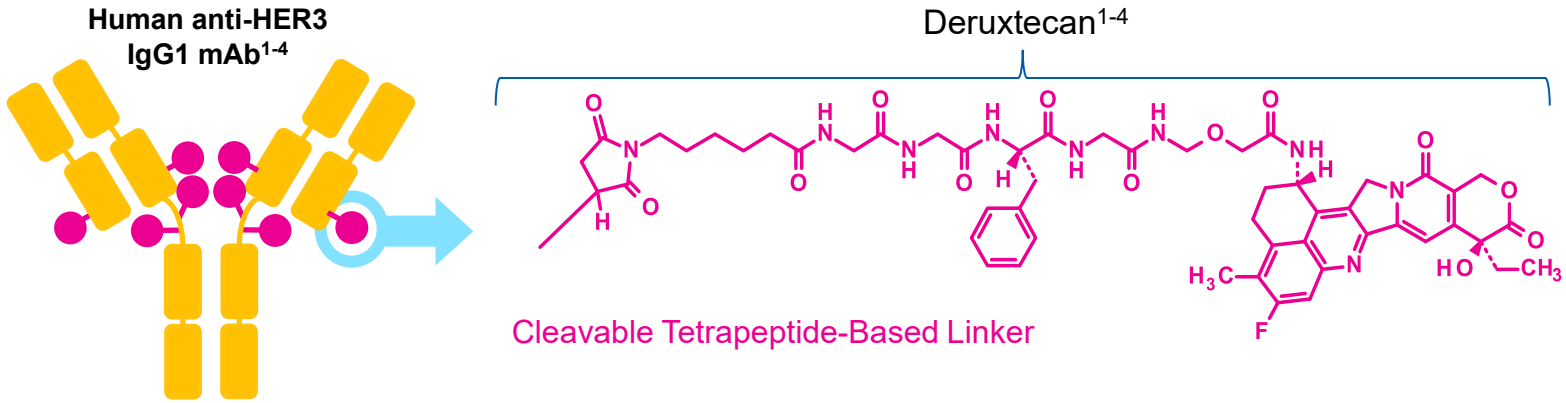
- **Confirmed ORR: 79%, median DOR: 15.5 months** and **median PFS: 13.8 months**
- Antitumor responses were observed **regardless of PD-L1 expression level**
- The most common AEs were gastrointestinal and generally of low grade
- There were 3 (5%) adjudicated treatment-related ILD/pneumonitis events (2 grade 2 events, 1 grade 1 event)

AEs: adverse events, CI: confidence interval, CR: complete response, DOR: duration of response, ILD: interstitial lung disease, NC: not calculable, ORR: objective response rate, PFS: progression-free survival, PR: partial response, TAP: tumor area positivity, TNBC: triple-negative breast cancer

# HER3-DXd

## HER3-DXd is an ADC composed of 3 components[1-4]:

- A fully human anti-HER3 IgG1 mAb (patritumab), covalently linked to:
- A topoisomerase I inhibitor payload, an exatecan derivative, via
- A tetrapeptide-based cleavable linker




[a] The clinical relevance of these features is under investigation.
[b] Based on animal data.


1. Hashimoto Y, et al. *Clin Cancer Res.* 2019;25:7151-7161.
2. Nakada T, et al. *Chem Pharm Bull (Tokyo).* 2019;67(3):173-185.
3. Ogitani Y, et al. *Clin Cancer Res*. 2016;22(20):5097-5108.
4. Koganemaru S, et al. *Mol Cancer Ther.* 2019;18:2043-2050.

# HER3 as ADC Target

Daiichi-Sankyo

## Feature 1: Dynamic expression on various cancer types

- HER3 expression is observed in several cancer tissues like breast cancer, NSCLC, colorectal cancer, ovarian cancer and melanoma

## Feature 2: Up-regulation of HER3 by pre-treatment

- HER3 upregulation related to resistance from anti-hormone, MAPKi, PI3K/AKTi therapeutic agents are observed in nonclinical / clinical studies
  - *J Steroid Biochem Mol Biol.* 2005 Feb;93(2-5):249-56.
  - *Int J Oncol.* 2007 Feb;30(2):509-20.
  - *Sci Signal.* 2014 Mar 25;7(318):ra29.

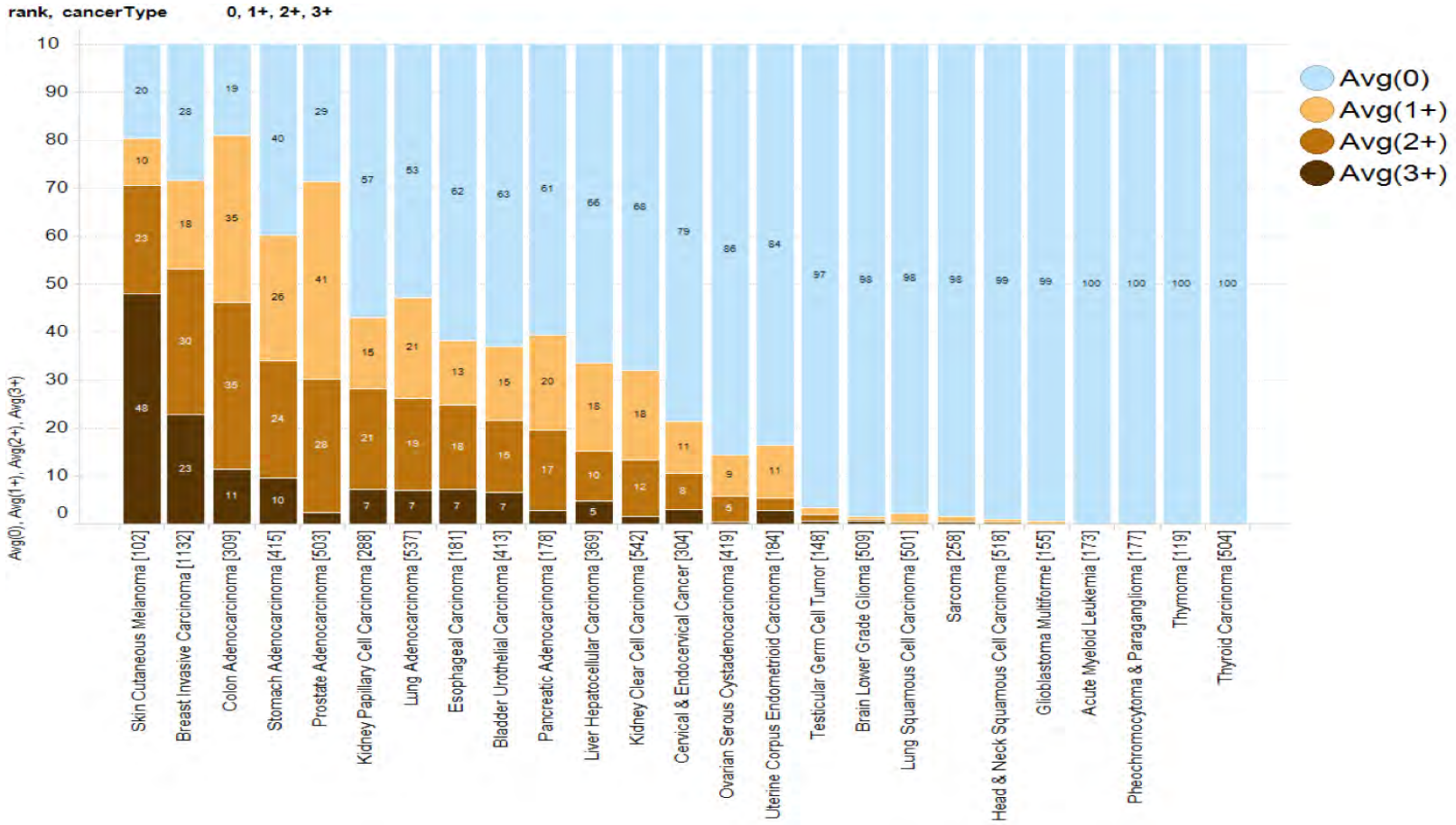
## Feature 3: Rapid and high internalization

- HER3 is well internalized into cancer cells (50-80%) comparing to EGFR or HER2

**Daiichi Sankyo renovated HER3 character as ADC target**

# HER3 Expression in Various Cancers

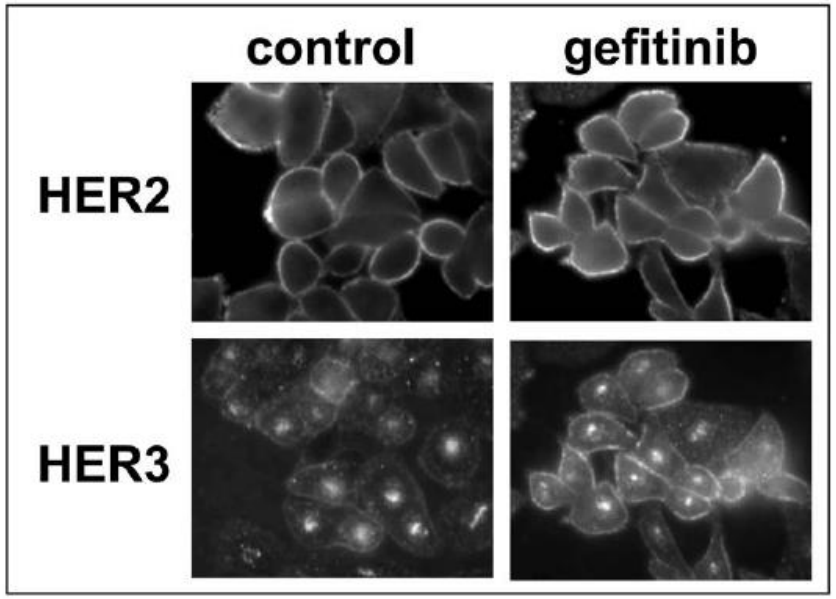
## TCGA* mRNA HER3



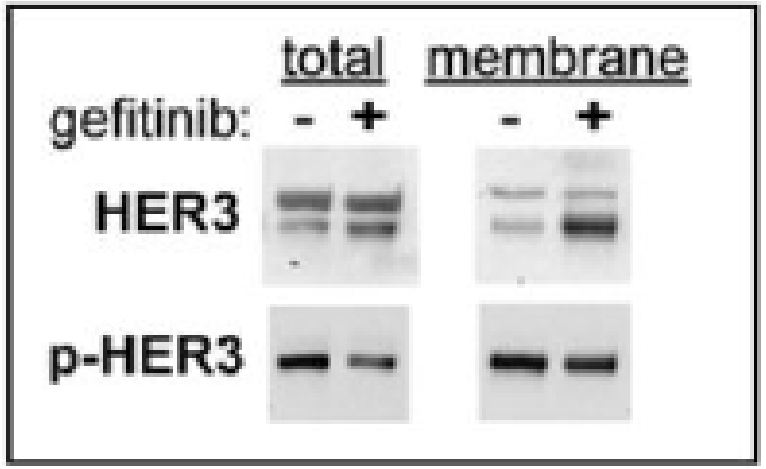

*The Cancer Genome Atlas

**High HER3 expression was observed in Melanoma, Breast, Colorectal, Lung cancer etc**

# HER3 Up-regulation by Tyrosine Kinase Inhibitor




*Nature*. 2007 January 25; 445(7126): 437–441.




- Gefitinib upregulates the total HER3 expression
- HER3 localization at membrane occurs after gefitinib treatment

**EGFR TKi promotes HER3 up-regulation**

HER3-DXd

# HERTHENA-Lung01 study

WCLC 2023

Daiichi-Sankyo

## HER3-DXd demonstrated clinically meaningful and durable efficacy in patients with EFGR-mutated NSCLC whose disease progressed after EGFR TKI and PBC

| Confirmed responses and survival | | Prior EGFR TKI (any) and PBC (N=225) | Subset with prior 3G EGFR TKI and PBC (n=209) |
|---|---|---|---|
| **cORR (95% CI), %** | | **29.8 (23.9-36.2)** | **29.2 (23.1-35.9)** |
| Best overall response (BICR), n (%) | CR | 1 (0.4) | 1 (0.5) |
| | PR | 66 (29.3) | 60 (28.7) |
| | SDa | 99 (44.0) | 91 (43.5) |
| | PD | 43 (19.1) | 41 (19.6) |
| | NEb | 16 (7.1) | 16 (7.7) |
| DCR (95% CI), % | | 73.8 (67.5-79.4) | 72.7 (66.2-78.6) |
| DOR, median (95% CI), mo | | 6.4 (4.9-7.8) | 6.4 (5.2-7.8) |
| PFS, median (95% CI), mo | | 5.5 (5.1-5.9) | 5.5 (5.1-6.4) |
| OS, median (95% CI), mo | | 11.9 (11.2-13.1) | 11.9 (10.9-13.1) |

[a] Includes non-CR/non-PD. [b] No adequate postbaseline tumor assessment (n=12); SD too early (SD <5 weeks after start of study treatment [n=4])

### HERTHENA-Lung01 Study

Registrational Ph2 study to evaluate antitumor activities of HER3-DXd in patients with EGFR mutated NSCLC previously treated with at least one EGFR TKI and PBC

- Primary endpoint is ORR, and secondary endpoints are DOR, PFS, OS etc
- FDA granted BTD in Dec 2021
- Regulatory submission in US is planned for FY2023
- The confirmatory Ph3 study HERTHENA-Lung02 study is ongoing

- Overall population: confirmed ORR 29.8%, median DOR 6.4 months, median PFS 5.5 months, median OS 11.9 months. Efficacy was observed **across diverse mechanisms of EGFR TKI resistance** and **across a broad range of pretreatment tumor HER3 membrane expression**
- The most common TEAEs were nausea, thrombocytopenia and decreased-appetite. Incidence of ILD was 5.3% and one patient experienced grade 5 ILD. Overall safety profile was manageable and consistent with previous reports

BICR: blinded independent central review, BTD: breakthrough therapy designation, CR: complete response, DOR: duration of response, ILD: interstitial lung disease, NE: not evaluable, NSCLC: non-small cell lung cancer, ORR: objective response rate, OS: overall survival, PBC: platinum-based chemotherapy, PFS: progression-free survival, PR: partial response, SD: stable disease, PD: progressive disease, TEAE: treatment emergent adverse event, TKI: tyrosine kinase inhibitor

HER3-DXd

# HERTHENA-Lung01 study – Efficacy in Brain Met

ESMO 2023

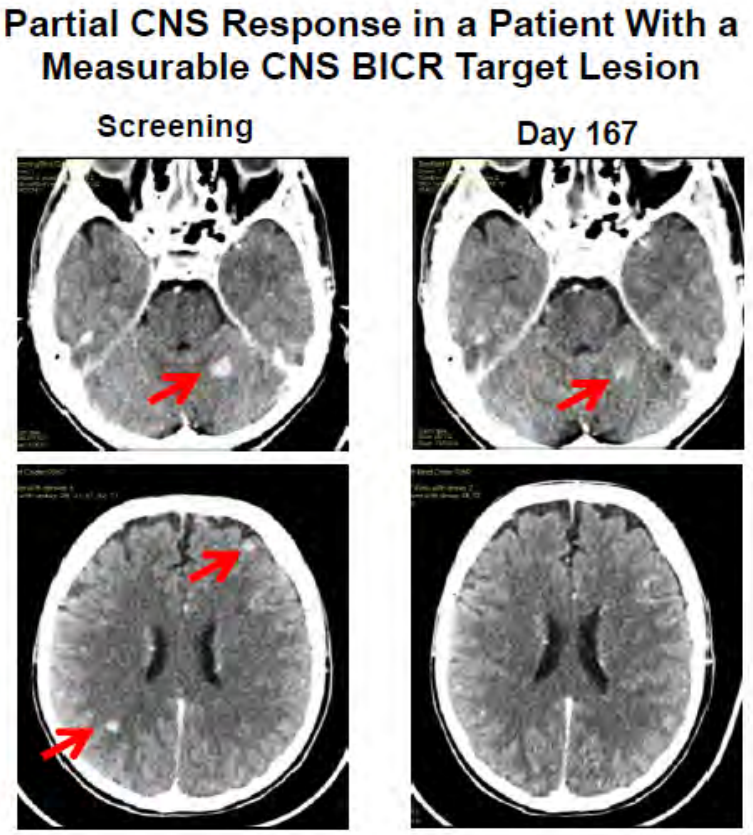
Daiichi-Sankyo

## HER3-DXd demonstrated clinically meaningful and durable intracranial responses in patients with no prior radiotherapy

### Intracranial Efficacy

| Responses by CNS BICR[a] | All patients with baseline BM by CNS BICR (n=95) | Patients whose baseline BM had not been irradiated (n=30)[b] |
|---|---|---|
| CNS cORR, n (%) [95% CI] | 19 (20.0) [12.5, 29.5] | 10 (33.3) [17.3-52.8] |
| CR, n (%) | 15 (15.8) | 9 (30.0)[c] |
| PR, n (%) | 4 (4.2) | 1 (3.3) |
| SD/non-CR/non-PD, n (%) | 57 (60.0) | 13 (43.3) |
| PD, n (%) | 13 (13.7) | 4 (13.3) |
| NE, n (%) | 6 (6.3) | 3 (10.0) |
| CNS DCR (95% CI), % | 80.0 (70.5, 87.5) | 76.7 (57.7-90.1) |
| CNS DOR, median (95% CI), mo | 9.2 (8.1-11.1) | 8.4 (5.8-9.2) |

Snapshot data cutoff, 18 May 2023.
Median study follow-up, 18.9 (range, 14.9-27.5) months.




