Company name: DAIICHI SANKYO COMPANY, LIMITED
Representative: Hiroyuki Okuzawa, Representative Director,
President and COO
(Code no.: 4568, Prime Market, Tokyo Stock Exchange)
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Vice President, Corporate Communications Department
Telephone: +81-3-6225-1126
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Daiichi Sankyo's "R&D Day 2023"

Tokyo, Japan (December 11, 2023) - Daiichi Sankyo Company, Limited will hold its "R&D Day 2023" at 7:30am JST on Tuesday, December 12, 2023 for institutional investors, security analysts and media.

In addition to the Zoom webinar, on-demand recorded video will be available at a later date.
URL: https://www.daiichisankyo.com/investors/library/materials/2023.html

Attachment: presentation material

Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

R&D Day 2023

DAIICHI SANKYO CO., LTD.

December 11th, 12th 2023

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.

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Agenda

1. Opening
2. R&D Strategy
3. Research Capability
4. Clinical Progress
5. Q&A

FY2023 R&D Day presenters

Sunao Manabe
Executive Chairperson and CEO

Ken Takeshita
Head of Global R&D

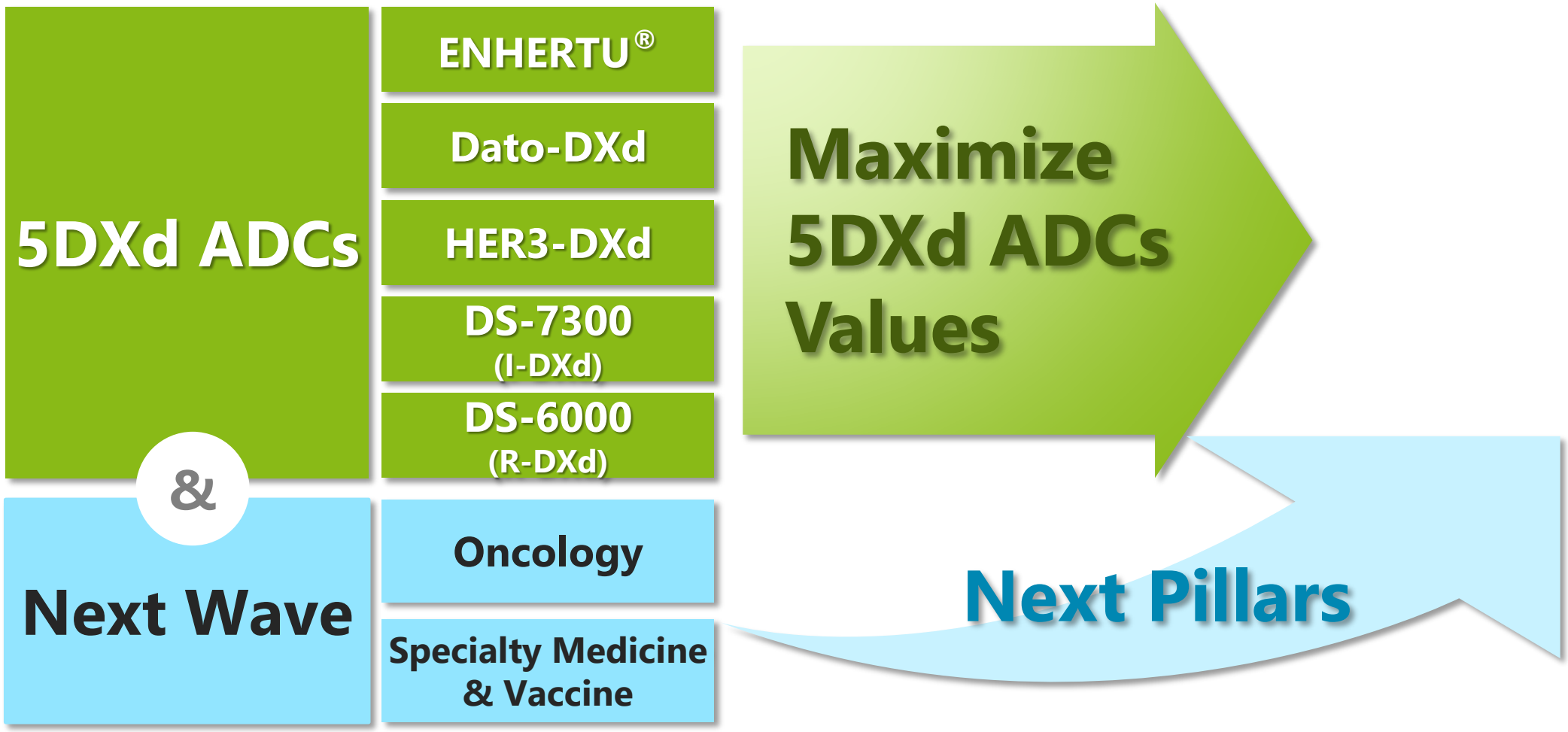
Toshinori Agatsuma
Head of Global Research

Mark Rutstein
Head of Global Oncology Clinical Development

Agenda

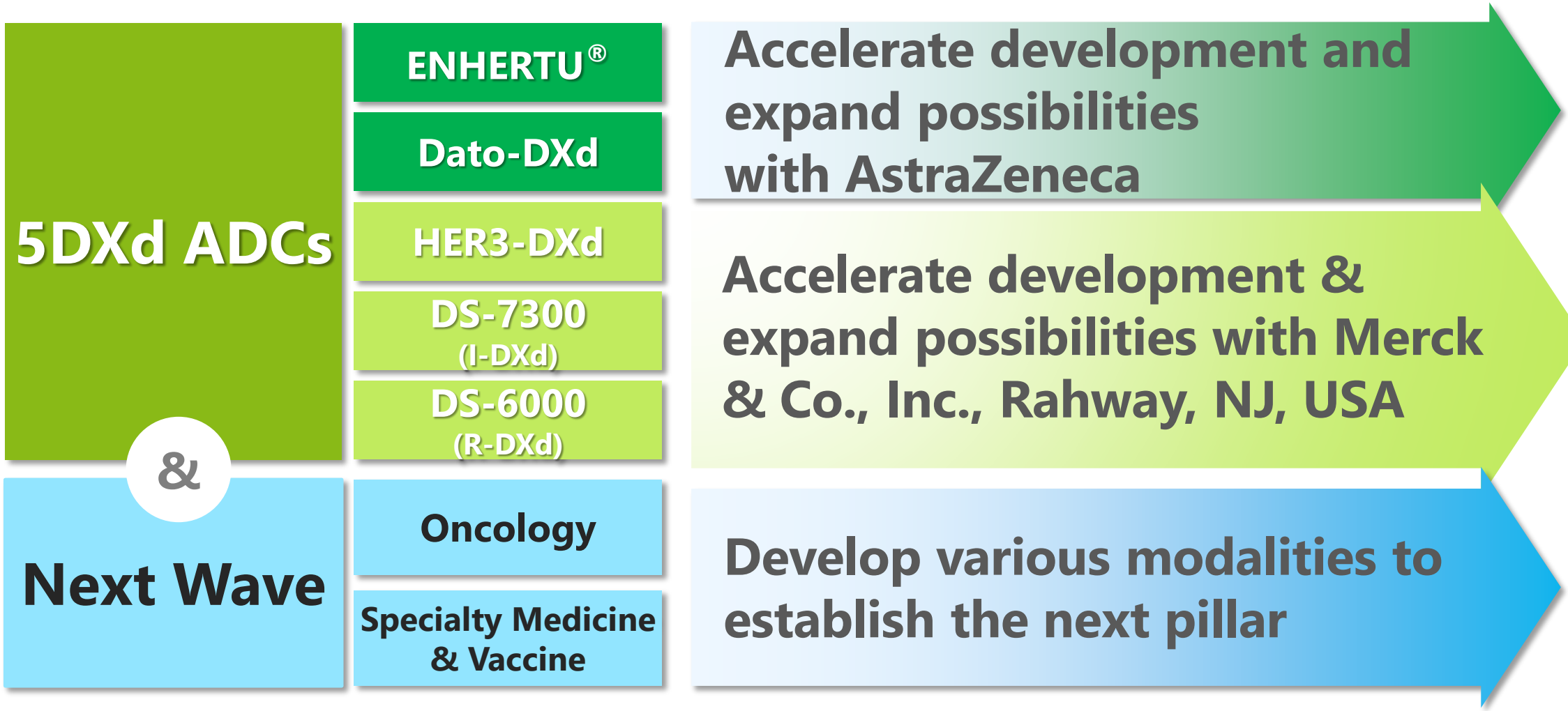
1. Opening
2. **R&D Strategy**
3. Research capability
4. Clinical Progress
5. Q&A

5DXd ADCs and Next Wave



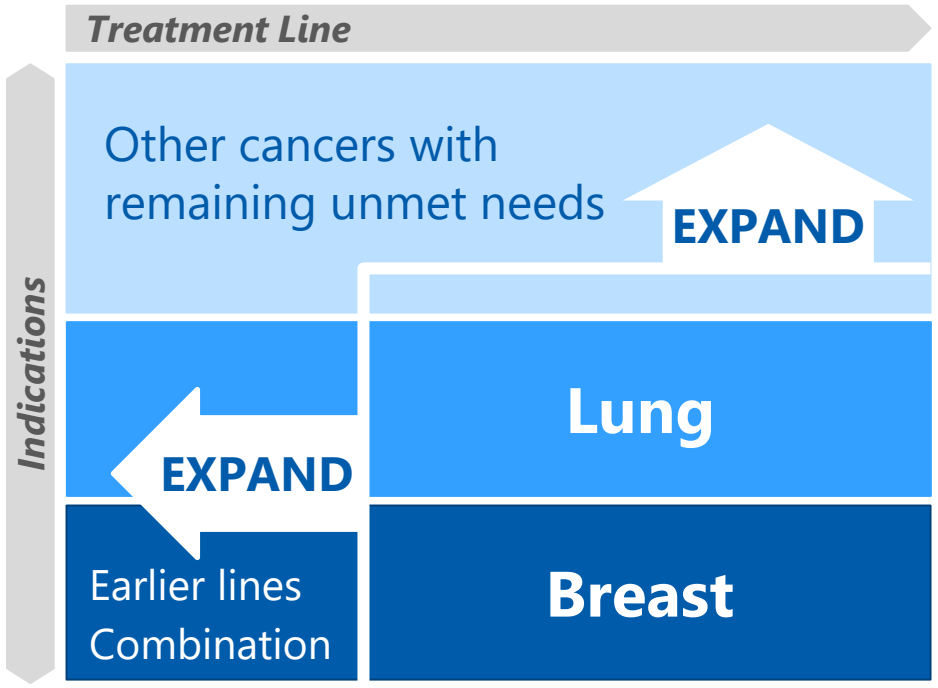
ENHERTU® : trastuzumab deruxtecan (International Nonproprietary Name: INN), T-DXd, DS-8201 (HER2-directed ADC), **Dato-DXd**: datopotamab deruxtecan (INN), DS-1062 (TROP2-directed ADC), **HER3-DXd**: patritumab deruxtecan (INN), U3-1402 (HER3-directed ADC), **DS-7300**: ifinatamab deruxtecan, I-DXd (B7-H3-directed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

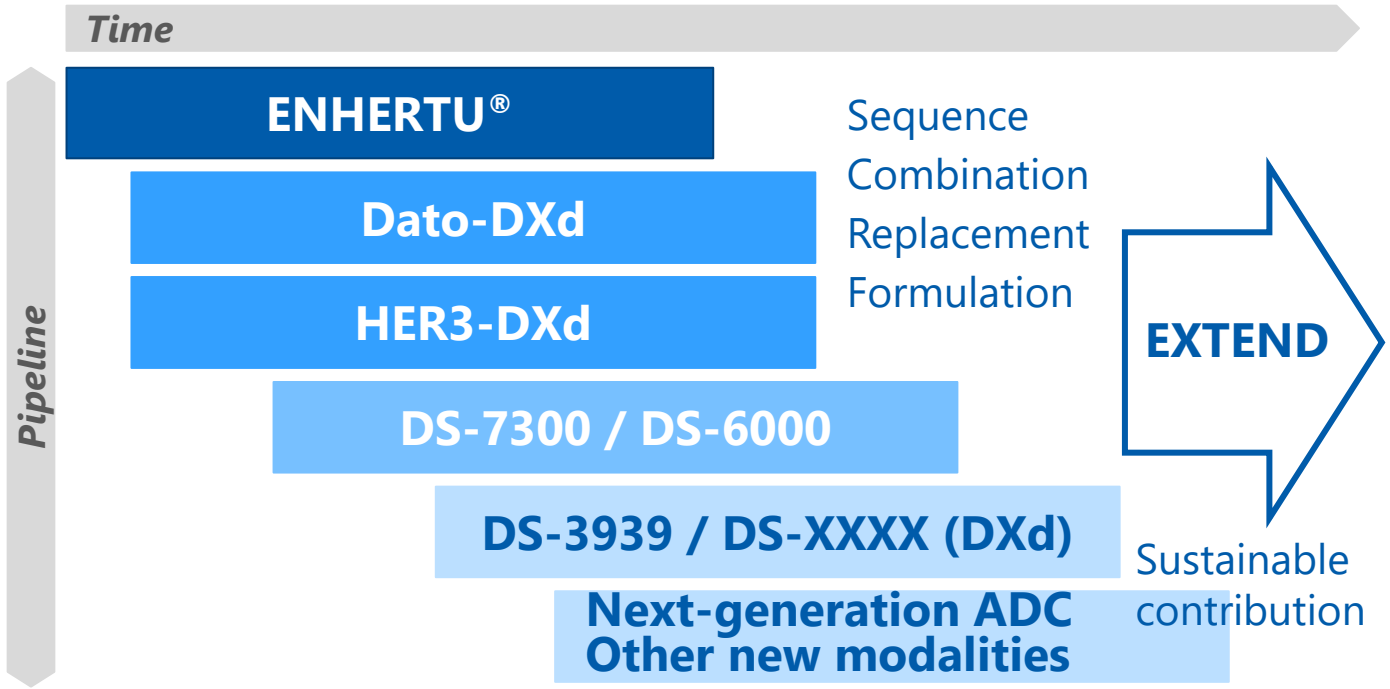
5DXd ADCs and Next Wave



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）

EXPAND & EXTEND to deliver our technology to more patients





- 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 patients in 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

3ADCs launch plan

As of Apr. 2023, FY2022 Q4 earnings call

Active R&D investment following 3ADCs development progress exceeding the initial plan

~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-Gastric04
- DESTINY-Lung01/02
- DESTINY-Lung04
- DESTINY-CRC01/02

Dato-DXd

- TROPION-Lung01
- TROPION-Lung08
- TROPION-Breast01
- TROPION-Breast02

HER3-DXd

- HERTHENA-Lung01
- HERTHENA-Lung02

FY2026 & Beyond

ENHERTU®

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

Dato-DXd

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

HER3-DXd

- Combo with targeted therapy in NSCLC
- Other cancer types

Study approved the indication during 5-Year Business Plan Major study only

ADC: antibody-drug conjugate, BC: breast cancer, DS: Daiichi Sankyo, I/O: immune oncology, NSCLC: non-small cell lung cancer

Timeline indicated is based on the forecast in Apr 2023 and subject to change.

Progress since R&D Day 2022

Steady progress in maximizing product value of DXd ADCs
New assets proceeded to clinical stage

ENHERTU® trastuzumab deruxtecan

Transform the course of HER2+ BC

- Approval in China as the first indication
- Strong market penetration

Pioneer HER2 low BC as a new clinically meaningful patient segment

- Approval in Japan, EU and China

Expand leadership across other HER2 targetable tumors

- Approval for HER2 mutant NSCLC in Japan and EU
- BTD was granted for HER2+ solid tumors and HER2+ CRC indication in US

Dato-DXd & HER3-DXd

Data readout of pivotal studies

- Dato-DXd
  - **NSCLC 2L/3L** (TROPION-Lung01 study)
  - **HR+/HER2 low or negative BC 2L/3L** (TROPION-Breast01 study)
- HER3-DXd
  - **EGFR mutated NSCLC 3L** (HERTHENA-Lung01 study)

Started New pivotal studies

- Dato-DXd
  - **PD-L1<50% NSCLC, 1L** (TROPION-Lung07 study)
  - **Neo-adjuvant/Adjuvant, TNBC** (TROPION-Breast04 study)
  - **PD-L1 positive TNBC, 1L** (TROPION-Breast05 study)

DXd ADCs in early phase

- **Obtained updated data and presented at medical congresses**
  - DS-7300：**SCLC, CRPC, ESCC, sqNSCLC** (Ph1/2 study and Ph2 study for SCLC ongoing)
  - DS-6000：**OVC** (Ph1 study ongoing)
- **FIH study for DS-3939 has started**

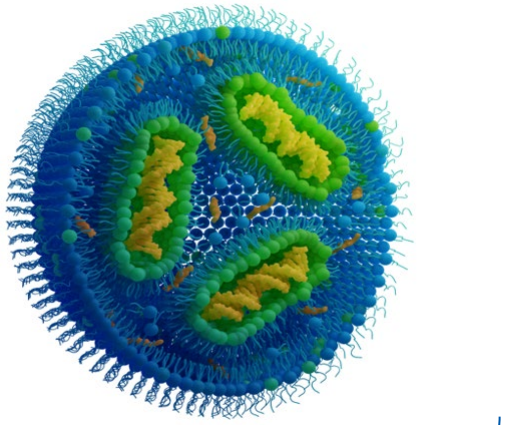
Next Wave

- Approval of quizartinib for *FLT3*-ITD positive AML 1L in Japan/US/EU
- FIH study for the next generation ADC, DS-9606 is ongoing
- FIH studies for new assets, DS-1103, DS-1471 have started

ADC: antibody-drug conjugate, AML: acute myeloid leukemia, BC: breast cancer, BTD: breakthrough therapy designation, CRC: colorectal cancer, CRPC: castration-resistant prostate cancer, ESCC: esophageal squamous cell carcinoma, FIH: first-in-human, HR: hormone receptor, NSCLC: non-small cell lung cancer, OVC: ovarian cancer, SCLC: small cell lung cancer, sqNSCLC: squamous non-small cell lung cancer, TNBC: triple-negative breast cancer

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).

Agenda

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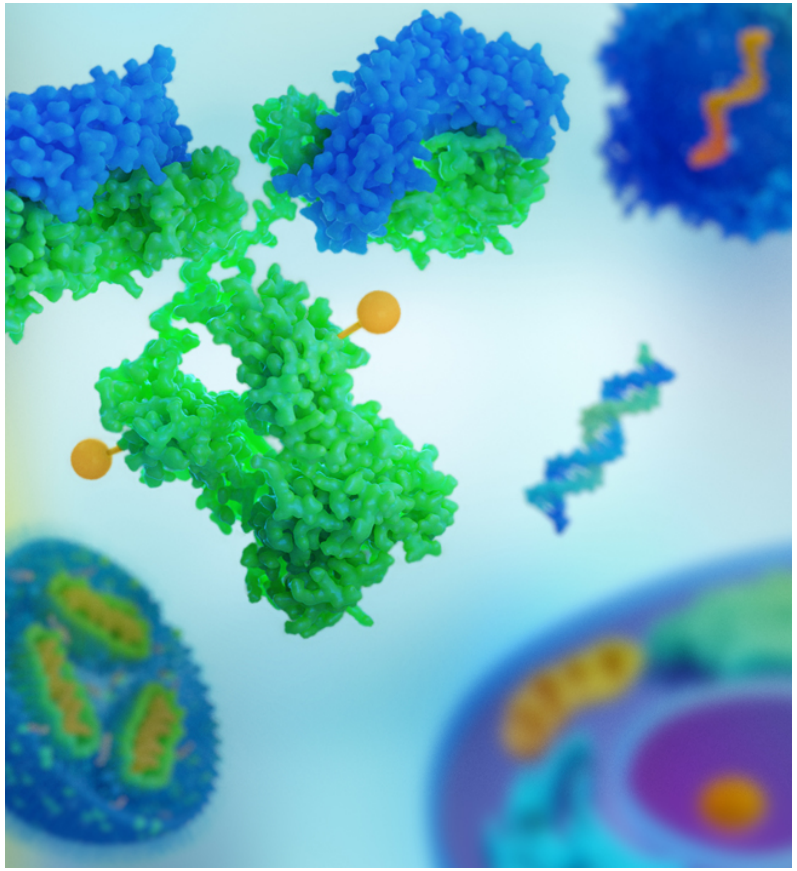
3. **Research Capability**
4. Clinical Progress
5. Q&A

Toshinori Agatsuma Career Highlights

Career

2023	Head of Global Research (Research Function Head of R&D Division)
2019	Global Oncology Research Head (Head of Oncology Research Labs. I)
2016	Head of Biologics & Immuno-Oncology Labs.
2013	Head of Biologics Pharmacology Research Labs.
2010	Group Leader of Biologics Research Labs.
2008	Group Leader of Antibody Drug Group of Drug Discovery Technology Research Labs.
2004	Group Leader of Biomedical Research Labs. in former Sankyo
1996	Biological Research Labs. II/ Biomedical Research Labs. in former Sankyo
1995	Division of Infectious Diseases in The Institute of Medical Science, The University of Tokyo
1994	MRC Collaborative Centre, London , UK
1991	Bioscience Research Labs in former Sankyo



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

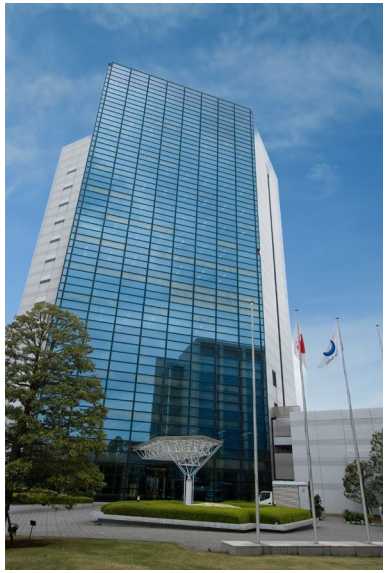
valemetostat

DAICHIRONA®

Shinagawa, 1908

Kasai,1938

Shinagawa



Kasai

Long history behind the birth of DXd ADC

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

Sankyo Co., Ltd.