The comparative efficacy in the CNS will be further evaluated in the randomized controlled trial HERTHENA-Lung02 study

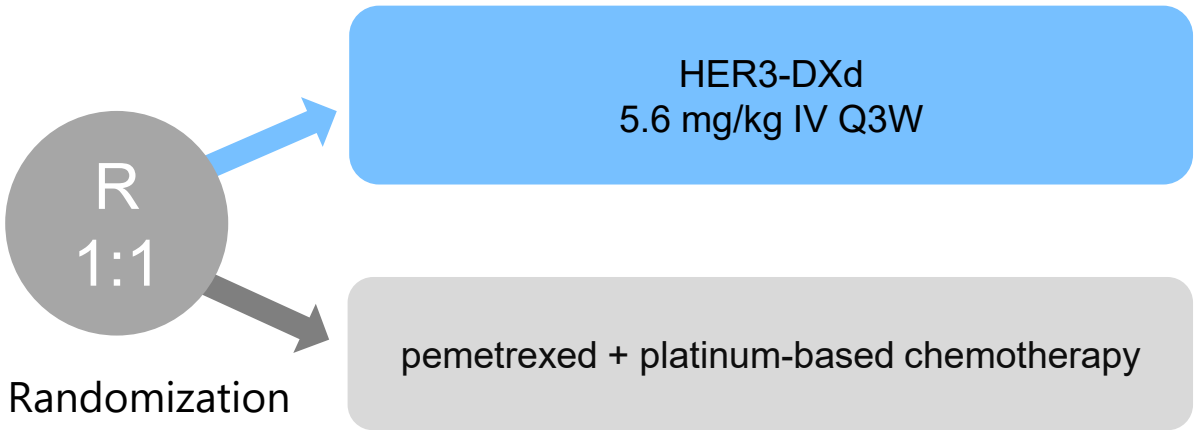
BICR: blinded independent central review, CNS: central nervous system, CR: complete response, DCR: disease control rate (CR+PR+SD), DOR: duration of response, MRI: magnetic resonance imaging, ORR: objective response rate, PD: progressive disease, PR: partial response, RECIST: Response Evaluation Criteria in Solid Tumors, SD: stable disease [a] 7 patients had measurable target lesions; 23 patients had only nontarget lesions. [b] 8 patients had only nontarget lesions. [c] Includes non-CR/non-PD.

# HERTHENA-Lung02: Study Design

## Initiated Ph3 study for post TKI EGFR mutated NSCLC patients in Aug 2022

**Patient Population (N≈560)**

- Metastatic or locally advanced non-squamous NSCLC with an EGFR-activating mutation (exon 19 deletion or L858R)
- Received 1 or 2 lines of EGFR TKI treatment including a third-generation EGFR TKI, and progression on or following treatment with a third-generation EGFR TKI




**HER3-DXd**

| NSCLC Dev. status | Advanced/metastatic 1L | Advanced/metastatic 2L | Advanced/metastatic 3L |
|---|---|---|---|
| EGFR mutated NSCLC | | **HERTHENA-Lung02** Ph3 Started in Aug 2022 | **HERTHENA-Lung01** Registrational Ph2 Started in Feb 2021 |
| | **Ph1b** Combination with osimertinib Started in Jun 2021 | | |

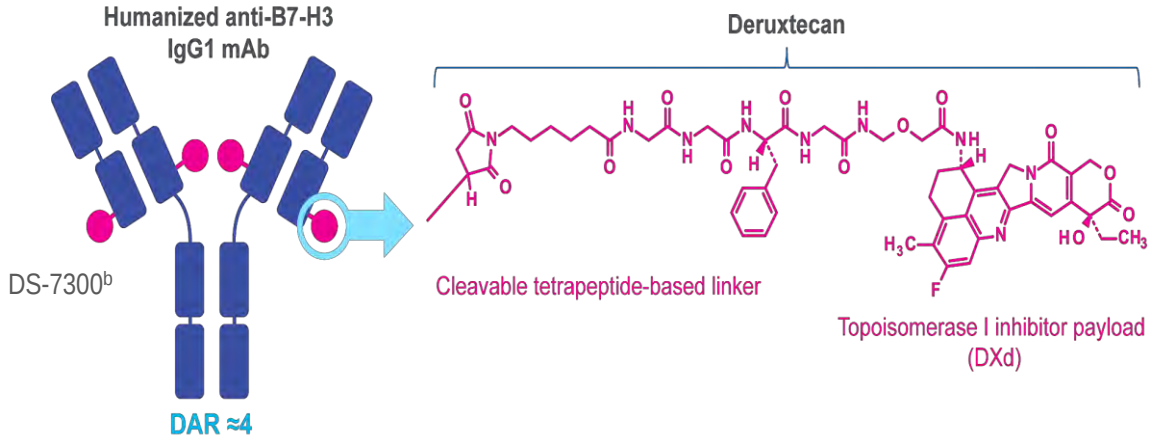
### HERTHENA-Lung02 study

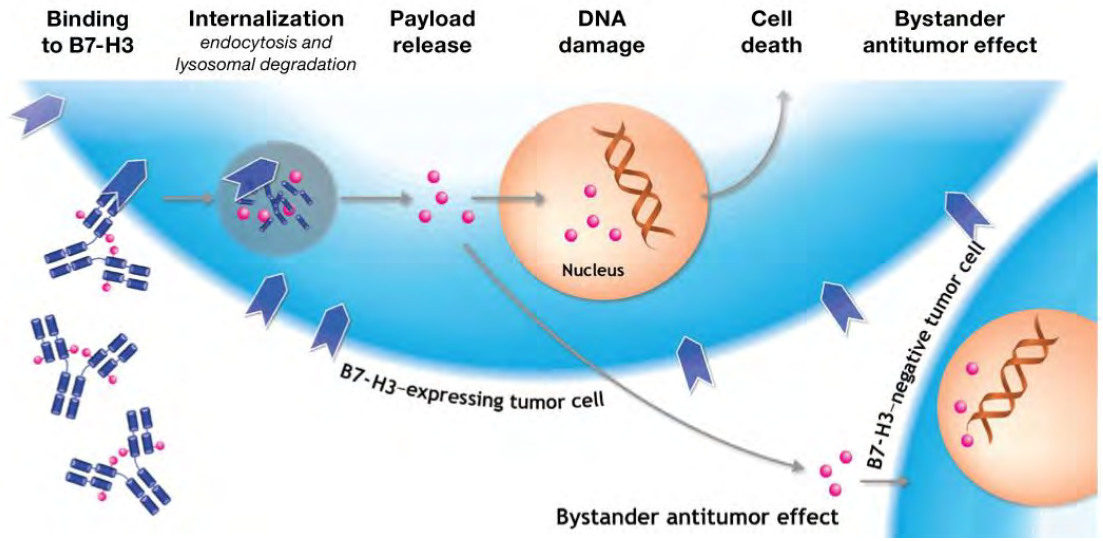
- Global study, open label
- Primary endpoint: PFS
  Secondary endpoint: OS. ORR, DoR, CBR, DCR, safety, etc.

CBR: clinical benefit rate, DCR: disease control rate, DoR: duration of response, NSCLC: non-small cell lung cancer, ORR: objective response rate, OS: overall survival, PFS: progression-free survival, TKI: tyrosine kinase inhibitor

# I-DXd (DS-7300): B7-H3 ADC

- Payload mechanism of action: topoisomerase I inhibitor [a,1-5]
- High potency of payload [a,2-5]
- Optimized drug-to-antibody ratio [a,c,1-4]
- Payload with short systemic half-life [a,c,2,3]
- Stable linker-payload [a,2,3,5]
- Tumor-selective cleavable linker [a,2-6]
- Bystander antitumor effect [a,2,7]



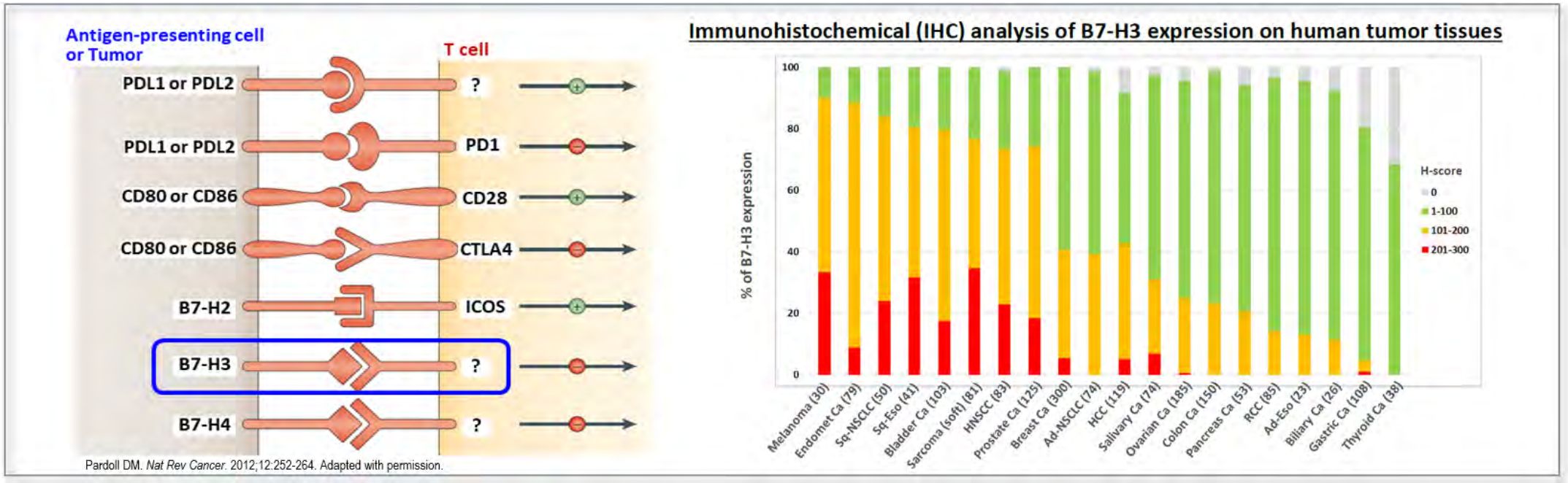




[a] The clinical relevance of these features is under investigation. [b] Image is for illustrative purposes only; actual drug-to-antibody ratio and drug positions may vary. [c] Based on animal data.

**1.** Okajima D, et al. Poster presented at: AACR-NCI-EORTC International Conference; October 26-30, 2019; Boston, MA. Abstract C026. **2.** Nakada T, et al. *Chem Pharm Bull* (Tokyo). 2019;67(3):173-185. **3.** Ogitani Y, et al. *Clin Cancer Res*. 2016;22(20):5097-5108. **4.** Hashimoto Y, et al. *Clin Cancer Res.* 2019;25(23):7151-7161. **5.** Koganemaru S, et al. *Mol Cancer Ther.* 2019;18(11):2043-2050. **6.** Haratani K, et al. *J Clin Invest.* 2020;130(1):374-388. **7.** Ogitani Y, et al. *Cancer Sci*. 2016;107(7):1039-1046.

# B7-H3 as ADC Target

- B7 homologue 3 (B7-H3, CD276) is a transmembrane protein overexpressed in various cancers, including lung, prostate, esophageal, and breast cancers, and head and neck squamous cell carcinoma (HNSCC)[1-4]
  - B7-H3 overexpression is associated with poor prognosis[1,2,4]




Ad, adenocarcinoma; Eso, esophageal cancer; HCC, hepatocellular carcinoma; HNSCC, head and neck squamous cell carcinoma; NSCLC, non-small cell lung cancer; RCC, renal cell carcinoma; Sq, squamous cell carcinoma

**1.** Yamoto M, et al. EORTC-NCI-AACR 2020. Abstract 28. **2.** Dong P, et al. *Front Oncol.* 2018;8:264. **3**. Picarda E, et al. *Clin Cancer Res.* 2016;22(14):3425-3431. **4.** Bendell JC, et al. *J Clin Oncol*. 2020;39(15 suppl 1). Abstract 2020.

DS-7300 (I-DXd)

# Ph1/2 Study Data Update

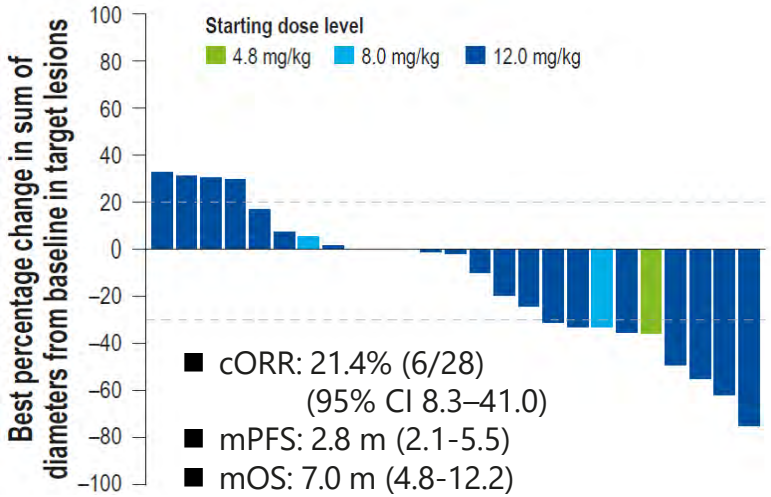
ESMO 2023

Daiichi-Sankyo

## DS-7300 continued to show durable efficacy in patients with heavily pretreated solid tumors, including ESCC, mCRPC, and sqNSCLC

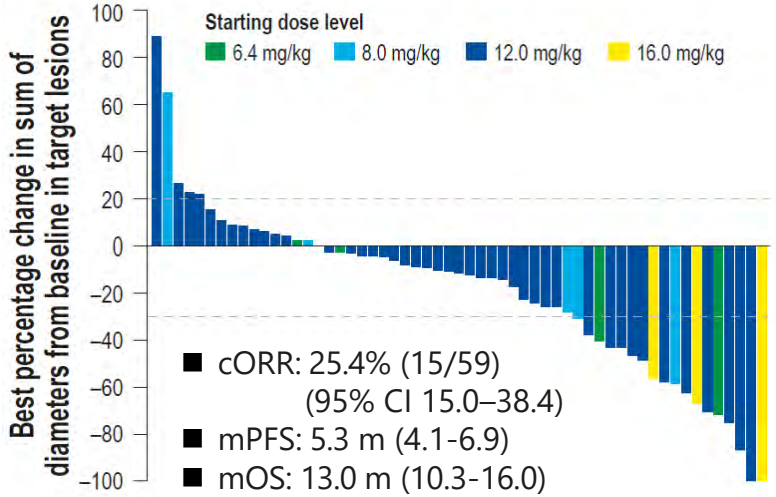
### Efficacy in selected tumor types

#### ESCC



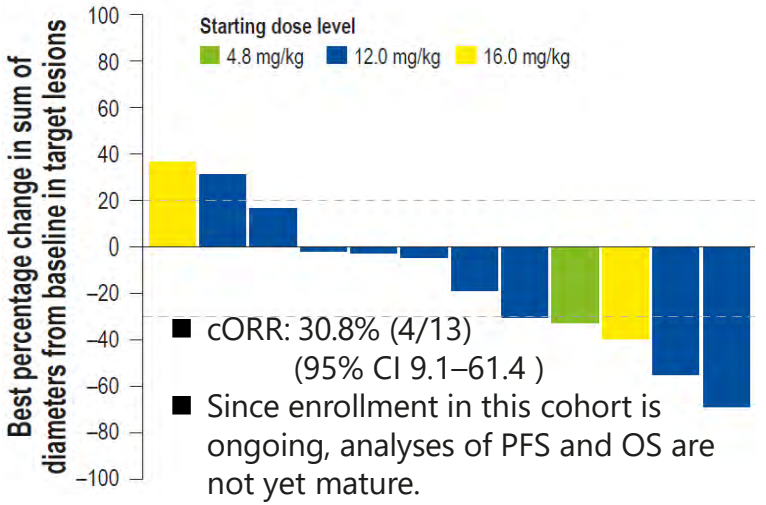

- cORR: 21.4% (6/28)
  (95% CI 8.3–41.0)
- mPFS: 2.8 m (2.1-5.5)
- mOS: 7.0 m (4.8-12.2)
- No. of prior treatments, median: 4 (1-7)

#### mCRPC*




- cORR: 25.4% (15/59)
  (95% CI 15.0–38.4)
- mPFS: 5.3 m (4.1-6.9)
- mOS: 13.0 m (10.3-16.0)
- No. of prior treatments, median: 6 (1-11)

#### sqNSCLC




- cORR: 30.8% (4/13)
  (95% CI 9.1–61.4 )
- Since enrollment in this cohort is ongoing, analyses of PFS and OS are not yet mature.
- No. of prior treatments, median: 3 (1-12)

Data cutoff: Jan 2023

- Observed safety profile was manageable and tolerable
- No new safety signals were observed, and the safety profile was consistent with previous data. The most common (≥3%) Grade ≥3 TEAEs were anemia (19.0%), neutropenia (4.0%), and nausea and lymphocyte count decreased (3.4% each)
- Incidence of ILD was consistent with the previously observed data; 10 (5.7%) confirmed cases of adjudicated ILD were observed, of which two cases were Grade ≥3 (one grade 4 in 12 mg/kg cohort and one grade 5 in 16 mg/kg cohort)

* n=73, including patients with bone metastases who were not evaluable for ORR. The ORR is calculated based on 59 patients who received ≥1 dose ≥4.8 mg/kg, had measurable disease at baseline, ≥2 postbaseline scans, and/or discontinued treatment for any reason at data cutoff.