Biologics

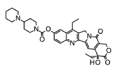
1990s
Humanization
Small-scale manufacturing (Anti CD95, anti-DR5)

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

Daiichi Pharmaceutical Co., Ltd.

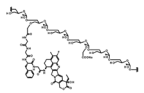
Topo I inhibitors

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

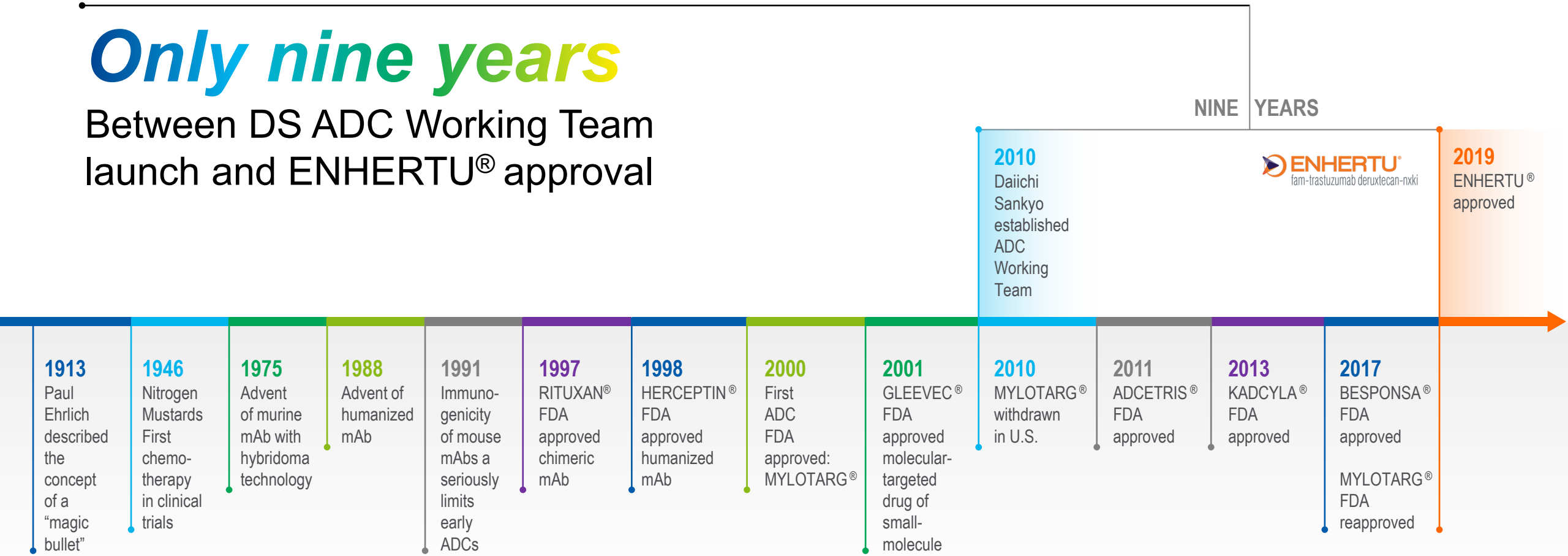
- They have long tenure at DS, leveraged their expertise and are now research leaders growing our future talent

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

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

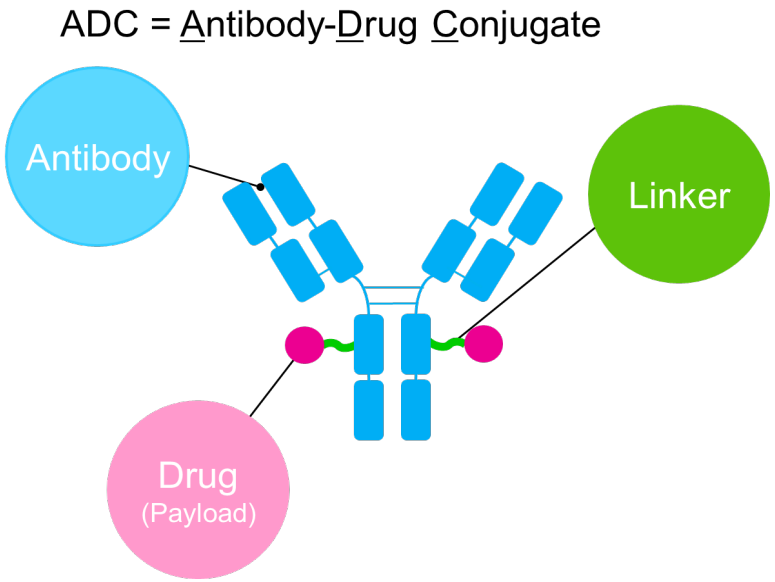
Establishment of ADC Working Team

- Experience and expertise in research and production of both antibodies and small molecules are important
- At the time, ADC technology was a new area – a trial-and-error approach was inevitable
- In addition to pharmacological research, pharmacokinetics and safety evaluation research were also crucial

Organized cross-functional working team specialized in the development of new ADC (Jun 2010)

ADC: antibody-drug conjugate

Challenges that new ADCs had to overcome



Limited variations of payload

Limitations in treatment options for non-responsive and drug resistant tumors

Heterogeneity in drug binding sites

Challenges in inter-batch variability and setting formulation specification

Instability of linker

Decreased efficacy due to a decrease in blood concentration of ADC
Toxicity due to an increase in free payload concentration in blood

Limited numbers of drugs to conjugate

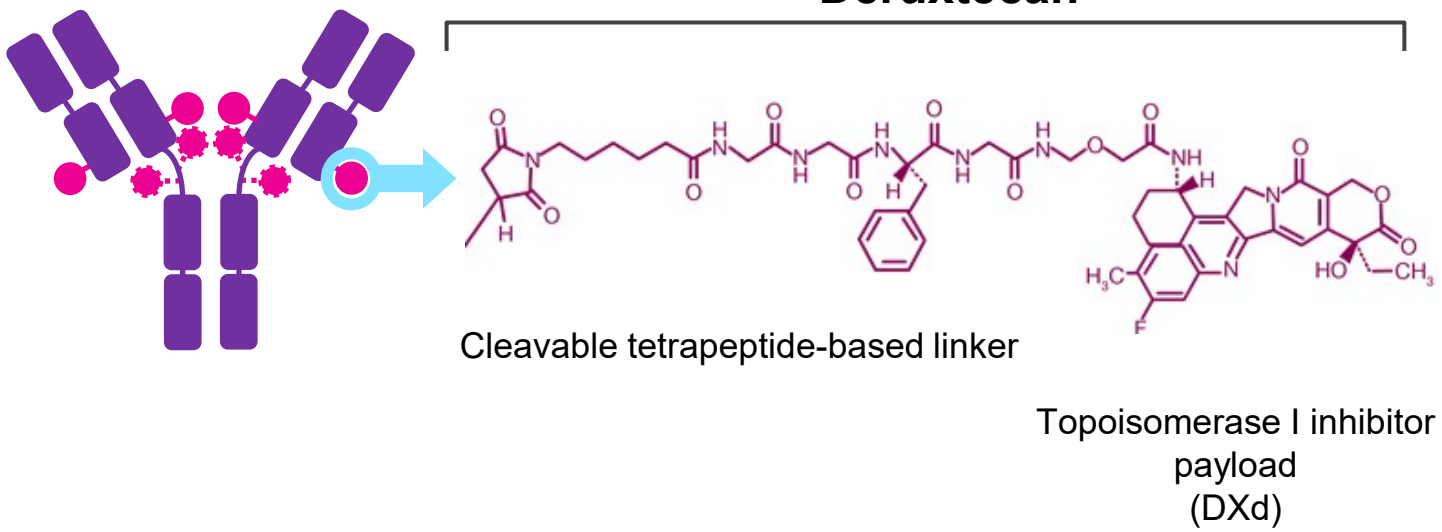
Limitation in therapeutic efficacy

ADC: antibody-drug conjugate

Daiichi Sankyo's DXd ADC technology solved conventional challenges

Widely applicable platform

DXd ADC Technology



7 Key Attributes[a] of DXd ADC

- Payload MOA: Topoisomerase I inhibitor
- High potency of payload
- High drug to antibody ratio (DAR)
- Stable linker-payload
- Payload with short systemic half-life
- Tumor-selective cleavable linker
- Bystander antitumor effect

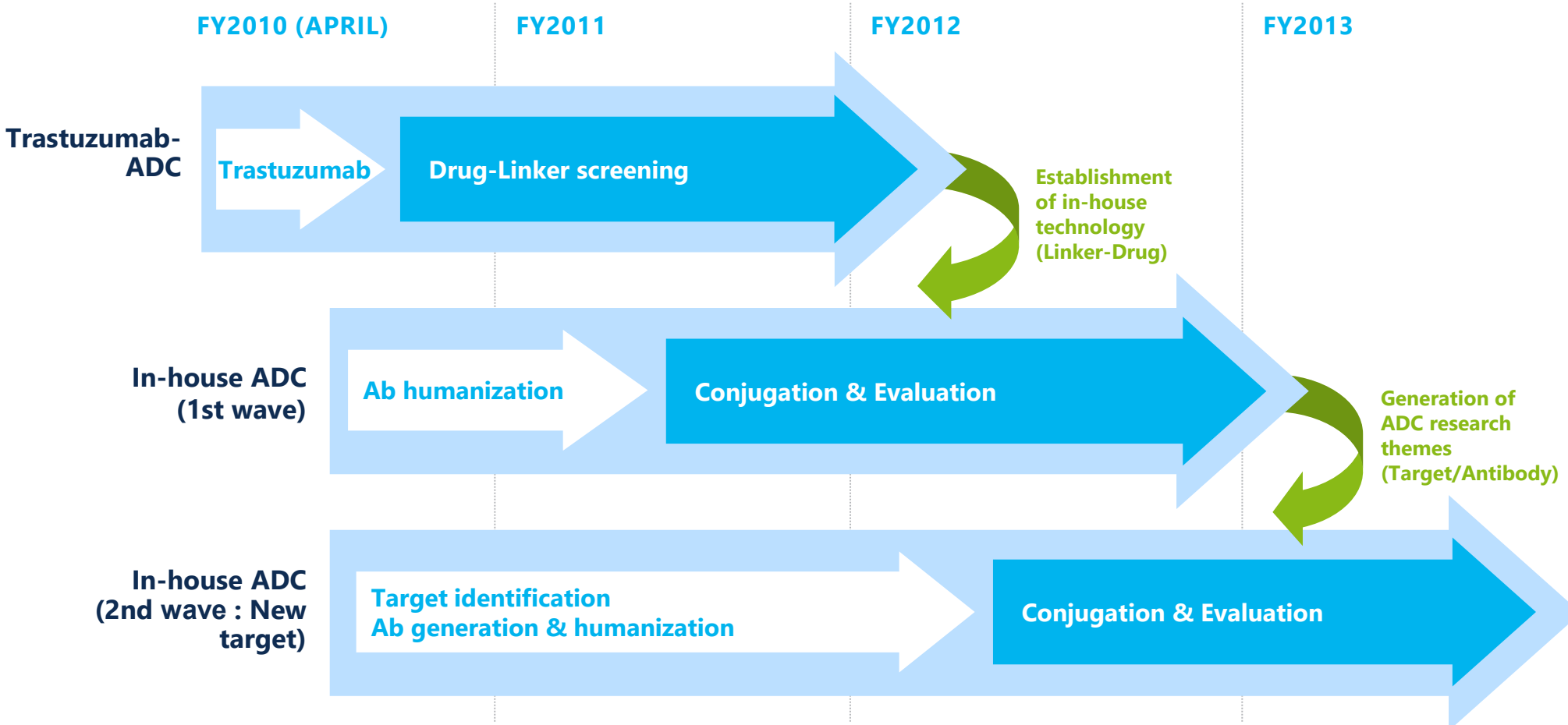
[a]The clinical relevance of these features is under investigation.

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

ADC: antibody-drug conjugate

Strategy for ADC research in Daiichi Sankyo as of 2010

Development of original ADC technology - Generation of innovative drugs for cancer patients



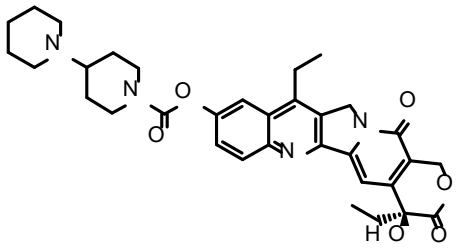
ADC: antibody-drug conjugate

Key point to success 1

Discovery of potent payload

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

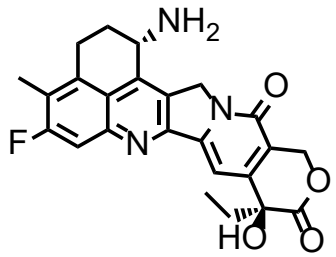
Irinotecan (CPT-11)



Prodrug of SN-38

Approved for refractory tumors in 1994.

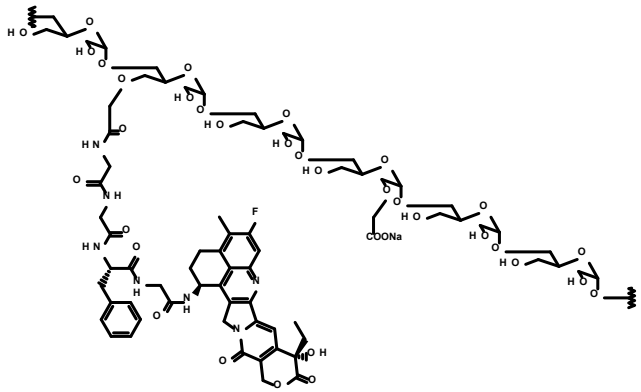
Exatecan (DX-8951)



10-fold more potent than SN-38

Discontinued (Ph3 study)

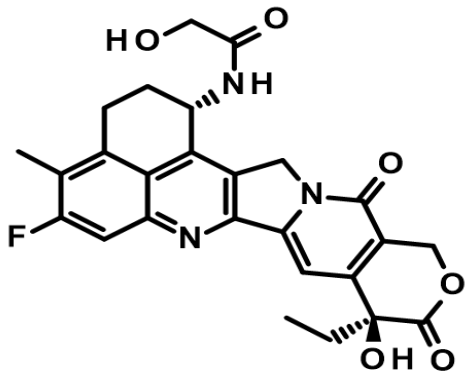
DE-310



Polymer-conjugate of exatecan

Discontinued (Ph1 study)

DXd (Exatecan derivative)

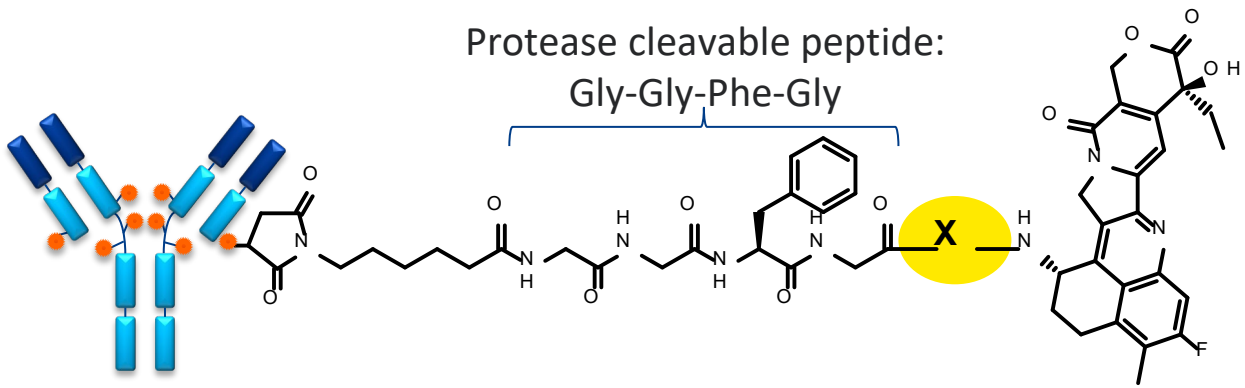


Source: *R De Jager et al., Ann N Y Acad Sci. 922:260-273 (2000), Soepenberg O et al., Clin Cancer Res 11:703-711 (2005)*

Key point to success 2

Design of drug-linker capable of demonstrating excellent efficacy

Development of unique drug-linker structure through the researchers' imagination and creativity, utilization of past knowledge & experience to leverage the benefits and improve the drawbacks



Entry	X	DAR	Aggregate (%)	KPL-4 IC_{50} (nM)
1	None	3.4	26	0.33
2	-NH-CH_2-(C=O)-	3.2	3	0.39
3	-NH-$(CH_2)_2$-(C=O)-	3.8	2	0.07
4	-NH-$(CH_2)_3$-(C=O)-	2.6	3	0.05
5	-NH-$(CH_2)_4$-(C=O)-	3.4	4	0.07
6	-NH-$(CH_2)_5$-(C=O)-	2.5	20	0.11
7	-NH-CH_2OCH_2-C(=O)-	7.7	0.6	0.19

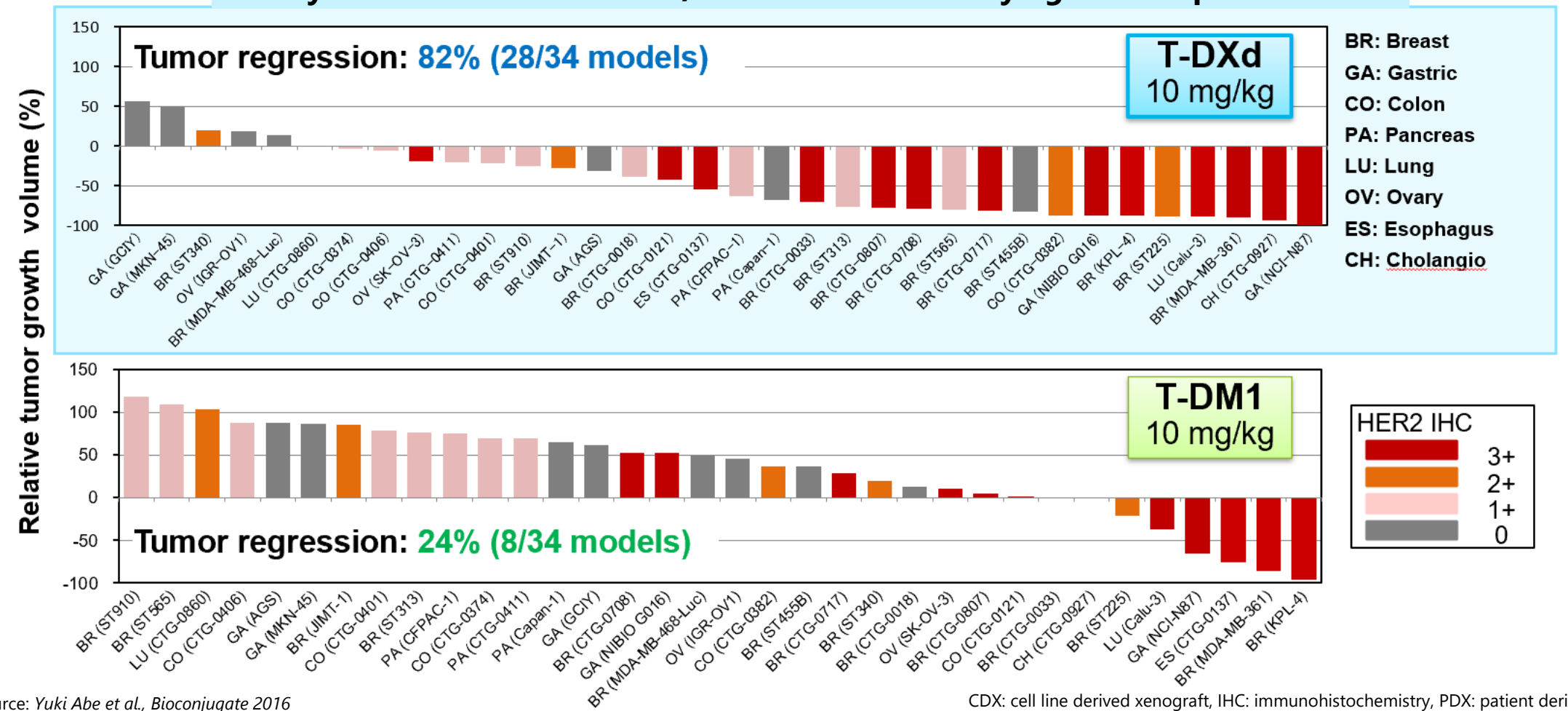
Source: *Abe Y et al. Drug Delivery System 34-1, pp.52-58* DAR: drug-antibody ratio