CI: confidence interval, cORR: confirmed objective response rate, ESCC: esophageal squamous cell carcinoma, ILD: interstitial lung disease, mCRPC: metastatic castration-resistant prostate cancer, mOS: median overall survival, mPFS: median progression-free survival, NE: not estimable, OS: overall survival, PFS: progression-free survival, SCLC: small cell lung cancer, sqNSCLC: squamous non-small cell lung cancer

**DS-7300 (I-DXd)**

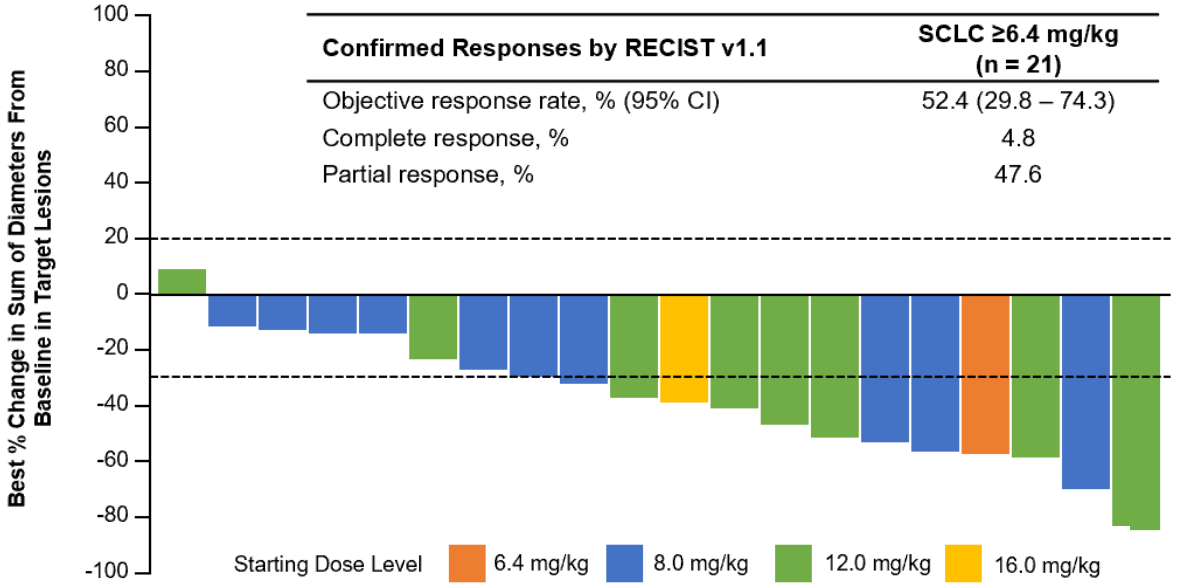
# Ph1/2 Study: SCLC subgroup analysis

WCLC 2023

Daiichi-Sankyo

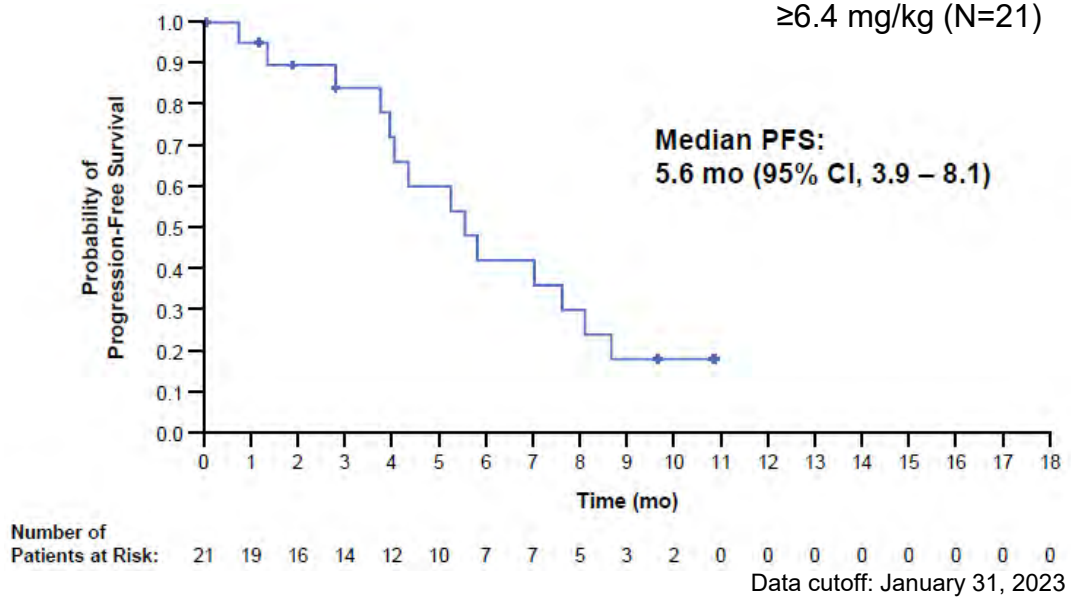
## DS-7300, a novel B7-H3-directd DXd ADC, continues to demonstrate robust and durable efficacy in patients with heavily pretreated SCLC

### ORR




| Confirmed Responses by RECIST v1.1 | SCLC ≥6.4 mg/kg (n = 21) |
|---|---|
| Objective response rate, % (95% CI) | 52.4 (29.8 – 74.3) |
| Complete response, % | 4.8 |
| Partial response, % | 47.6 |

### PFS




Data cutoff: January 31, 2023

- Median number of prior systemic treatments: 2 (range: 1-7)
- ORR 52.4% (95% CI, 29.8-74.3), mDOR 5.9 months (2.8-7.5), mPFS 5.6 months (3.9-8.1), mOS 12.2 months (6.4-NA)
- Generally well tolerated; no new safety signals and safety profile was consistent with previous reports
- Data support further development including a Ph2 of patients with extensive stage SCLC (IDeate-1)

ADC: antibody-drug conjugate, CI: confidence interval, RECIST: response evaluation criteria in solid tumors, mDOR: median duration od response, mo: months, mOS: median overall survival, mPFS: median progression free survival, ORR,: objective response rate, SCLC: small cell lung cancer

**DS-7300 (I-DXd)**

# IDeate-Lung01: ES-SCLC Ph2 study

Daiichi-Sankyo

## Patient eligibility:

- Histologically or cytologically documented ES-SCLC
- Age ≥18 years[a]
- ≥1 prior line of PBC and ≤3 prior lines of systemic therapy
- Radiologically documented PD on or after most recent prior systemic therapy
- ECOG PS 0–1
- ≥1 measurable lesion per RECIST 1.1[b]
- Patients with asymptomatic brain metastases (untreated or previously treated) are eligible

R 1:1

**Arm 1:** I-DXd 8 mg/kg Q3W (n≈40)

**Arm 2:** I-DXd 12 mg/kg Q3W (n≈40)

Extended enrollment at RP3D (n≈70 3L+)

**Stratification**:

- 2L CTFI <90 days, 2L CTFI ≥90 days, 3L or 4L
- Prior anti–PD-(L)1 treatment (yes or no)

## Primary endpoint:

- ORR by BICR[c]

## Secondary endpoints:

- DOR by BICR and inv[c]
- PFS by BICR and inv[c]
- OS
- DCR[c]
- TTR by BICR and inv[c]
- ORR by inv[c]
- Safety
- Pharmacokinetics
- Immmunogenicity

## Exploratory analysis:

- Intracranial ORR by BICR[d]

[a]Or local legal age of consent. [b]Patients must also have ≥1 lesion that has not been irradiated and is amenable to biopsy. [c]Per RECIST 1.1. [d]Per CNS RECIST.
2L, second-line; 3L+, third-line and beyond; 4L, fourth-line; BICR, blinded independent central review; CTFI, chemotherapy treatment-free interval; DCR, disease control rate; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; ES-SCLC, extensive-stage small cell lung cancer; inv, investigator; ORR, objective response rate; OS, overall survival; PBC, platinum-based chemotherapy; PD, progressive disease; PD-(L)1; programmed death (ligand) 1; PFS, progression-free survival; Q3W, every 3 weeks; R, randomization; RECIST 1.1, Response Evaluation Criteria in Solid Tumors, version 1.1; RP3D, recommended Phase 3 dose; TTR, time to response.

I-DXd

# IDeate-Lung03 study

## Plan to start combination study in 1L in FY2024 H1 to maximize the value of I-DXd in SCLC

### IDeate-Lung03 study design (N=149)

**Cohort 1**

**Part A: Maintenance Only**
Patients who completed 1L induction with 4 cycles of SOC without PD

**Part B: SOC induction + Maintenance**
Treatment naïve ES-SCLC patients

**Part A: Safety Run-in**

**Maintenance**

**I-DXd 12 mg/kg** + Atezolizumab q3w

**Part B:Dose Optimization**

**Induction**

Etoposide + Atezolizumab + Carboplatin

**R 1:1**

Patients with CR, PR or SD

**Maintenance**
Arm 1: I-DXd 8 mg/kg
Arm 2: I-DXd 12 mg/kg

**I-DXd** + Atezolizumab q3w

**Cohort 2**

**Induction + Maintenance**
Treatment naïve ES-SCLC patients

**Part A: Safety Run-in**

**Induction**

**I-DXd 8 mg/kg or 12 mg/kg** + Atezolizumab + Carboplatin q3w

**Maintenance**

**I-DXd 8 mg/kg or 12 mg/kg** + Atezolizumab q3w

**Part B: Dose Optimization**

**Induction**
Arm 3: I-DXd 8 mg/kg
Arm 4: I-DXd 12 mg/kg

**I-DXd** + Atezolizumab + Carboplatin q3w

**Maintenance**
Arm 3: I-DXd 8 mg/kg
Arm 4: I-DXd 12 mg/kg

**I-DXd** + Atezolizumab q3w

**Primary endpoint**
- Safety

**Secondary endpoint**
- PFS, ORR, DOR, etc

CR: complete response, DOR: duration of response, ES-SCLC: extensive stage small cell lung cancer, ORR: objective response rate, PD: progressive disease, PFS: progression-free survival, PR: partial response, q3w: every 3 weeks, SCLC: small cell lung cancer, SD: stable disease, SOC: standard of care

I-DXd

# Ph2 study targeting multiple solid tumors

## Started a new signal seeking Ph2 study in multiple cancers to investigate further possibility of I-DXd

### Study Design

**Population**
- Recurrent or Metastatic solid tumors
- Previously treated with one or more systemic therapy for the selected tumor indication

**N=260**
**I-DXd 12 mg/kg**

- Endometrial cancer
- SCCHN
- PDAC
- CRC
- HCC
- Ad-Eso/GEJ/GC
- Nonsquamous NSCLC
- Urothelial carcinoma

**Endpoints**

**Primary:**
ORR

**Secondary:**
safety, DOR, PFS, DCR, OS, PK, immunogenicity

Ad-Eso: esophageal adenocarcinoma, CRC: colorectal cancer, DCR: disease control rate, DOR: duration of response, GC: gastric cancer, GEJ: gastroesophageal junction, HCC: hepatocellular carcinoma, NSCLC: non-small cell lung cancer, ORR: objective response rate, OS: overall survival, PDAC: pancreatic ducatal adenocarcinoma, PFS: progression-free survival, PK: pharmacokinetics, SCCHN: squamous cell carcinoma of head and neck

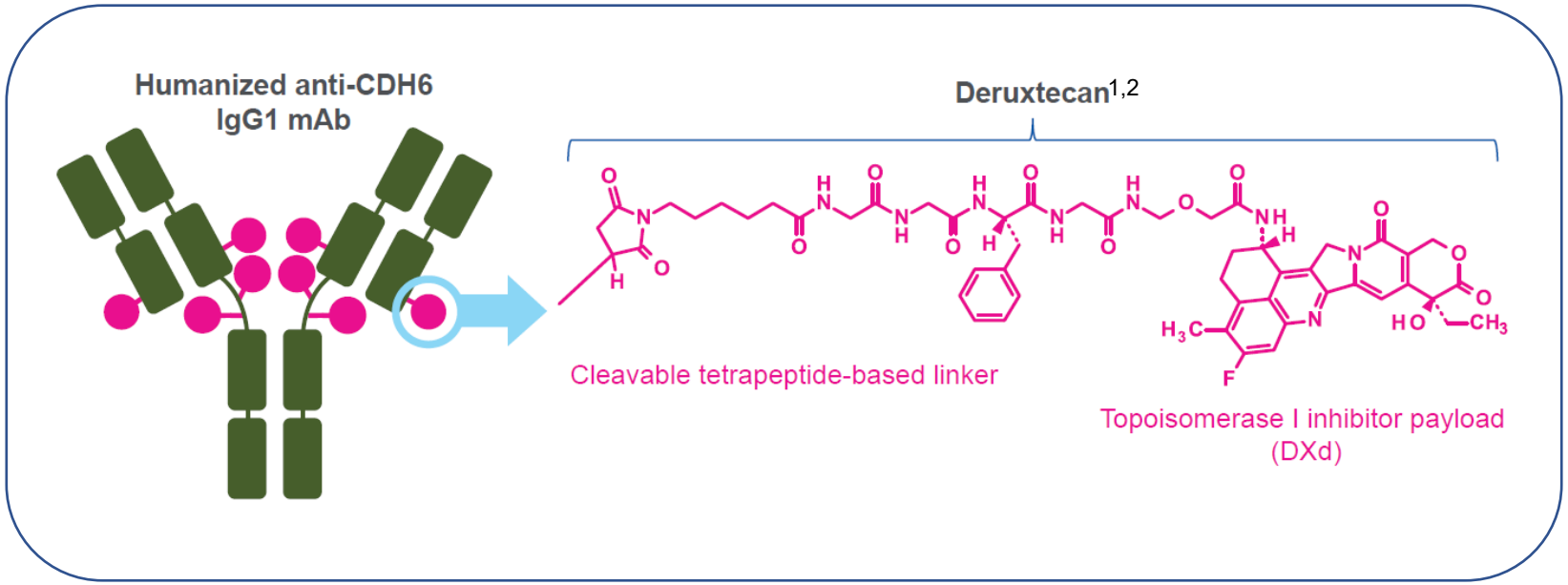
# DS-6000a Was Designed With 7 Key Attributes

## DS-6000a is a cadherin 6 (CDH6) directed ADC composed of 3 components:[1-3]

A humanized anti-CDH6 IgG1 monoclonal antibody covalently linked to:

A topoisomerase I inhibitor payload, an exatecan derivative, via

A tetrapeptide-based cleavable linker



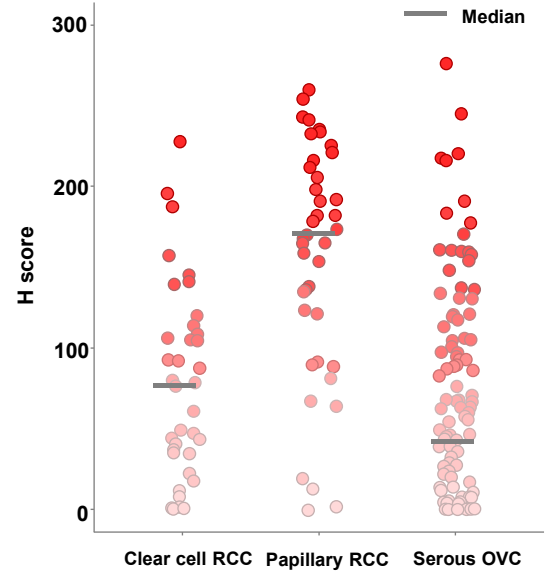

- Payload mechanism of action: topoisomerase I inhibitor [a,1,2]
- High potency of payload [a,1,2]
- High drug-to-antibody ratio ≈8 [a,1,2]
- Payload with short systemic half-life [a,b,1,2]
- Stable linker-payload [a,1,2]
- Tumor-selective cleavable linker [a,1,2]
- Bystander antitumor effect [a,1,2]

ADC, antibody-drug conjugate; DXd, a novel topoisomerase 1 inhibitor that is a derivative of exatecan; IgG1, immunoglobulin G1; mAb, monoclonal antibody.
[a] The clinical relevance of these features is under investigation. [b] Based on animal data.
**1.** Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67(3):173-185. **2.** Ogitani Y, et al. *Clin Cancer Res*. 2016;22(20):5097-5108. **3.** Ogitani Y, et al. *Cancer Sci*. 2016;107(7):1039-1046.