Key point to success 3

Confirmation of drug potential through animal models

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®)

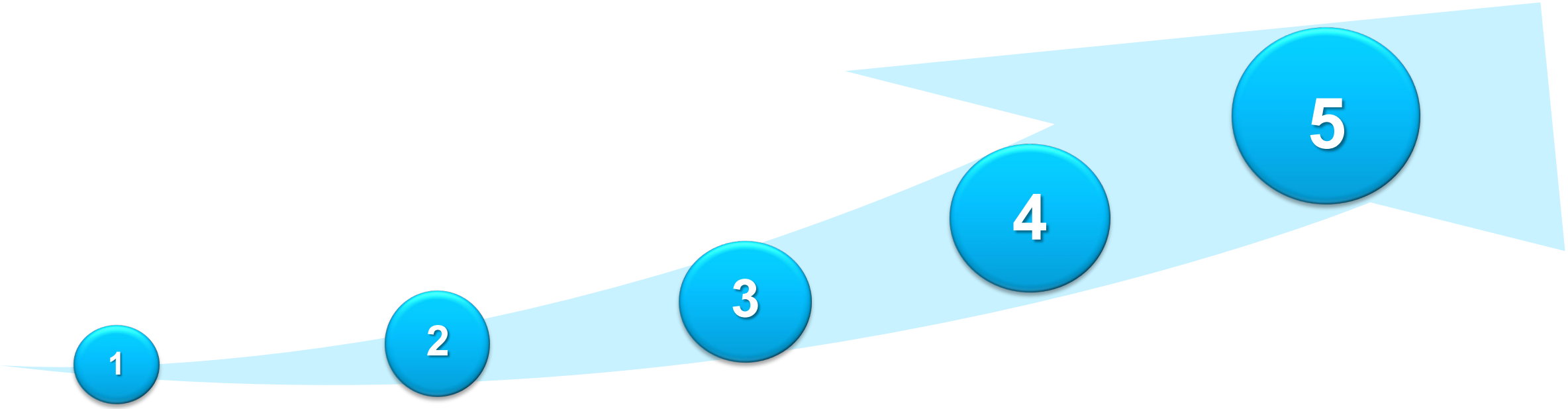
The Future of ADC research and development

- **Further increase in ADC products and expansion of target indications**
- **Investigation of drug combinations with ADC to show broader efficacy**
- **Develop new technologies to lessen adverse effects and seek cures**
  - **Establishment of new ADC technologies beyond next generation ADC through further investigation of payload, linker, DAR, etc.**

Further enhance Daiichi Sankyo as a global leader in ADC technology

ADC: antibody-drug conjugate, DAR: drug-antibody ratio

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

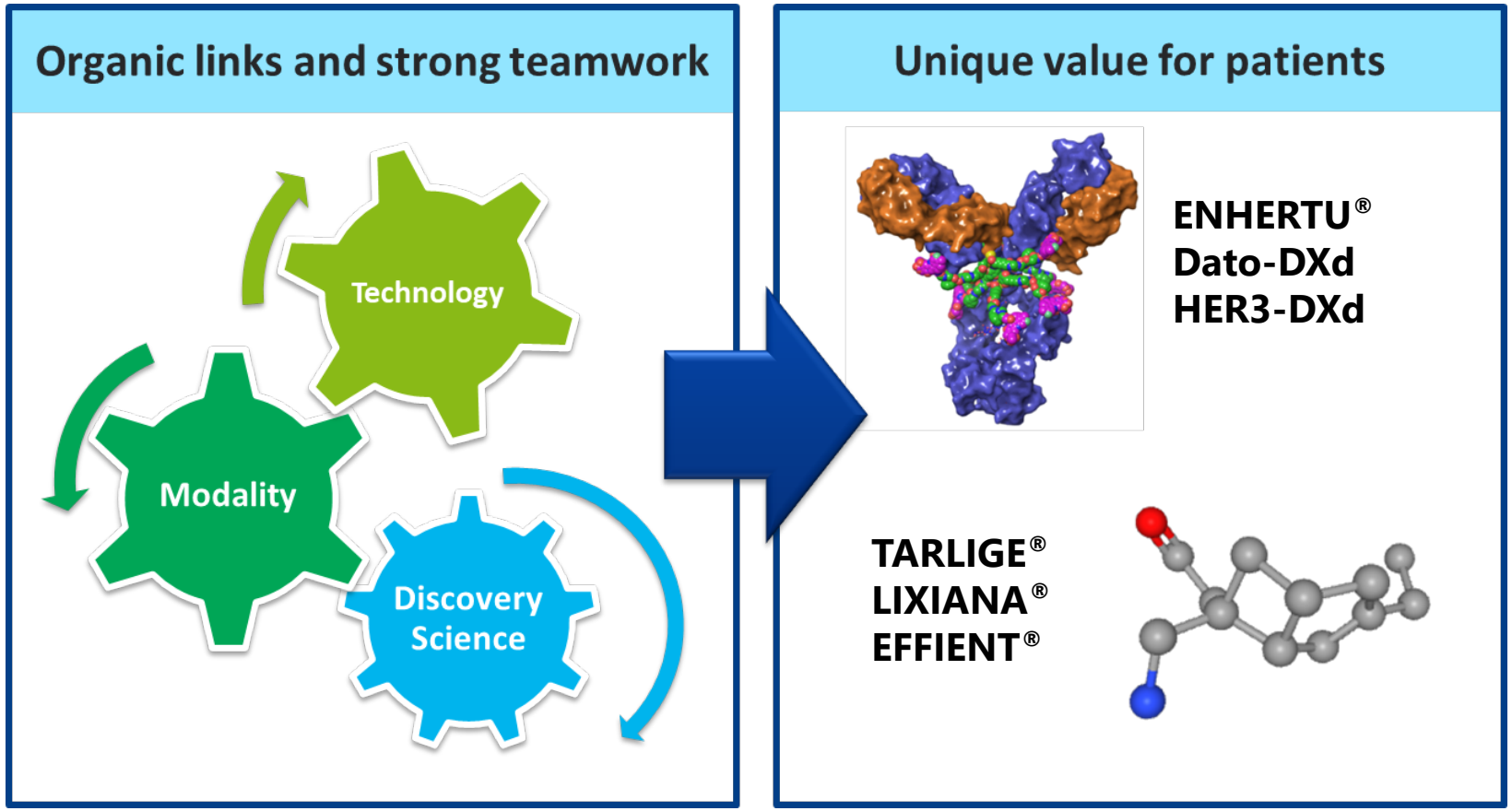
cept 4

cept 5

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

Key success factors of Daiichi Sankyo drug discovery:

Science & Technology through Craftspersonship

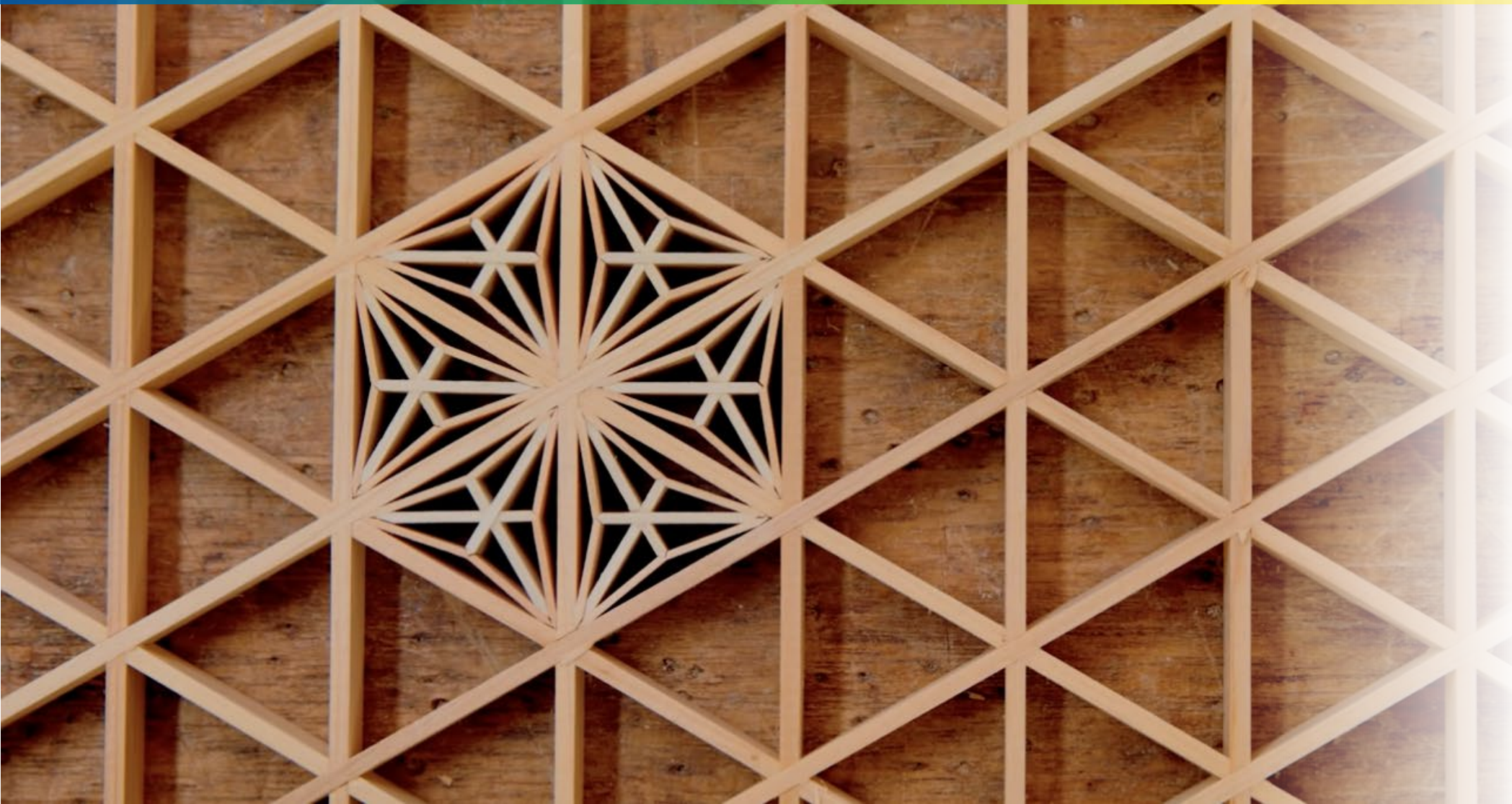


At DS, we

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

Crafting New Standards of Care

Daiichi-Sankyo

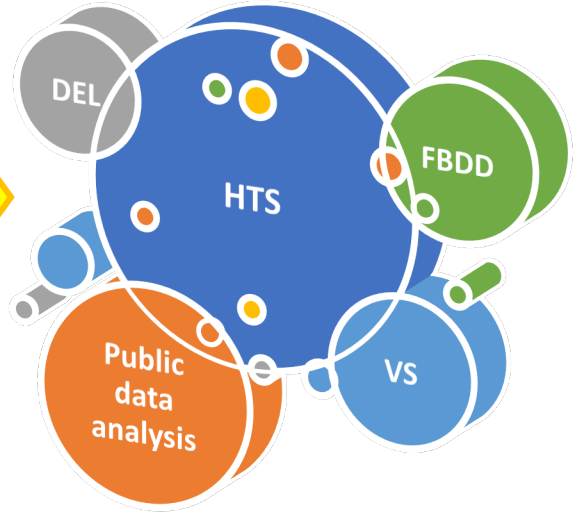


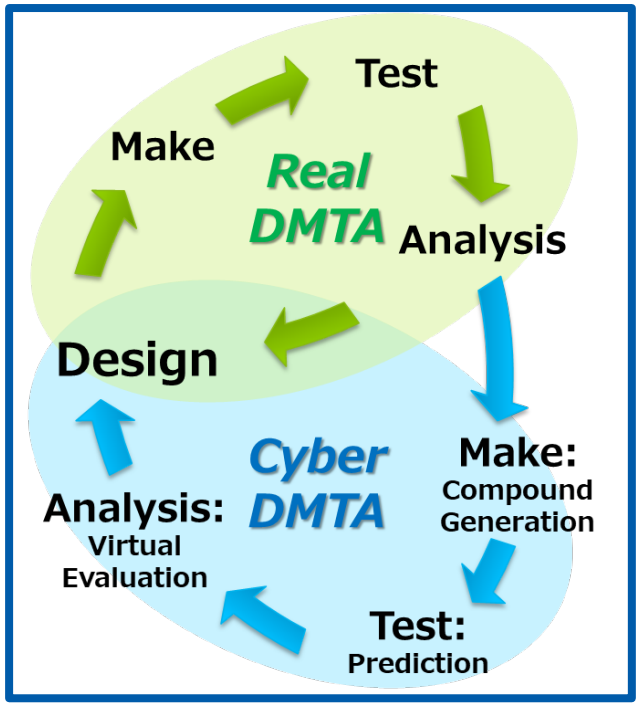
Data-Driven Drug Discovery (D4)

Effectively utilizing internal & external data to help deliver multiple clinical development candidates by enhancing the success rate and research speed of drug discovery research

Exploratory → **Hit discovery** → **Hit to lead / Lead optimization** → **Pre-Clinical**

Disease & target information





Clinical development candidate

We will expand D4 to include various modalities and accelerate drug discovery through cutting-edge computer-driven lab automation

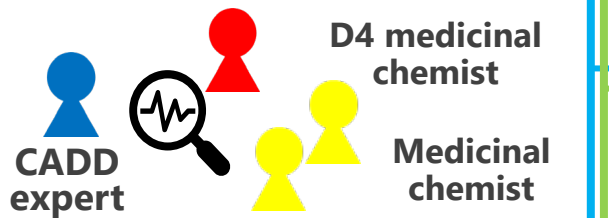
Source: *R. Kunimoto, J. Bajorath, K. Aoki., Drug Discovery Today, 2022* (the figure is partially modified)
DMTA: Design-Make-Test-Analysis

DEL: DNA encoded library, DMTA: Design-Make-Test-Analysis, FBDD: fragment-based drug discovery, HTS: high throuput screening, VS: virtual screening

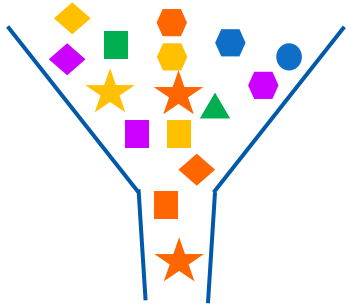
Improvement of research efficiency and quality of compound design through Cyber DMTA

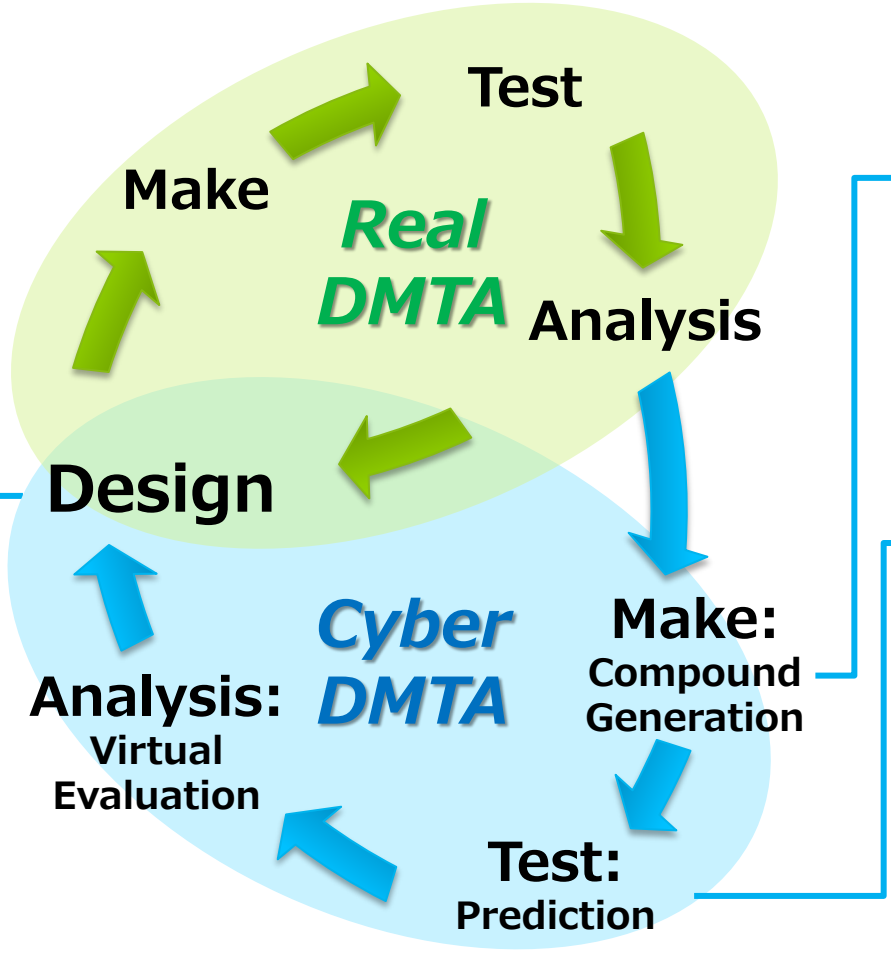
Daiichi-Sankyo

Determine the next compound to be created

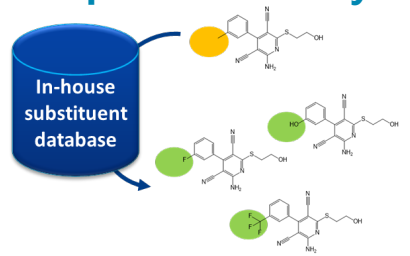


Narrow down to promising compounds

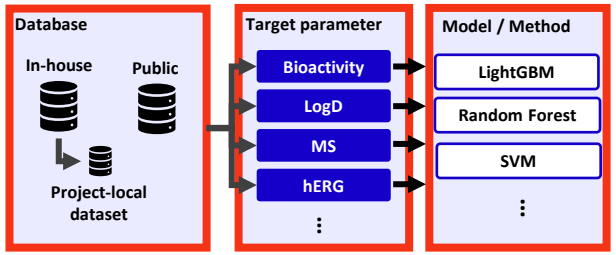




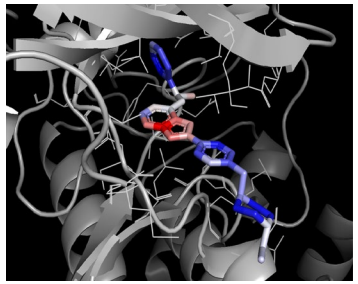
Generate a large number of various compounds virtually



Property prediction by ML



Target binding simulation with precise calculation



- **New tools allowed us to attain higher-quality compound designs through data analysis**