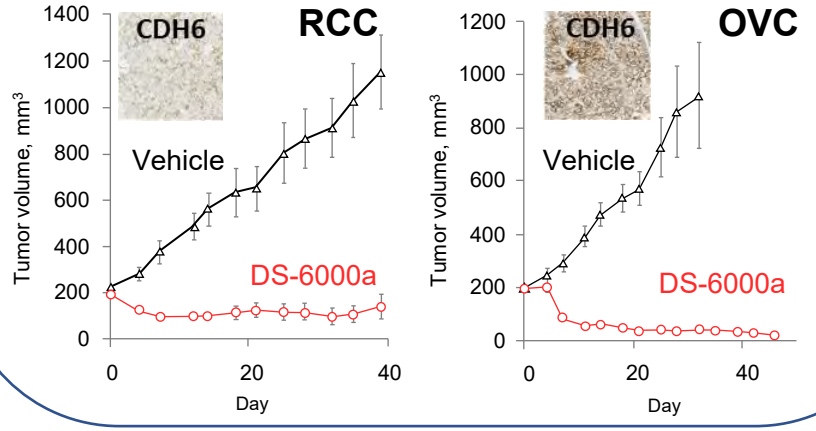
# Cadherin 6

- Cadherin 6 (CDH6) is part of the cadherin family, which is involved with cell-cell adhesion, organ development, and epithelial-mesenchymal transition
- CDH6 is found to be overexpressed in various cancers, particularly ovarian cancer (OVC) and renal cell carcinoma (RCC)[1]
- In preclinical studies, DS-6000a inhibited tumor growth and induced tumor regression in CDH6-expressing OVC and RCC[1]
- Here, we report initial results from the dose-escalation portion of a first-in-human trial in patients with advanced OVC and RCC (NCT04707248)

**CDH6 Expression in RCC/Serous OVC[1]**




**Antitumor Activity of DS-6000a in RCC and OVC PDX Model[1]**




PDX, patient-derived xenograft.

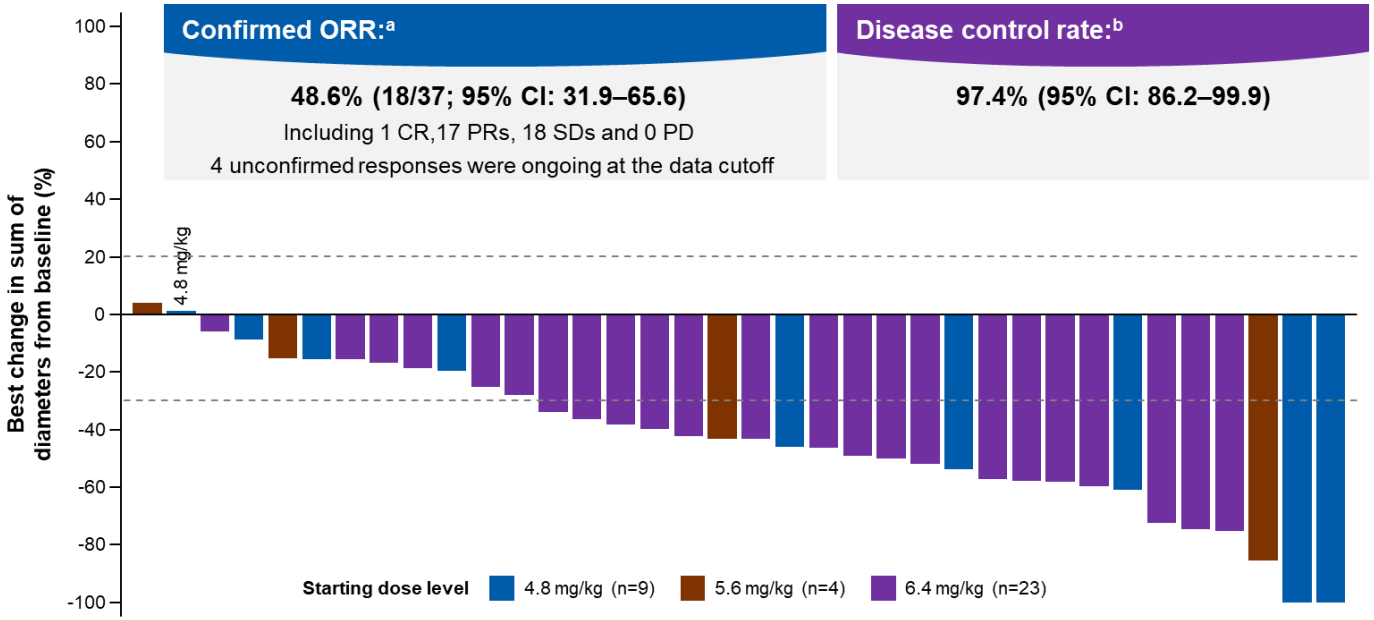
**1.** Hirokazu S, et al. ESMO 2021. Abstract 10P.

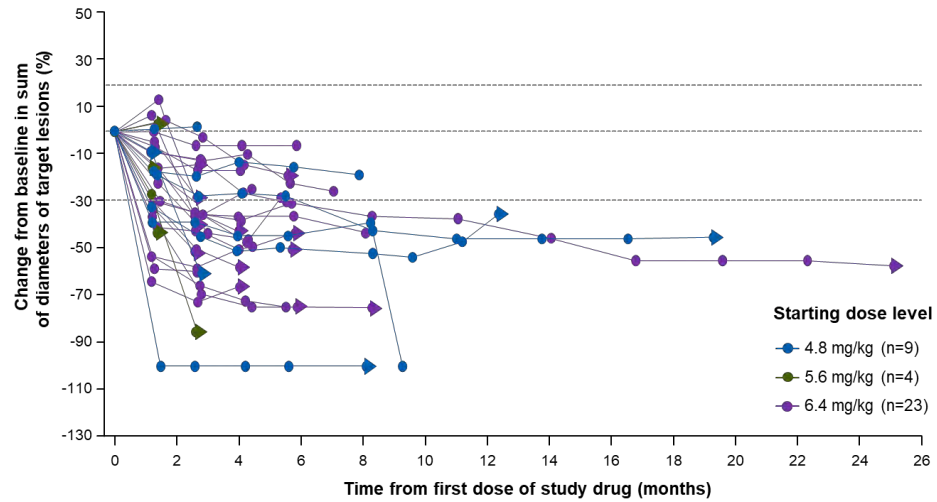
DS-6000 (R-DXd)

# Progress in FY2023

## Promising data were obtained in platinum resistant ovarian cancer and new Ph2/3 study started

### Efficacy in Ph1 study (SGO 2024)




**Median DOR:**
11.2 months (95% CI: 3.1–NE)
Median (range) FU: 6.7 months (1.4–16.8)

**Median TTR:**
5.7 weeks (95% CI: 5.3–11.4)

**Median PFS:**
8.1 months (95% CI: 5.3–NE)
Median (range) FU: 4.0 months (0–25.1)

Data Cutoff: July 2023

- DS-6000 demonstrated strong clinical activity and manageable safety profile in Ph1 study platinum resistant ovarian cancer cohort
- **REJOICE-Ovarian01 study (Ph2/3)** for platinum resistant ovarian, primary peritoneal or fallopian tube cancer **started in Apr 2024** based on the data from Ph1 study

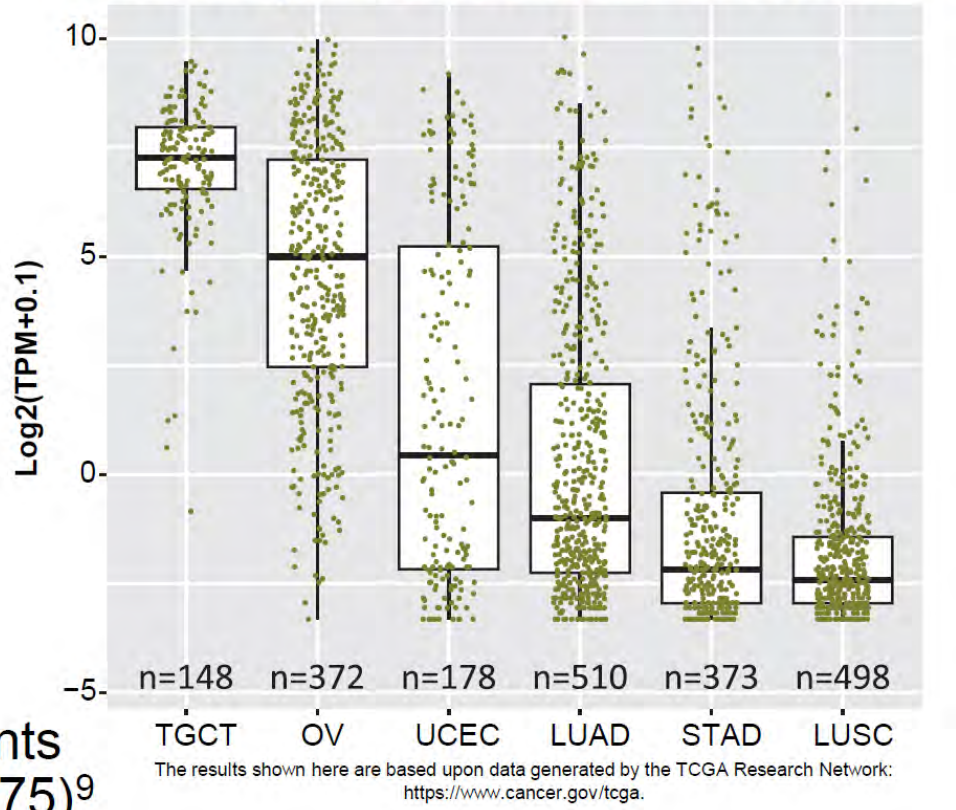
CI: confidence interval, CR: complete response, DOR: duration of response, FU: follow up, NE: not estimable, ORR: objective response rate, PD: progressive disease, PFS: progression-free survival, PR: partial response, SD: stable disease, SGO: Society of Gynecologic Annual Meeting on Women's Cancer, TTR: time to response

DS-9606

# Background

- **DS-9606 is an ADC composed of[1]:**
  - Humanized anti-CLDN6 mAb
  - Cleavable linker
  - Modified PBD payload
- **CLDN6**
  - Important component of cell-to-cell tight junctions[2]
  - Plays a role in the regulation of epithelial and endothelial cell proliferation and differentiation[2]
  - Nearly absent in normal adult tissue but expressed in several tumor types, including ovarian, endometrial, and gastric cancers, GCTs, and NSCLC[3–8]
  - Can be associated with poor prognosis[7]
- First report from an ongoing Phase 1 trial of DS-9606 in patients with locally advanced or metastatic solid tumors (NCT05394675)[9]

**CLDN6 expression in select solid tumors**




The results shown here are based upon data generated by the TCGA Research Network: https://www.cancer.gov/tcga.

ADC, antibody–drug conjugate; CLDN6, Claudin 6; GCT, germ cell tumor; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; mAb, monoclonal antibody; NSCLC, non-small cell lung cancer; OV, ovarian serous cystadenocarcoma; PBD, pyrrolobenzodiazepine; STAD, stomach adenocarcinoma; TCGA, The Cancer Genome Atlas; TGCT, testicular GCT; TPM, transcripts per million; UCEC, uterine corpus endometrial carcinoma.

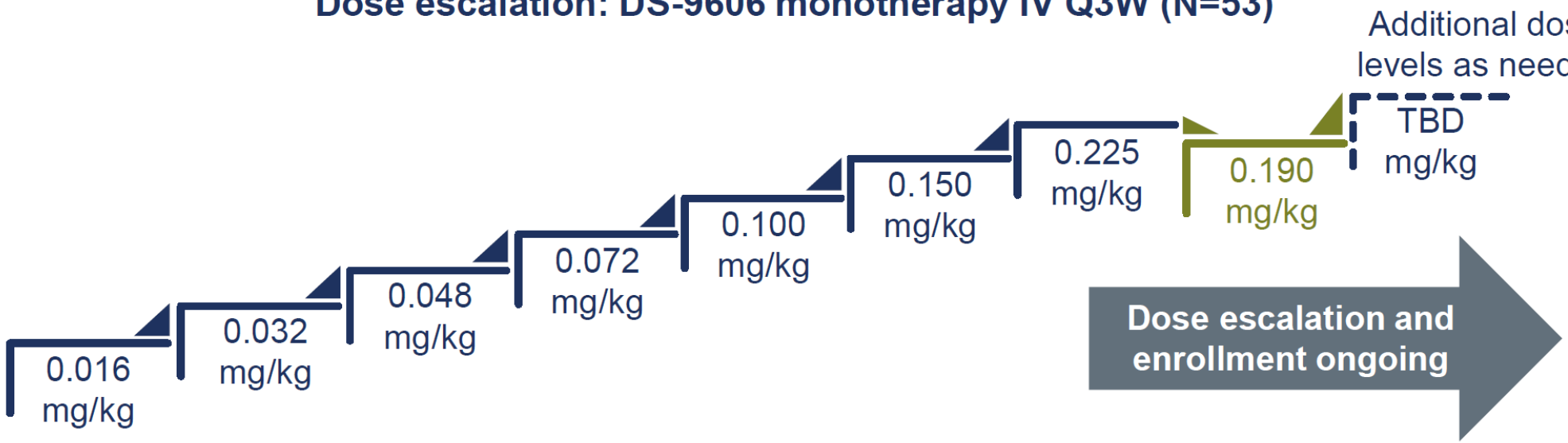
1. Data on file. Daiichi Sankyo, Inc. DS9606-137 protocol, version 6; 2023. 2. Du H, et al. *Mol Med Rep*. 2021;24:677. 3. Wang L, et al. *Diagn Pathol*. 2013;8:190. 4. Ushiku T, et al. *Histopathology*. 2012;61:1043–1056. 5. Kojima M, et al. *Cancers (Basel)*. 2020;12:2748. 6. Micke P, et al. *Int J Cancer*. 2014;135:2206–2214. 7. Zhang C, et al. *Front Cell Dev Biol*. 2021;9:726656. 8. Yu S, et al. *Cell Death Dis*. 2019;10:949. 9. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT05394675. Accessed August 15, 2024.