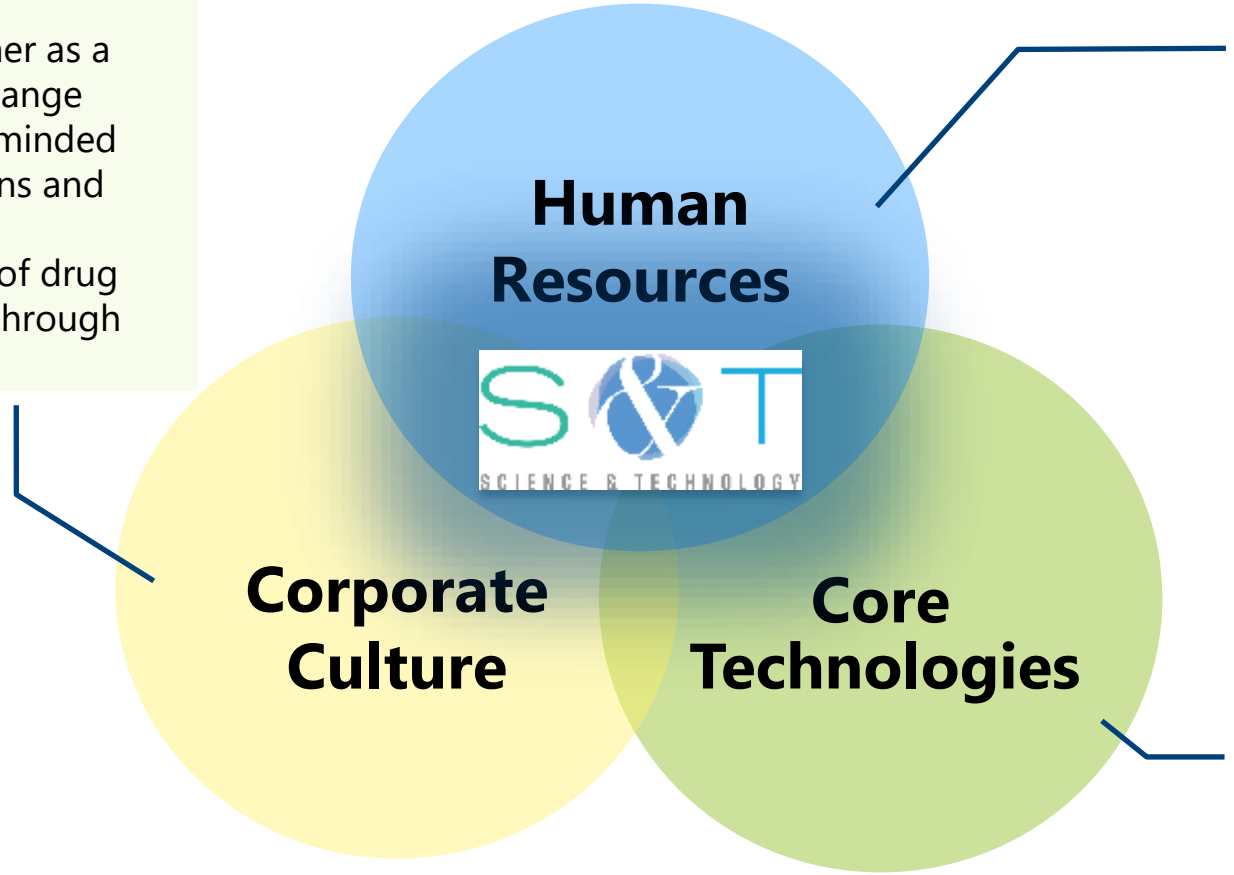
CADD: computer aided drug design, DMTA: Design-Make-Test-Analysis, D4: Data-Driven Drug Discovery, ML: machine learning

Identifying Our Next Growth Driver

Further enhancement of our strengths "Science & Technology" is essential for sustainable growth

Our Strength

- Our corporate culture:
  Researchers respect each other as a specialist in science and exchange opinions in a free and open-minded manner regardless of positions and tenure
- Techniques and experiences of drug development handed down through our history



- Pursue cutting-edge science
- Scientific assessment capabilities
- Technologies originated from craftspersonship
- A high level of engagement
- Eagerness for innovation

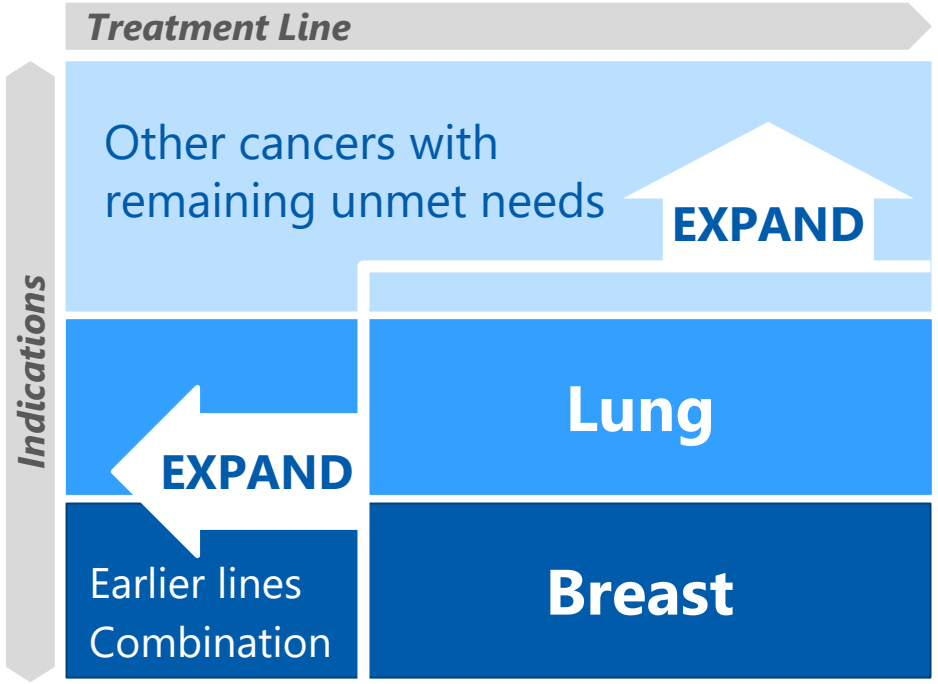
- Our proprietary ADC technology platform
- Medicinal chemistry, protein engineering, drug evaluation, computational science and translational research

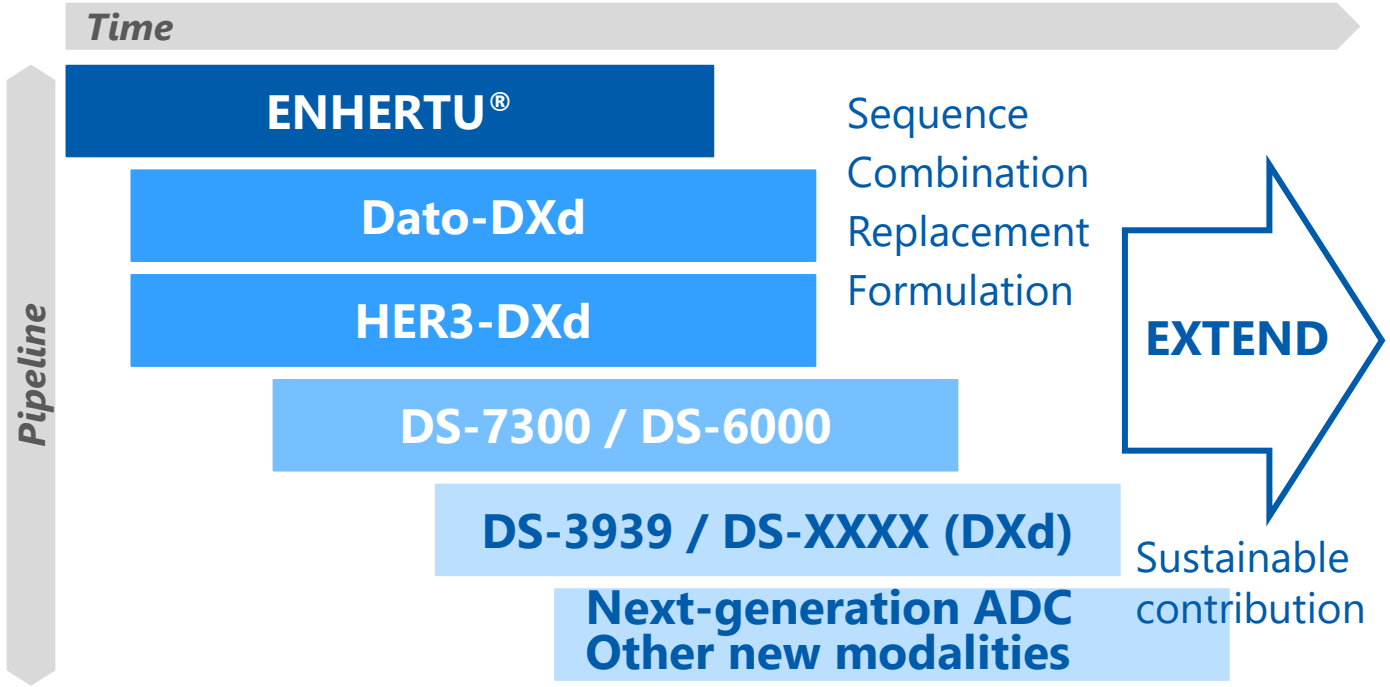
ADC: antibody-drug conjugate

Agenda

1. Opening
2. R&D Strategy
3. Research Capability
4. **Clinical Progress**
5. Q&A

EXPAND & EXTEND to deliver our technology to more patients



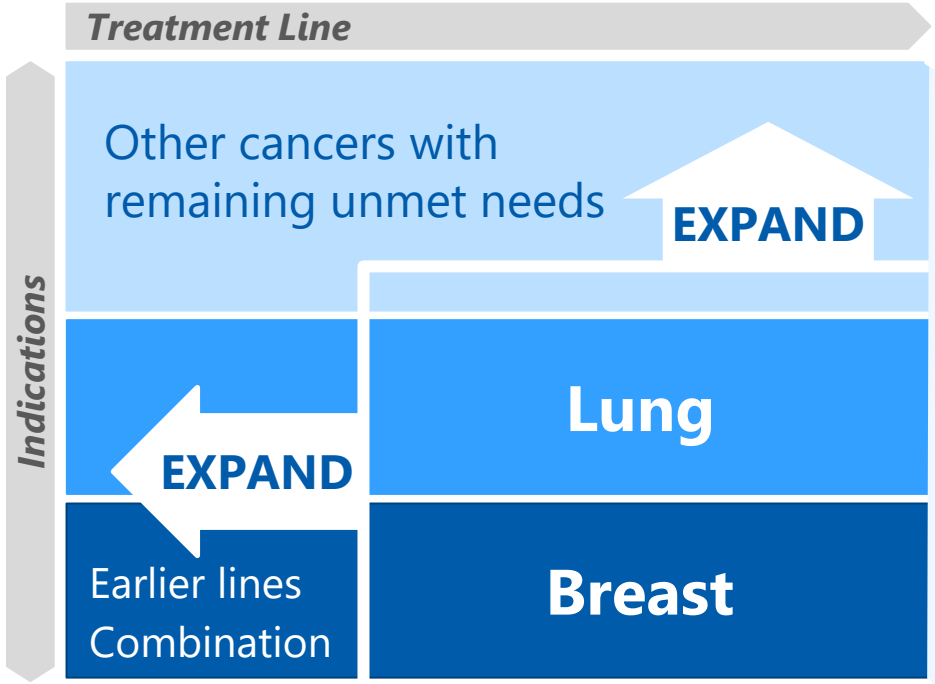


- Establish and expand DXd ADC therapies in **Breast** and **Lung** cancers
- **Go Earlier:** explore early lines of therapy/ stage of diseases; replace chemotherapy
- **Go Wider:** into new diseases beyond currently focusing areas to serve more patients in needs