DS-9606

# First-in-human Phase 1 study of DS-9606

## Preliminary safety and efficacy analysis of dose-escalation

### Dose escalation: DS-9606 monotherapy IV Q3W (N=53)




**Key enrollment criteria:**

- Adults with locally advanced or metastatic solid tumors known to express CLDN6 (CLDN6 expression was not required for selection[a])
- PD with SOC treatment for metastatic disease (any number of prior LOTs)
- ECOG PS 0–1
- No prior CLDN6-targeted agents or ADCs that deliver a PBD payload
- Adequate cardiac and pulmonary function, including no history of or current ILD/pneumonitis

**Data cutoff: June 14, 2024**

[a]Archived tumor tissue, or fresh tumor biopsy if archived tissue was not available, was tested retrospectively; patients with GCTs without archived tumor tissue may be allowed with medical monitor approval.

ADC, antibody–drug conjugate; CLDN6, Claudin 6; ECOG PS, Eastern Cooperative Oncology Group performance status; GCT, germ cell tumor; ILD, interstitial lung disease; IV, intravenous; LOT, line of therapy; PBD, pyrrolobenzodiazepine; PD, progressive disease; Q3W, every 3 weeks; SOC, standard-of-care; TBD, to be determined.

1. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT05394675. Accessed August 15, 2024. 2. Data on file. Daiichi Sankyo, Inc. DS9606-137 protocol, version 6; 2023.

DS-9606

# Safety: Overview of TEAEs and related TEAEs

Daiichi-Sankyo

- 45 patients (84.9%) had TEAEs; 28 patients (52.8%) had related TEAEs
- No treatment withdrawals due to related TEAEs; related TESAEs occurred at the highest dose level
- No DLTs to date; MTD and RDE not yet determined

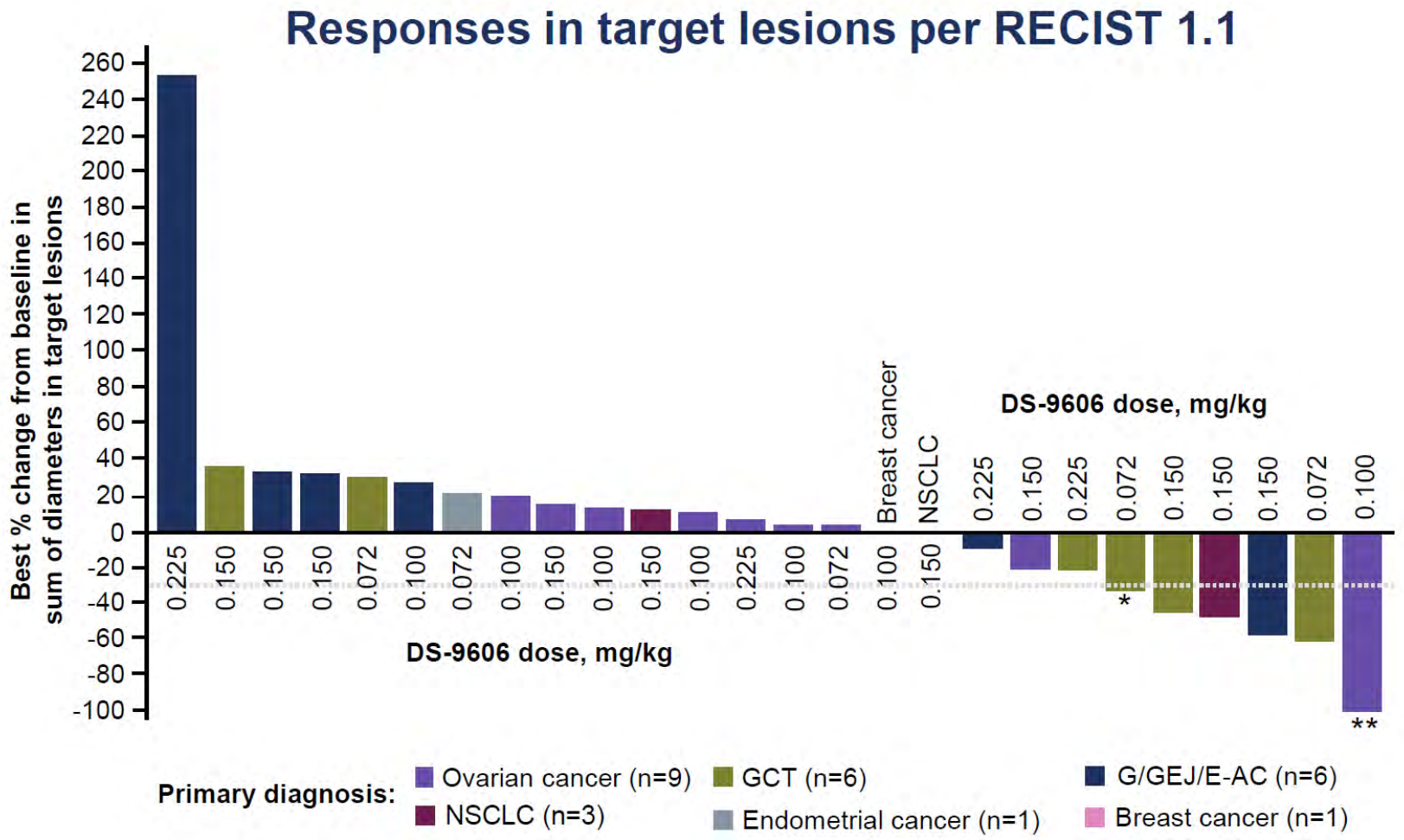
| DS-9606 dose, mg/kg | 0.016 (n=3) | 0.032 (n=7) | 0.048 (n=7) | 0.072 (n=6) | 0.100 (n=7) | 0.150 (n=14) | 0.190 (n=3) | 0.225 (n=6) | Total (N=53) |
|---|---|---|---|---|---|---|---|---|---|
| **TEAEs, n with event (%)** | | | | | | | | | |
| **Any grade** | 3 (100.0) | 6 (85.7) | 7 (100)[a] | 6 (100) | 5 (71.4) | 13 (92.9) | 1 (33.3) | 4 (66.7) | 45 (84.9) |
| Related | 0 | 5 (71.4) | 5 (71.4)[a] | 4 (66.7) | 2 (28.6) | 8 (57.1) | 0 | 4 (66.7) | 28 (52.8) |
| **Grade ≥3** | 1 (33.3) | 2 (28.6) | 3 (42.9) | 2 (33.3) | 2 (28.6) | 4 (28.6) | 0 | 2 (33.3) | 16 (30.2) |
| Related | 0 | 1 (14.3) | 1 (14.3) | 0 | 0 | 0 | 0 | 1 (16.7) | 3 (5.7) |
| **Serious[b]** | 1 (33.3) | 1 (14.3) | 3 (42.9) | 2 (33.3) | 2 (28.6) | 4 (28.6) | 0 | 3 (50.0) | 16 (30.2) |
| Related | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 (33.3) | 2 (3.8) |
| **Associated with:** | | | | | | | | | |
| Treatment interruption | 0 | 2 (28.6)[c] | 2 (28.6) | 2 (33.3) | 0 | 2 (14.3) | 0 | 1 (16.7) | 9 (17.0) |
| Related | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (16.7) | 1 (1.9) |
| Dose reduction | 0 | 0 | 1 (14.3)[a] | 0 | 0 | 1 (7.1) | 0 | 1 (16.7) | 3 (5.7) |
| Related | 0 | 0 | 1 (14.3)[a] | 0 | 0 | 1 (7.1) | 0 | 1 (16.7) | 3 (5.7) |
| Treatment withdrawal | 0 | 0 | 0 | 0 | 0 | 1 (7.1) | 0 | 0 | 1 (1.9) |
| Related | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Death | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

**Data cutoff: June 14, 2024**

[a]One intra-patient dose escalation (IPDE), with the patient receiving DS-9606 0.048 mg/kg from Cycle 1–10, 0.100 mg/kg from Cycle 11–14, and then 0.048 mg/kg from Cycle 15 through end of treatment. Dose reduction occurred at 0.100 mg/kg. Per the protocol, IPDE was allowed if the investigator determined IPDE was favorable from a benefit–risk standpoint; the patient had completed at least 6 cycles of treatment at the current dose level; no Grade ≥3 related TEAEs or any AE leading to dose reduction were observed at the current dose level; the totality of the patient's available data had been reviewed by the medical monitor; and the sponsor had granted approval. [b]Per the protocol, AEs were considered serious if they resulted in any of death, a life-threatening AE, inpatient hospitalization of ≥24 hours or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, a congenital anomaly/birth defect, or an important medical event. [c]Includes 1 IPDE, with the patient receiving DS-9606 0.032 mg/kg from Cycle 1–23, 0.048 mg/kg from Cycle 24–25, and 0.032 mg/kg from Cycle 26 through end of treatment. AE, adverse event; DLT, dose-limiting toxicity; IPDE, intra-patient dose escalation; MTD, maximum tolerated dose; RDE, recommended dose for expansion; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

DS-9606

# Preliminary efficacy[a]: All tumor types




- Confirmed objective responses seen across tumor types (RECIST 1.1)
  - GCT, n=2
  - G/GEJ/E-AC, n=1
  - NSCLC, n=1
  - Response highest with 0.150 mg/kg (3/12[b] patients)

**Data cutoff: June 14, 2024**

[a]DS-9606 doses ≥0.072 mg/kg, except 0.190 mg/kg due to immature data. [b]Includes only 12 of 14 patients; patients were included if they had ≥2 post-baseline scans and/or had discontinued treatment for any reason.
*Patient did not have confirmed PR due to new lesion observed at disease assessment. **Patient did not have a confirmed PR due to progression at subsequent assessment.

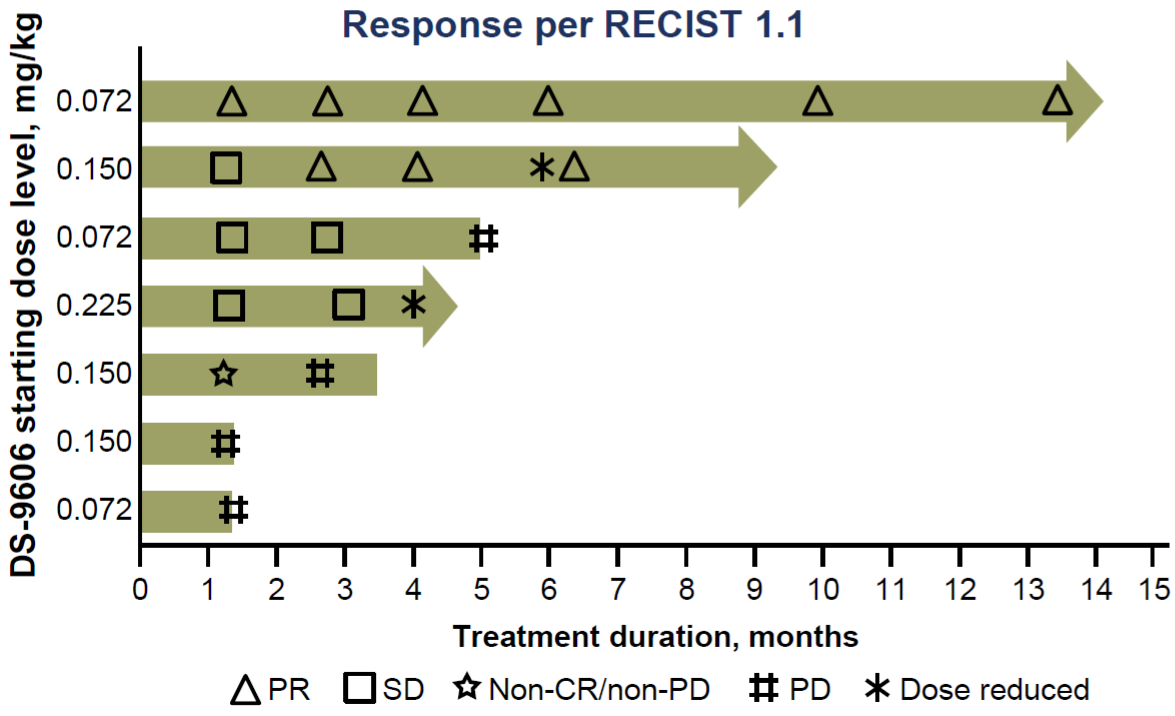
GCT, germ cell tumor; G/GEJ/E-AC, gastric/gastroesophageal junction/esophageal adenocarcinoma; NSCLC, non-small cell lung cancer; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumours, version 1.1.

DS-9606

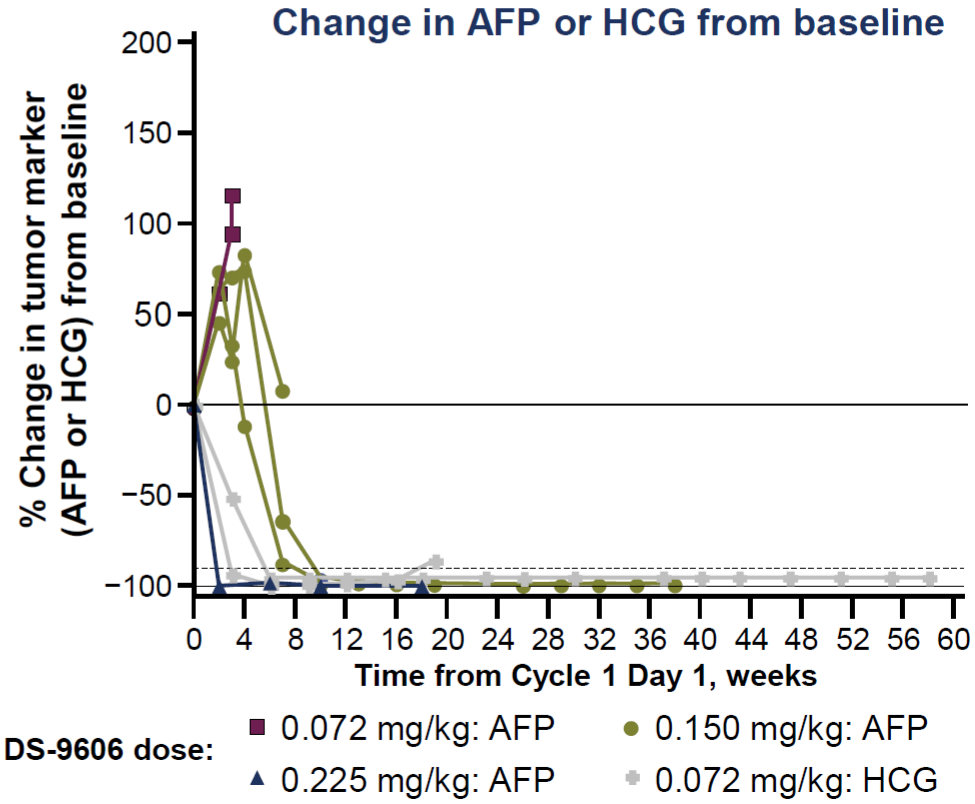
# Preliminary efficacy[a]: GCT responses

## Responses in patients with GCTs who were heavily pretreated/refractory to prior treatment

- 2/7 patients had PR as best response (RECIST 1.1) and remained on treatment >6 months




- 5/7 patients had ≥90% reduction in tumor markers

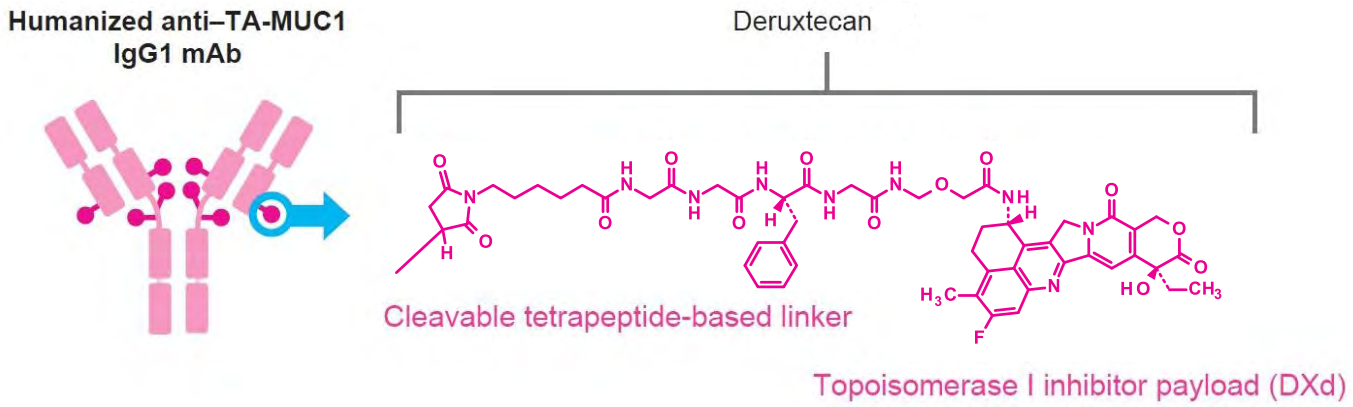



**Data cutoff: June 14, 2024**

[a]DS-9606 doses ≥0.072 mg/kg, excluding 0.190 mg/kg due to lack of efficacy data availability.

AFP, alpha-fetoprotein; CR, complete response, GCT, germ cell tumor; HCG, human chorionic gonadotropin; PD, progressive disease; PR, partial response; SD, stable disease.

# DS-3939 is the 6th DXd ADC and Directed Against TA-MUC1




## What is TA-MUC1?

- MUC1 is a transmembrane glycoprotein that is highly glycosylated in normal tissues and is localized to the apical membrane of epithelial surfaces.
- In cancers, MUC1 loses cell polarity and is redistributed over the cell surface and within the cytoplasm. Glycosylation of MUC1 is dysregulated in cancers and predominantly modified with shorter glycans, leading to the emergence of aberrantly glycosylated MUC1, known as tumor-associated MUC1 (TA-MUC1).
- TA-MUC1 is overexpressed in **broad range of tumors** including NSCLC, BC, UC, OVC, BTC and PDAC

## DS-3939 features

- High drug-to-antibody ratio ≈8
- DS-3939 specifically binds to TA-MUC1 by recognizing both the tumor specific glycan and backbone peptide moieties
- DS-3939 exhibited tumor regression against various preclinical in vivo models and also induced tumor regression after treatment of other FDA approved ADCs in xenograft model

BC; breast cancer, BTC: biliary tract cancer, FDA: Food and Drug Association, NSCLC: non-small cell lung cancer, OVC: ovarian cancer, PDAC: Pancreatic invasive ducatal adenocarcinoma, UC: urothelial cancer

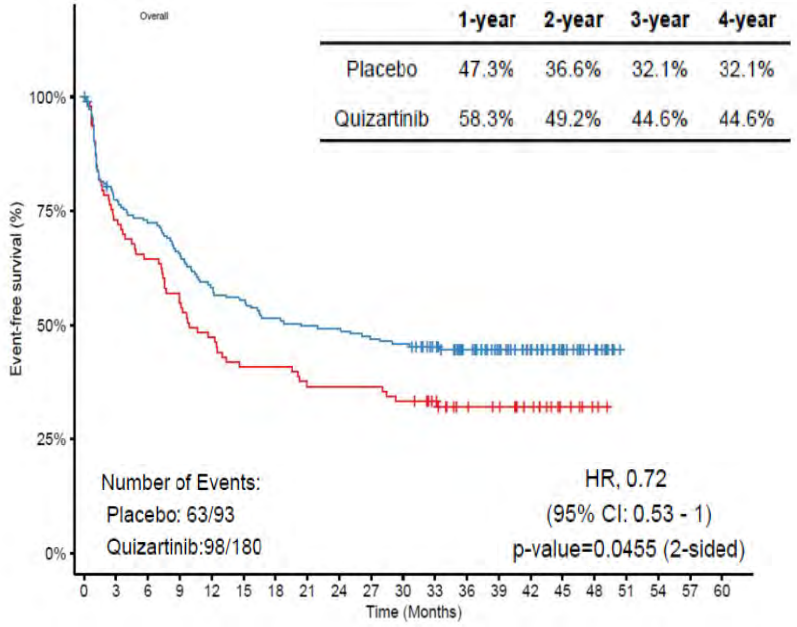
# Final Results of Ph2 PETHEMA-QUIWI study

ASH 2024

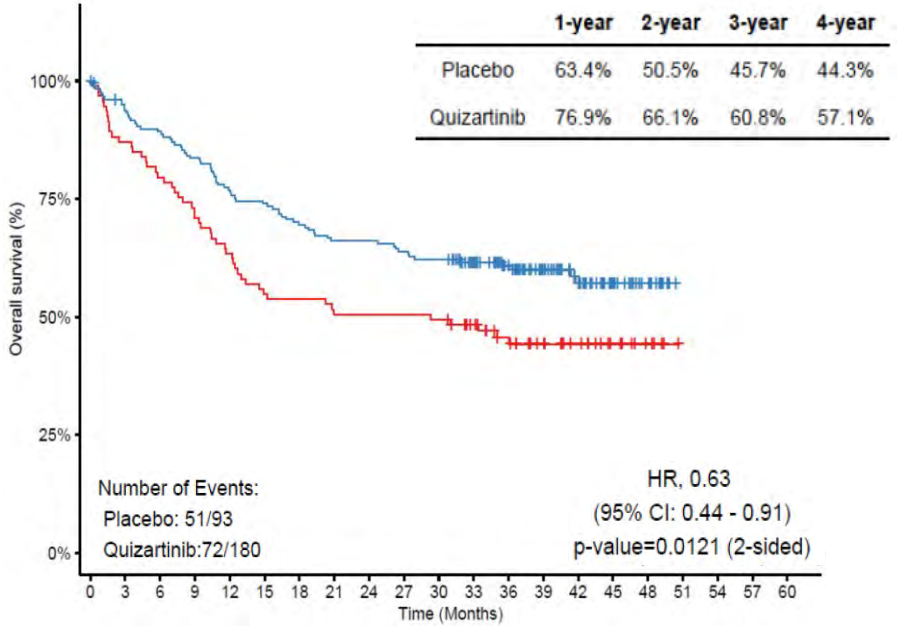
Daiichi-Sankyo

## Data supports indication expansion potential of VANFLYTA® to newly diagnosed *FLT3*-ITD negative AML

### ■ Primary Endpoint: EFS




### ■ Secondary Endpoint: OS




### ■ Secondary Endpoint: CR/CRi

CR/CRi rate after 2 cycles was 77.2% in the VANFLYTA® arm and 76.3% in the placebo arm

### ■ Secondary Endpoint: Safety

No new safety signals were observed among VANFLYTA® and placebo arms

AML: acute myeloid leukemia, ASH: American Society of Hematology, CR: complete remissions, CRi: complete remissions with incomplete recovery, EFS: event-free survival, HR: hazard ratio, OS: overall survival

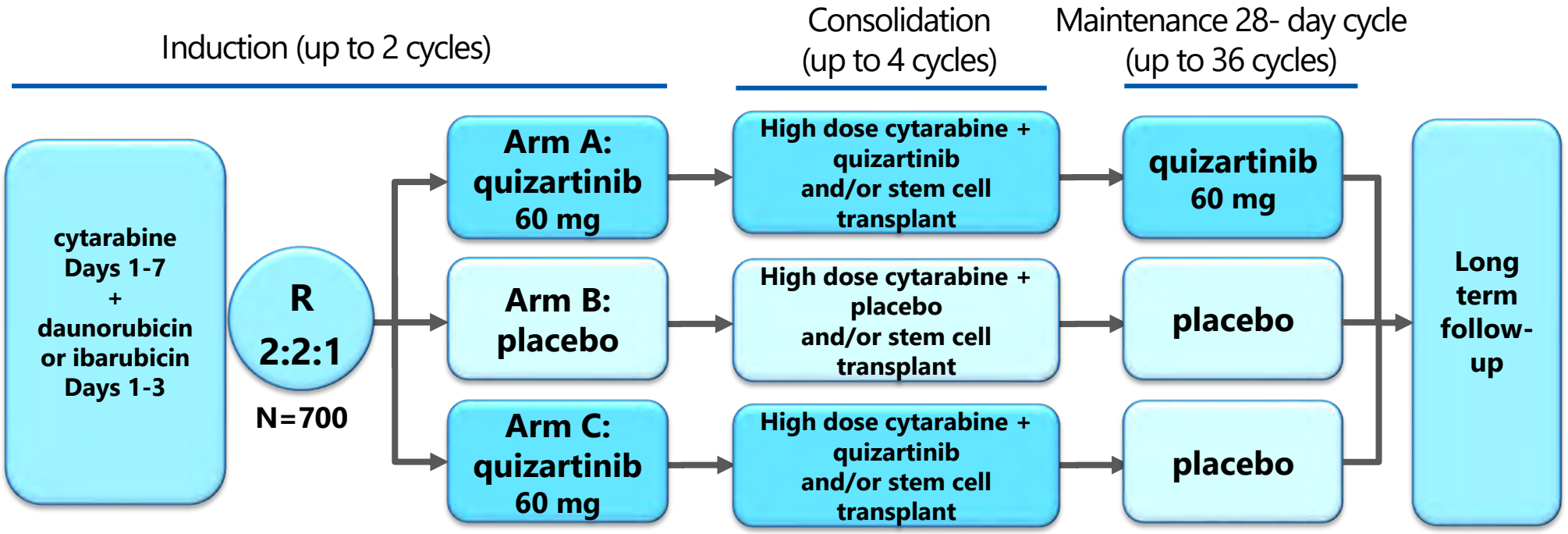
VANFLYTA®

# QuANTUM-Wild Study Design

## Started QuANTUM-Wild Ph3 study for *FLT3*-ITD negative AML based on data from QUIWI study

### QuANTUM-Wild study design

**Eligible patients**
- Newly diagnosed AML
- Without *FLT3*-ITD mutations




- VANFLYTA® + chemotherapy demonstrated preliminary efficacy in patients with newly diagnosed *FLT3*-ITD negative AML compared to placebo+ chemotherapy in the interim analysis of QUIWI study (EHA 2023)
- Started the study in Dec 2024 to expand indication for *FLT3*-ITD negative AML based on QUIWI study results

Primary endpoint
- OS

Secondary endpoint
- EFS, DCR, RFS, CR rate etc.

AML: acute myeloid leukemia, CR: complete response, DCR: disease control rate:, EFS: event-free survival, EHA: European Hematology Association, OS: overall survival, RFS: relapse-free survival

Valemetostat

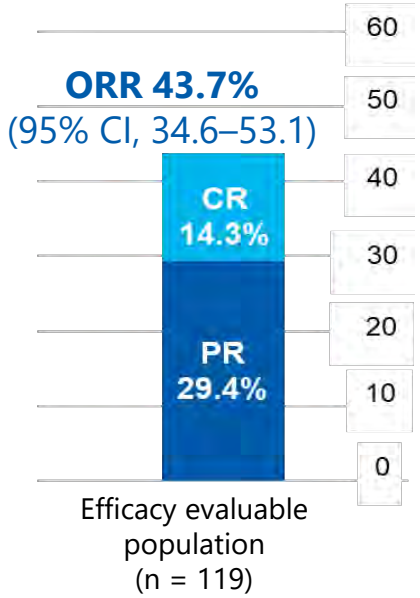
# VALENTINE-PTCL01 Primary Results

ASH 2023

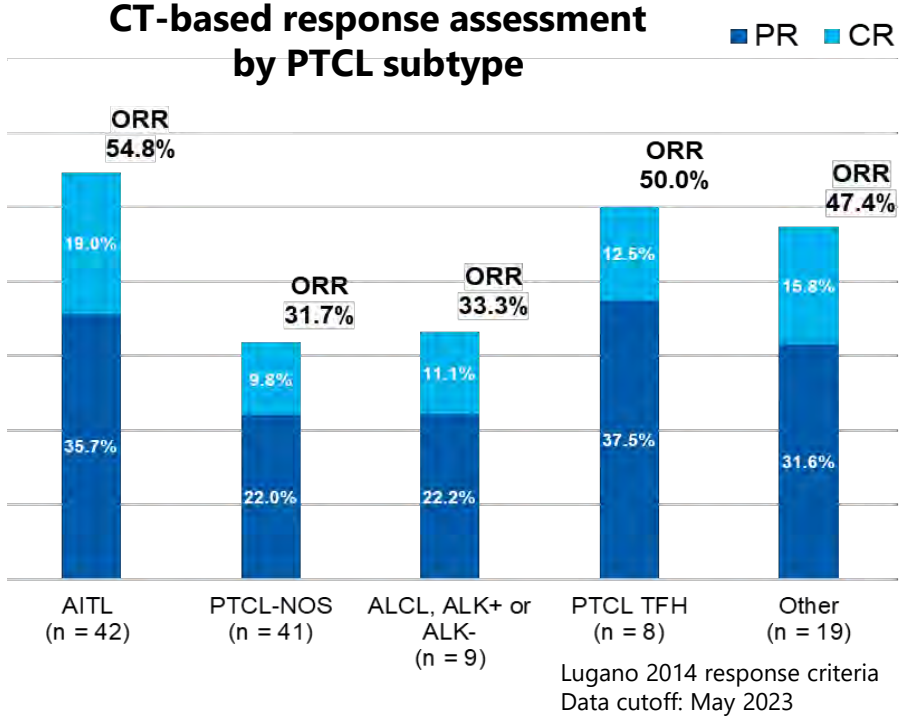
## Valemetostat monotherapy provides a clinically meaningful benefit for patients with R/R PTCL

### Clinical Response

**CT-based BICR assessment (primary endpoint)**




**CT-based response assessment by PTCL subtype**




Lugano 2014 response criteria
Data cutoff: May 2023

**VALENTINE-PTCL01**

A Ph2 single-arm study in R/R PTCL (N=133) treated with 200 mg/day valemetostat

- Valemetostat monotherapy demonstrated a high ORR of 43.7% with CR rate 14.3%
- Responses were durable (mDoR 11.9 months)
- The safety profile was acceptable and AEs were generally manageable; 57.9% patients experienced grade ≥3 TEAEs (cytopenias were the most common)

AITL: angioimmunoblastic T-cell lymphoma, ALCL: anaplastic large cell lymphoma, ALK: anaplastic lymphoma kinase, BICR: blinded independent central review, CI: confidence interval, CT: computed tomography, CR: complete response, ORR: objective response rate, PTCL-NOS: PTCL-not otherwise specified, R/R-PTCL: relapsed or refractory peripheral T-cell lymphomas, TEAEs: treatment emergent adverse events, TFH: T follicular helper

Valemetostat

# Rationale of combination with DXd ADC

## Hypothesis: DXd ADC and valemetostat combination would increase anti-tumor activity of DXd ADC through upregulation of SLFN11

**Hypothesis**

**Valemetostat**
(Inhibit EZH1/2)

↓

Decrease trimethylation at lysine 27 of histone H3

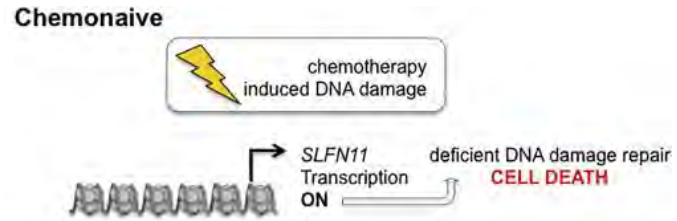
↓

Increase SLFN11 expression

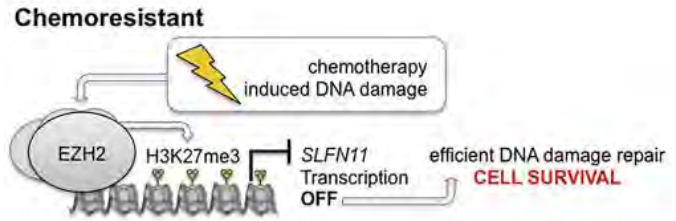
↓

**Increase sensitivity to DXd payload**

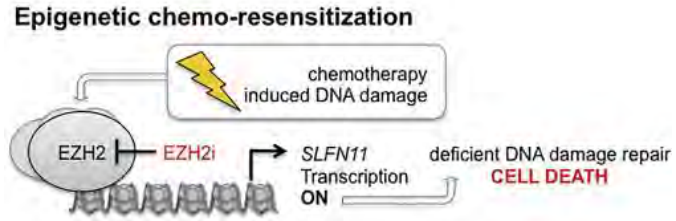
- SLFN11 is a dominant determinant of sensitivity to DNA-damaging agents




- SLFN11 expression is down regulated by EZH2 in chemo-resistant tumors




- EZH2 inhibition can upregulate SLFN11 expression and sensitize to DNA-damaging agents such as Topoisomerase I inhibitor DXd




Cancer Cell 31:169-71 (2017)

ADC: antibody-drug conjugate

Valemetostat

# Evaluating potential of combination with DXd ADC in clinical trial

■ **A Ph1b study is ongoing for valemetostat combination with ENHERTU® in patients with HER2 low/ultra-low/null mBC (collaboration with MDACC)**

**Key Eligibility Criteria**

- Unresectable or mBC with HER2 IHC 0, 1+, 2+/ISH-
- Received >1 line of chemo in mBC
- Progressed and no longer benefit from ET in HR+


Continuous 21-days cycle until PD or unacceptable toxicities

| Dose level | valemetostat | ENHERTU® |
|---|---|---|
| Level 1 | 100 mg/day QD | 5.4 mg/kg Q3W |
| Level 2 | 150 mg/day QD | 5.4 mg/kg Q3W |
| Level 3 | 200 mg/day QD | 5.4 mg/kg Q3W |

**Primary objectives**
- Safety
- MTD
- RP2D

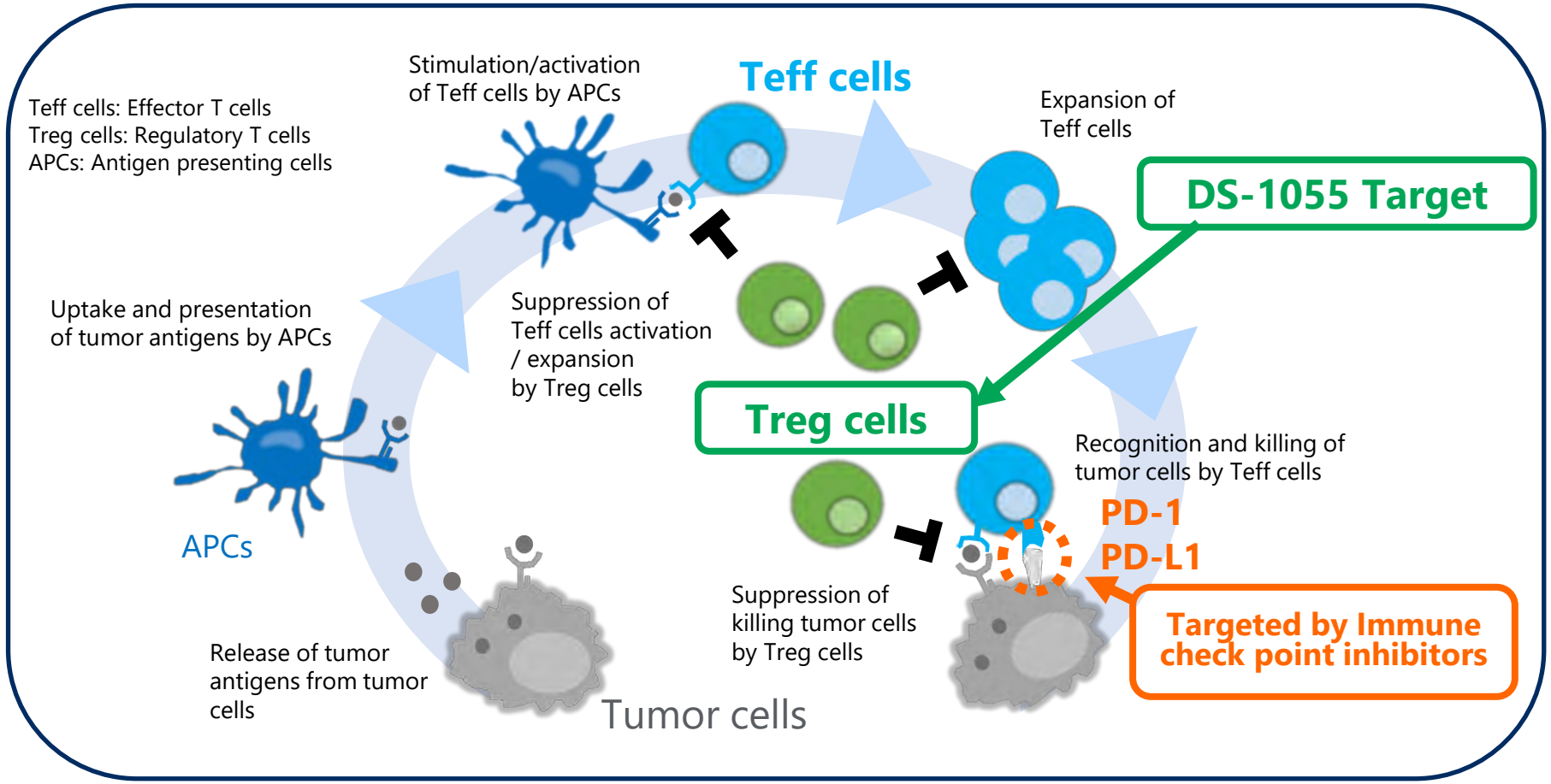
**Secondary objectives**
- PK
- Efficacy (ORR, DOR)
- Biomarkers

■ **Another combination study (company-sponsored Ph1b) is ongoing to investigate valemetostat combinations with ENHERTU® in HER2+ GC and HER2 low BC and with Dato-DXd in nonsquamous NSCLC**

ADC: antibody-drug conjugate, DOR: duration of response, ET: endocrine therapy, HR: hormone receptor, IHC: immunohistochemistry, ISH: *in situ* hybridization, MDACC: MD Anderson Cancer Center, Q3W: every 3 weeks, QD: quaque die (once daily), mBC: metastatic breast cancer, MTD: maximum tolerated dose, ORR: objective response rate, PD: progressive disease, PK: pharmacokinetics, RDE: recommended dose for expansion, RP2D: recommended Ph2 dose

# DS-1055 Target: Regulatory T Cells

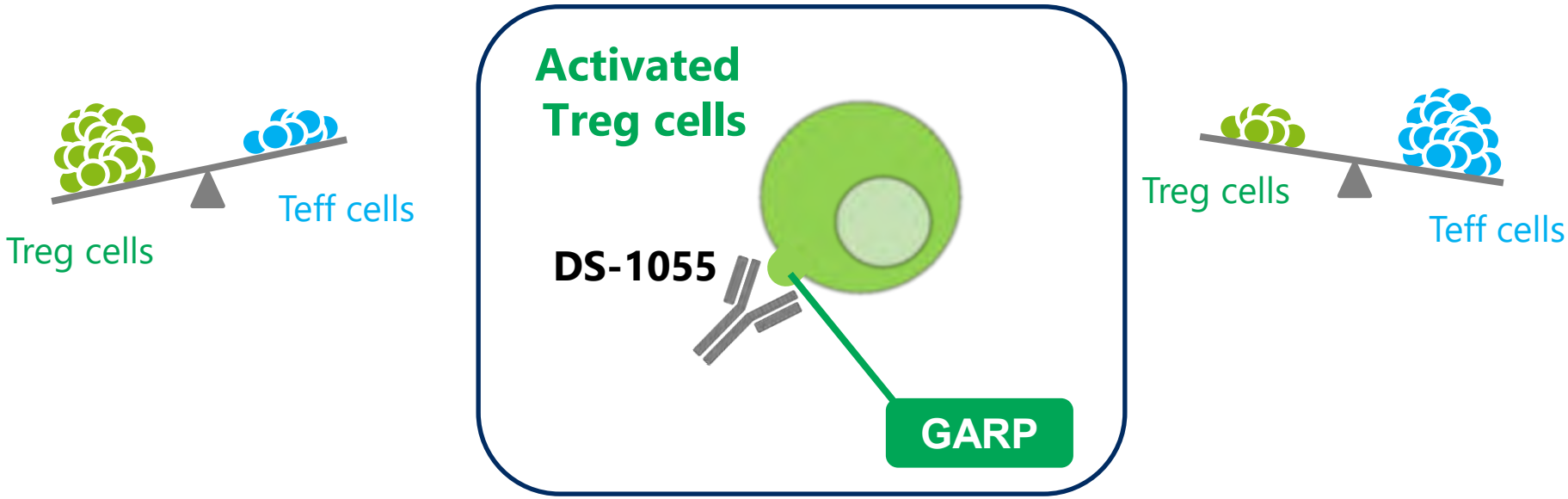
- **DS-1055 is anti-GARP antibody with different MOA from that of anti-PD-1 / PD-L1 antibody**
- **Activates anti-tumor immunity by targeting regulatory T cells (Treg cells) involved in immune escape of cancer cells**




GARP：Glycoprotein A repetitions predominant

# DS-1055: MOA of Anti-GARP Antibody

| Treg cells > Teff cells | | Treg cells < Teff cells |
|---|---|---|
| Immune escape of tumor by suppression of Treg cells | → | Elimination of tumor by activated Teff cells |

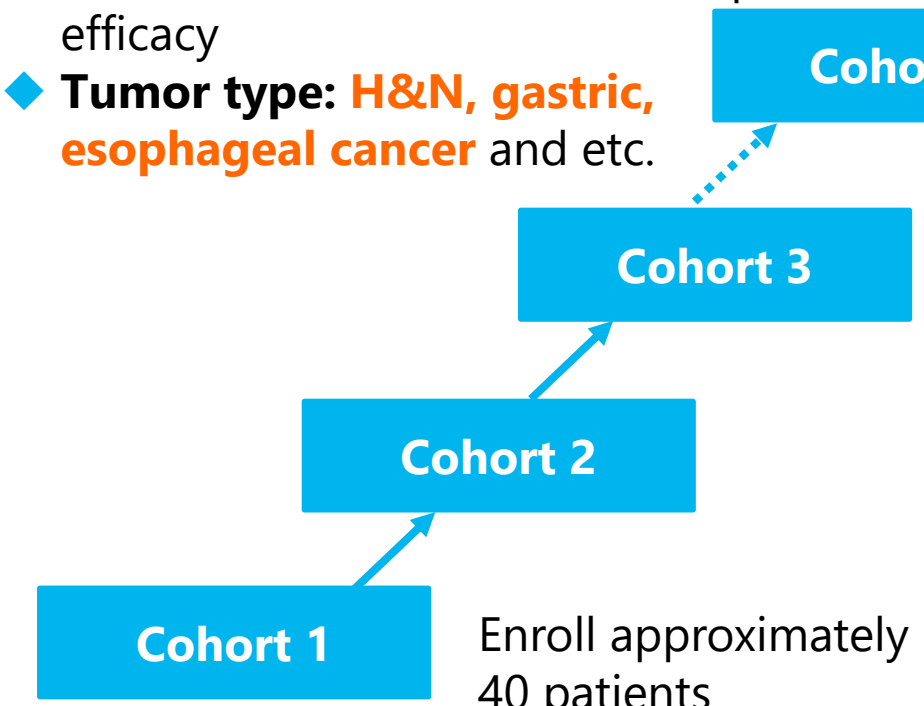



- **By recognizing GARP specifically expressed on activated Treg cells and depleting activated Treg cells, Teff cells can work as its original nature (anti-tumor activity)**

# DS-1055: FIH Phase 1 Study Design

## Dose Escalation

- **Purpose:** Safety and tolerability, determine the recommended dose for dose expansion, initial efficacy
- **Tumor type:** **H&N, gastric, esophageal cancer** and etc.




Enroll approximately 40 patients

## Dose Expansion

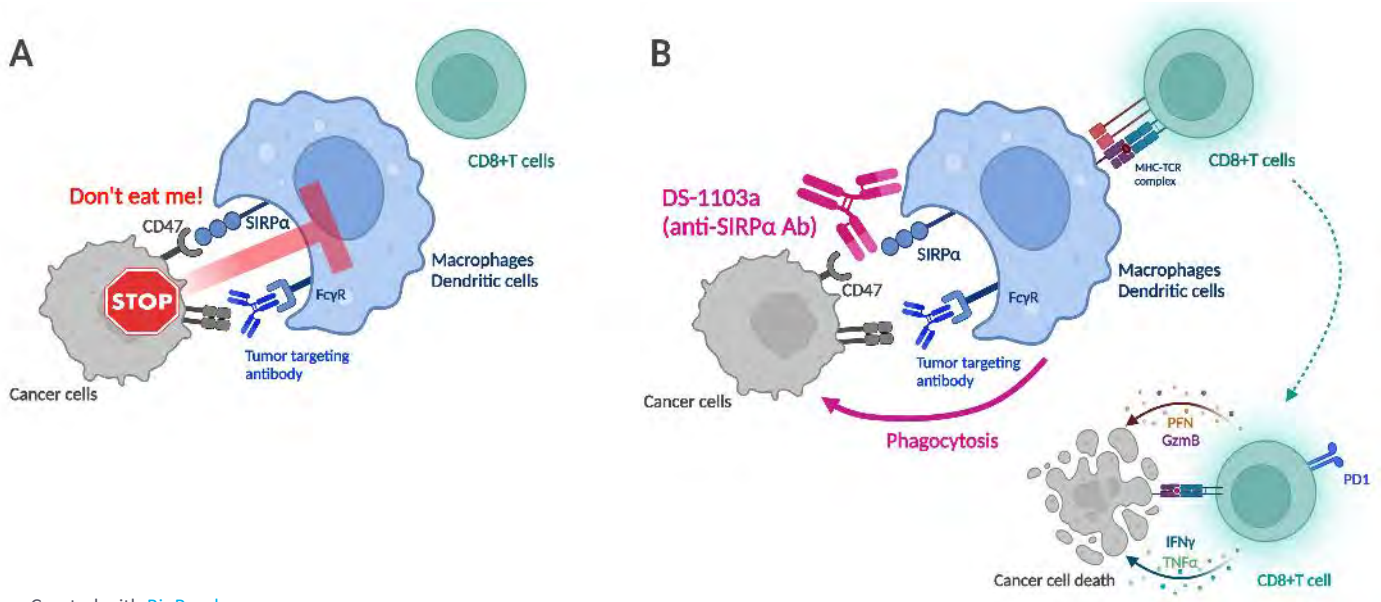
Choose recommended dose from appropriate cancer type from dose escalation part

- **Study started in Oct. 2020**
- **Combination with immune checkpoint inhibitor is under discussion**

JapicCTI-205292, NCT04419532

# DS-1103: anti-SIRPα antibody

- A new combination study of ENHERTU® with anti-SIRPα antibody DS-1103 starts in FY2023 H1




Created with BioRender.com.

- DS-1103 is designed to block the "Don't eat me" signal of the SIRPα-CD47 axis in macrophages and dendric cells, leading to phagocytosis of tumor cells and subsequent activation of anti-tumor immunity
- DS-1103 could potentiate efficacy of anti-tumor antibody drugs, including DXd-ADCs
- A related E-publication at ASCO 2023 (Abstract# e14509) on a QSP model informing DS-1103 dosing

**Ph1 study design**

**Dose escalation part**
DS-1103 + ENHERTU® (5.4 mg/kg Q3W)
HER2-expressing or HER2-mutant advanced metastatic solid tumors

→

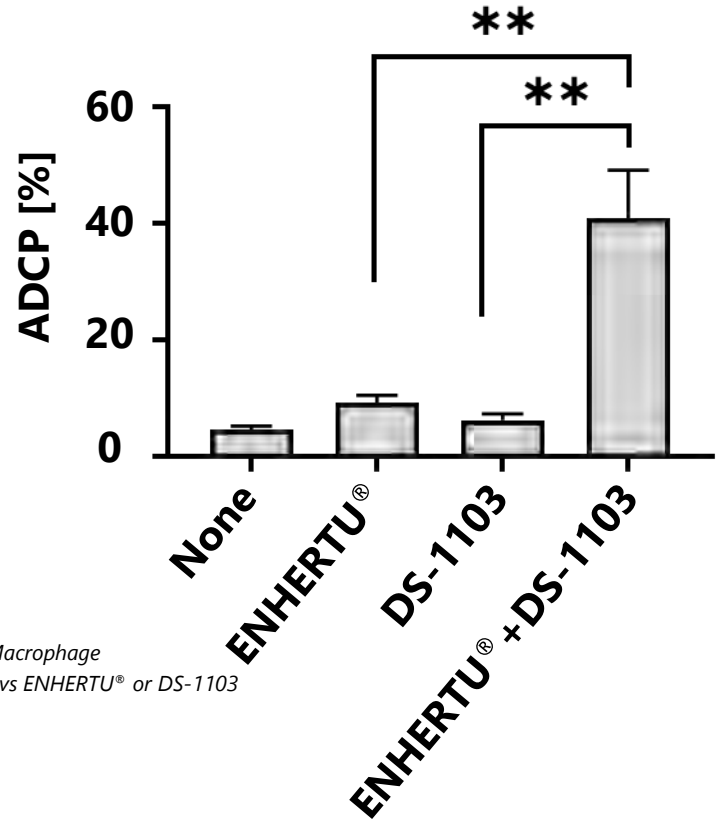
**Dose expansion part**
DS-1103 + ENHERTU® (5.4 mg/kg Q3W)
HER2 low BC

BC: breast cancer, FIH: first-in-human, Q3W: once every 3 weeks, QSP: quantitative systems pharmacology, SIRPα, signal-regulatory protein alpha

DS-1103

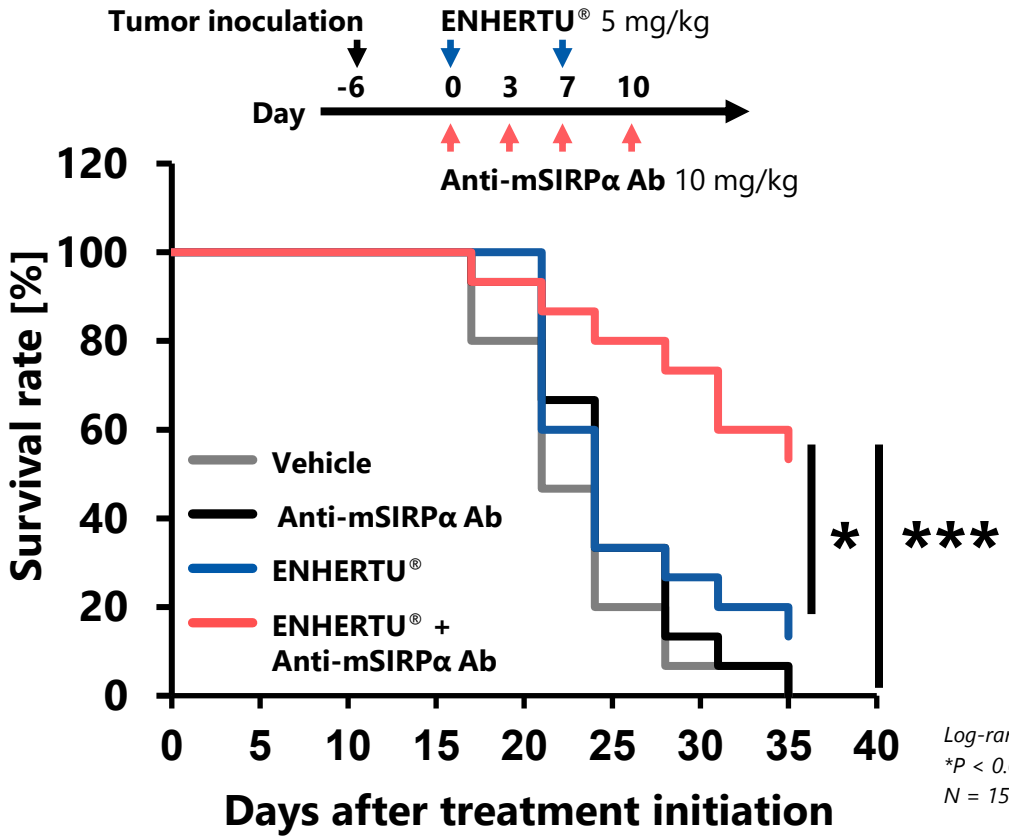
# Preclinical data support the rationale for the combination of ENHERTU® and DS-1103

- DS-1103, an anti-SIRPα antibody, effectively blocked the "don't eat me" signal from cancer cells
- Combining DS-1103 with ENHERTU® significantly enhanced antibody-dependent cellular phagocytosis (ADCP)
- The combination of an anti-mouse SIRPα surrogate antibody with ENHERTU® demonstrated a survival benefit in mice bearing HER2-expressing tumor cells




*SITC 2022 Poster #808*

*ADCs: 5 nM, Antibodies 50 nM*
*Tumor: HER2+ BC cell line, Effector: Macrophage*
*Dunnett's test: ENHERTU® +DS-1103 vs ENHERTU® or DS-1103*
**P < 0.05 and **P < 0.01, N = 4*



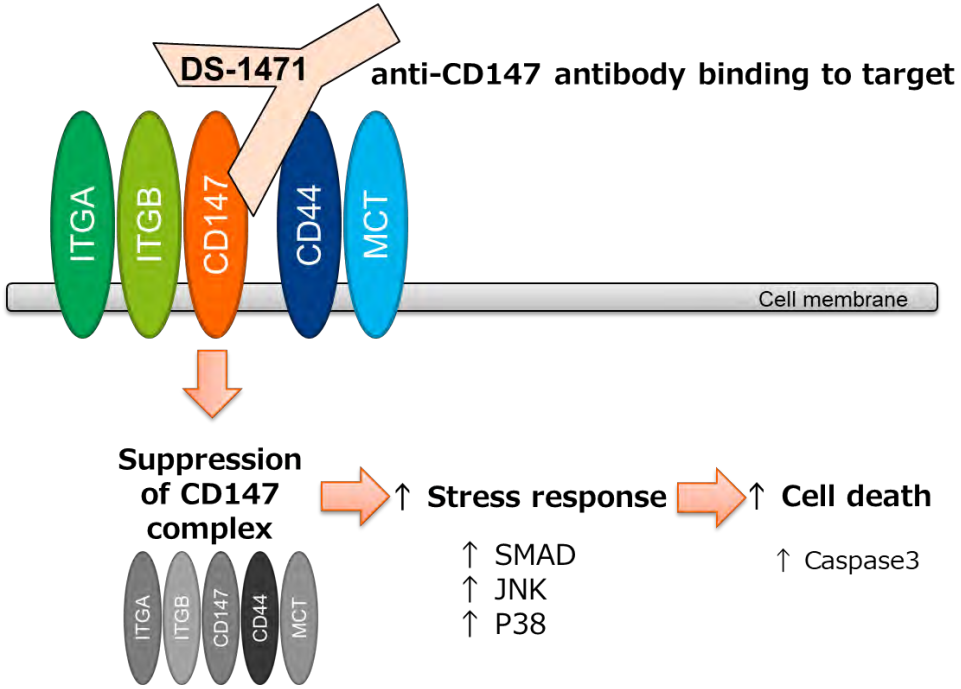

*Log-rank test;*
**P < 0.05 and ***P < 0.001*
*N = 15 per group*

ab: antibody

DS-1471

# A potential first-in-class anti-CD147 Antibody

## DS-1471 is a monoclonal antibody with targeting CD147
## A Ph1 first-in-human study is ongoing in solid tumors




- CD147 is known as a potential prognostic biomarker for various types of cancer including HCC, CRC etc.
- CD147 complex is also reported to play important roles in survival, invasion and metastasis in cancer tissues
- DS-1471 exhibits **unique mechanism of action** by downregulating CD147 complex which leads to cellular stress response and apoptotic cell death
- Ph1 dose escalation part is ongoing

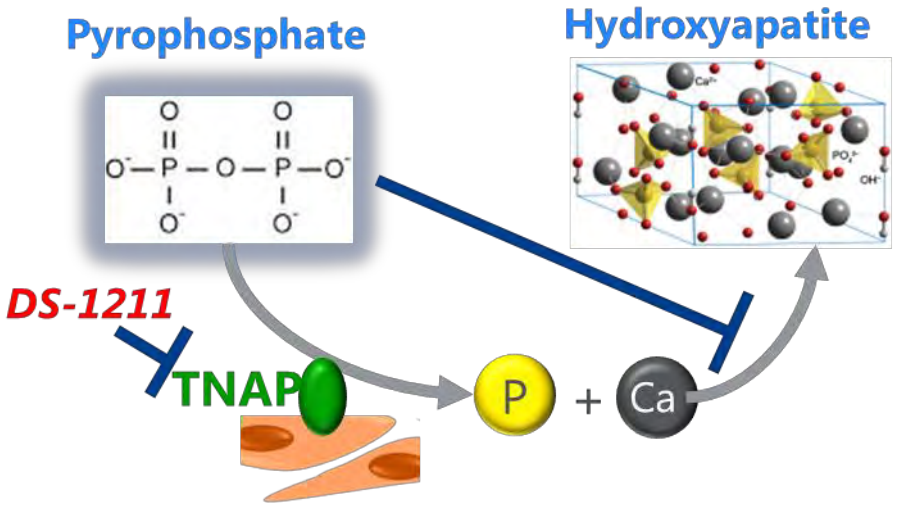
CRC: colorectal cancer, HCC: hepatocellular carcinoma

# DS-1211

Daiichi-Sankyo

**Stage: Phase 2** ➢ **Positive TLR from Ph2 study in Apr 2024**

**Small Molecule**

| Mode of Action | Target Disease |
|---|---|
| **TNAP* inhibitor**<br>  <br> | **Pseudoxanthoma elasticum (PXE)**<br>◆ Mutation in *ABCC6* gene results in low level of a calcification inhibitor, pyrophosphate, leading to skin lesions, visual impairments and cardiovascular diseases |
| **Approved Drug Therapy** | **Estimated Number of Patients** |
| ◆ No medical therapy currently available | JP/US/EU5: 16,000<br>Source: Calculated based on Uitto et al., Expert Opin Orphan Drugs. 2014 |

*TNAP: tissue nonspecific alkaline phosphatase

# DS-7011

- **Target indication: Systemic lupus erythematosus (SLE)**
  - Chronic autoimmune disease characterized by autoantibody production, inflammation, and tissue damage in multiple organs
  - Important cause of morbidity and mortality and unmet medical need
- It is estimated that 5 million people worldwide live with lupus
- Supported by AMED (Japan Agency for Medical Research and Development) CiCLE program since April 2020

## Mechanism of Action

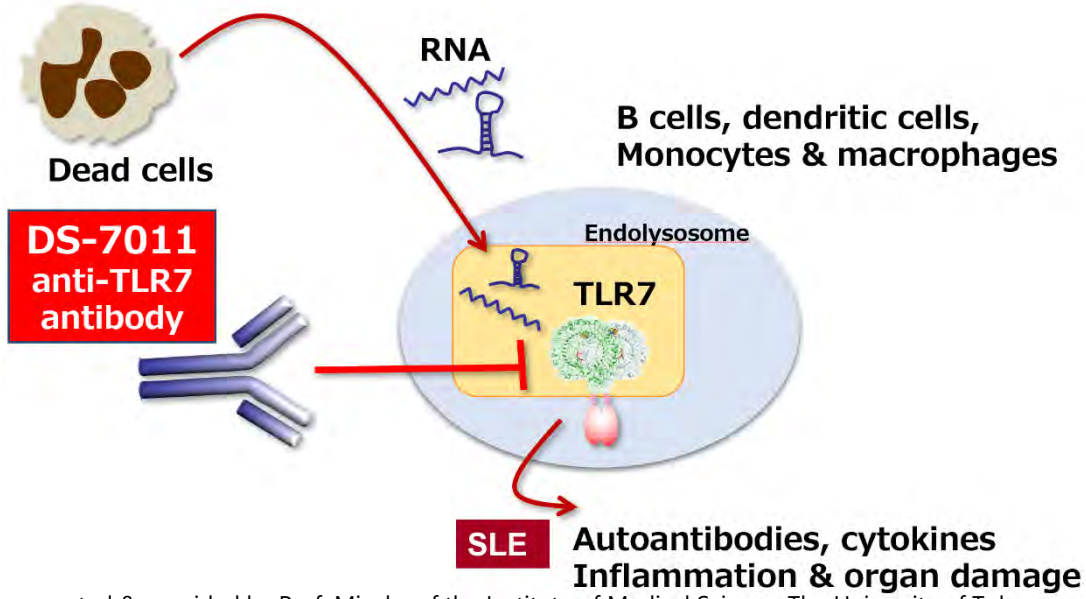


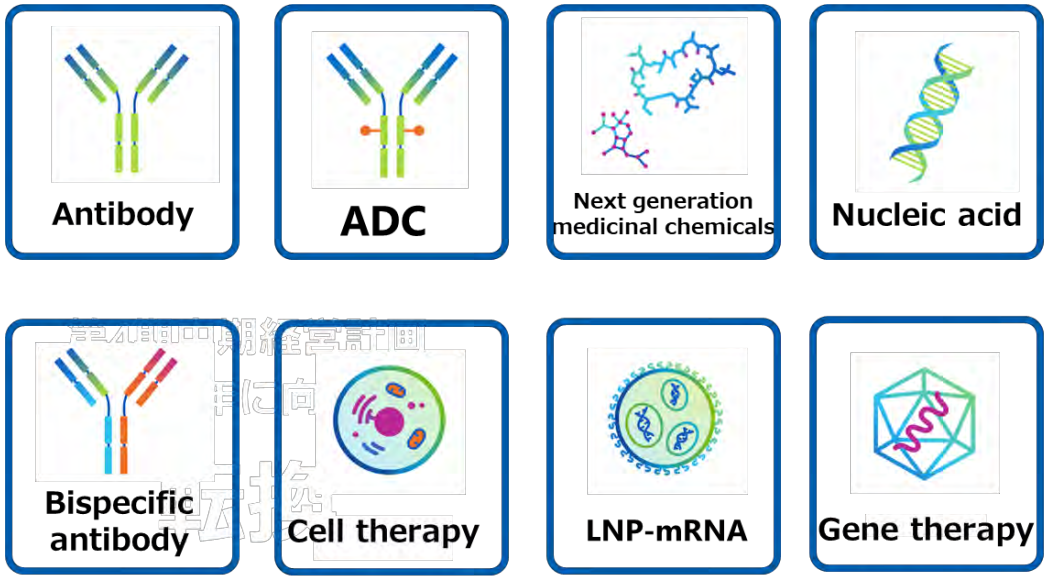

Diagram created & provided by Prof. Miyake of the Institute of Medical Science, The University of Tokyo

## Clinical Studies

- **Phase 1b/2**
  - Double-blinded, placebo-controlled, randomized
  - Multiple intravenous doses (3 doses, one every 4 weeks)
  - Two parallel arms of SLE patients
  - Objectives: Safety, pharmacokinetics, pharmacodynamics, immunogenicity, and preliminary efficacy
  - Started in July 2023

# Daiichi Sankyo's Multi-modality Strategy

## Optimized modality



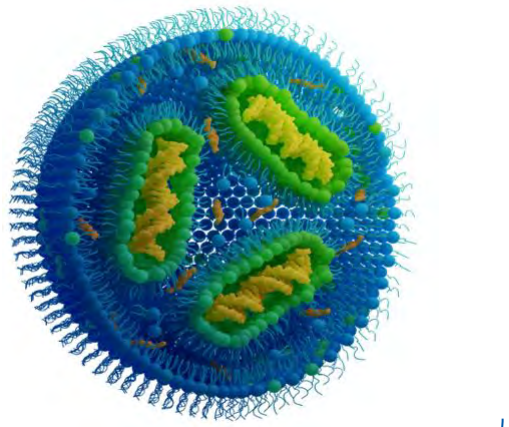

**High Unmet Medical Need**

- **Select and develop** the most suitable modality for a target disease/etiology from optimized or newly established modalities
- **Appropriate assessment/judgement** of our next growth drivers is the key for sustainable growth
  - Ensure continuous flow of high potential drug candidates by appropriate assessment and prioritization
  - Ensure acceleration of drug development once promising drug candidates are identified

DAICHIRONA®
(DS-5670)

# Approval of COVID-19 vaccine and progress

## DAICHIRONA®FOR INTRAMUSCULAR INJECTION*



Lipid nanoparticle(LNP)-mRNA

- **DS original cationic lipid** is applied
  - Best lipid and lipid composition ratio are selected based on efficacy & safety perspectives
- **The first mRNA vaccine made in Japan**
- mRNA vaccine for Omicron XBB.1.5 strain was **approved in Japan** against COVID-19 in Nov 2023

## Seasonal Flu/ COVID-19 combination vaccine**

Daiichi Sankyo's R&D activity on seasonal Flu/ COVID-19 combination vaccine was adopted the funding program for development of vaccines toward key infectious disease conducted by AMED

* The research and development of DAICHIRONA® FOR INTRAMUSCULAR INJECTION-is being conducted through the "Vaccine development project" promoted by the Japan Agency for Medical Research and Development (AMED) and the "Urgent improvement project for vaccine manufacturing systems" supported by the Japanese Ministry of Health, Labour and Welfare (MHLW).

* * The research and development of Seasonal Flu/COVID-19 combination vaccine is being conducted through the "Vaccine development project" promoted by the Strategic Center of Biomedical Advanced Vaccine Research and Development for Preparedness and Response （SCARDA）for Japan Agency for Medical Research and Development (AMED).