- 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

ADC: antibody-drug conjugate

EXPAND & EXTEND to deliver our technology to more patients



5DXd ADCs Progress and Future

- **Breast cancer**
- Lung cancer
- New disease areas

ADC: antibody-drug conjugate

Our Breast Cancer Strategy

Expand on our leadership in breast cancer to deliver additional novel treatment options to improve patient outcomes for a broad set of distinct patient segments

- Establish our assets as **a foundational treatment option** across early to metastatic disease
- Identify novel **combination** and **sequencing** strategies to improve patient outcomes
- Enhance our **knowledge of the underlying biology** across the disease spectrum of breast cancer

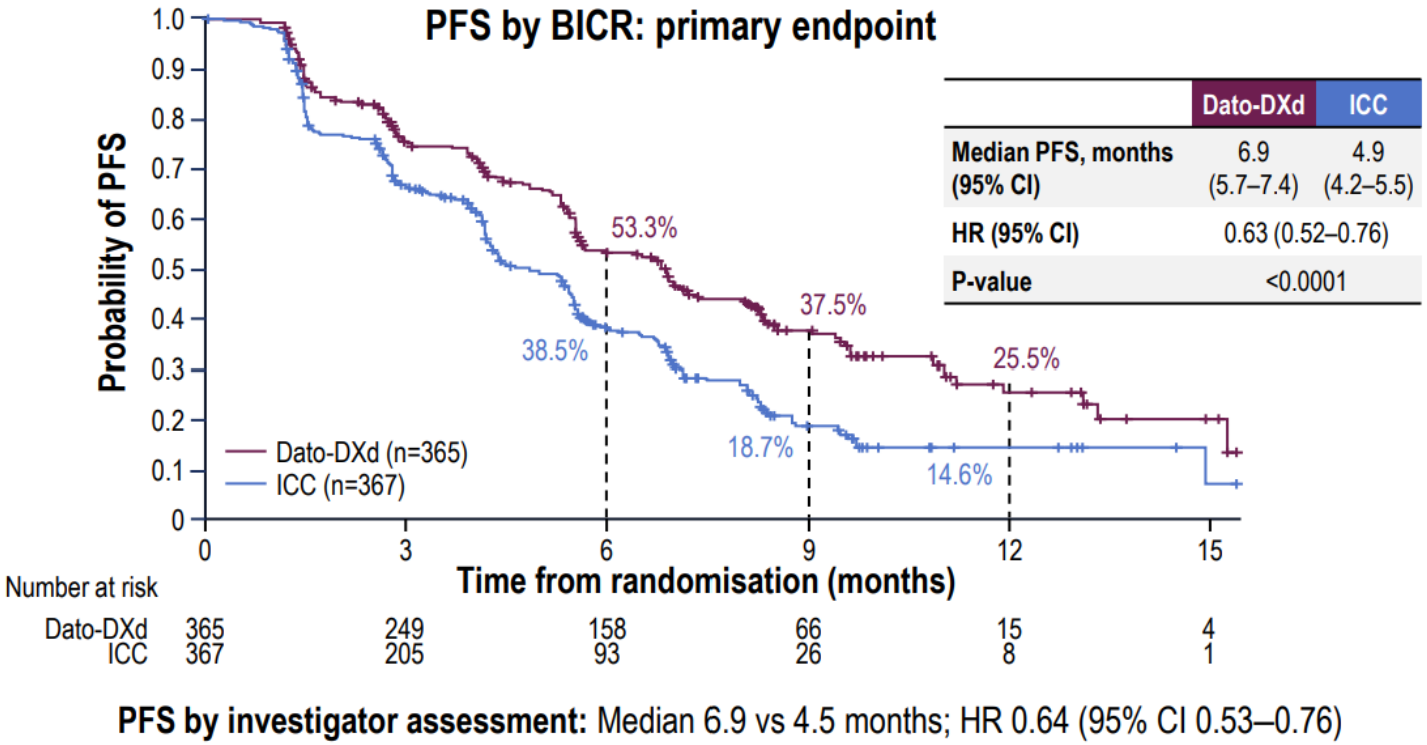
TROPION-Breast01

ESMO 2023

Daiichi-Sankyo

TROPION-Breat01 enables Dato-DXd to aim to set a new standard for TROP2 ADCs in HR+/HER2 low or negative BC

PFS



	Dato-DXd	ICC
Median PFS, months (95% CI)	6.9 (5.7–7.4)	4.9 (4.2–5.5)
HR (95% CI)	0.63 (0.52–0.76)	
P-value	<0.0001	

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

Dato-DXd

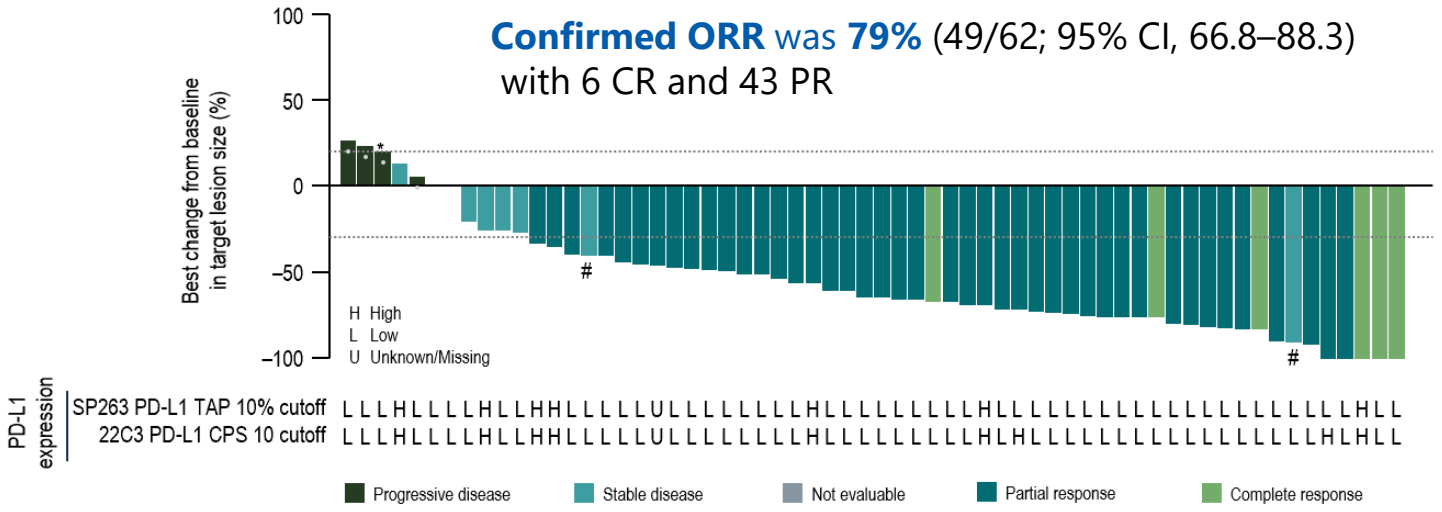
BEGONIA Data Update

ESMO 2023

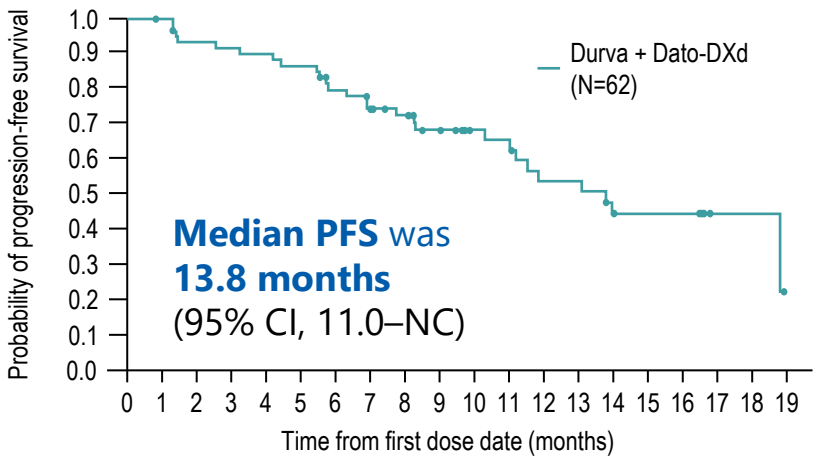
Daiichi-Sankyo

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

DESTINY-Breast01/02/03 pooled analysis for BM

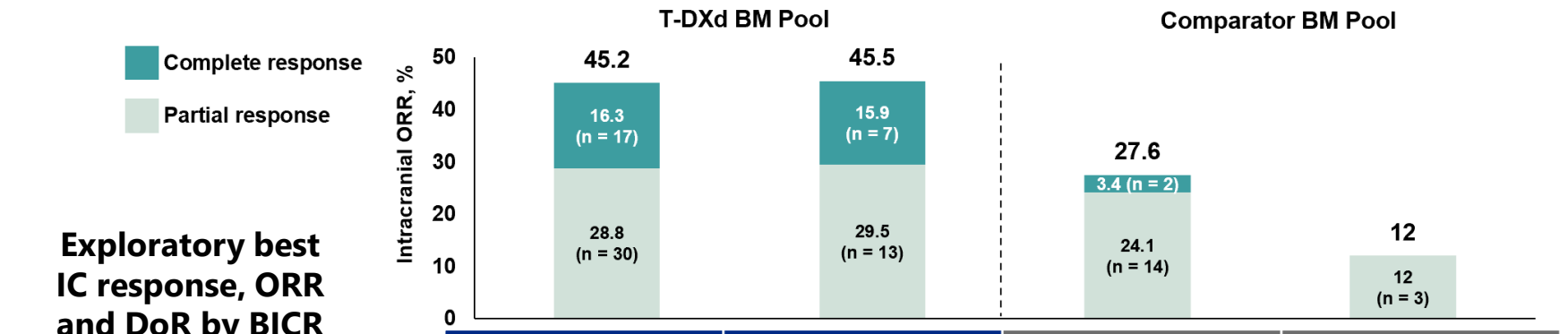
ESMO 2023

Daiichi-Sankyo

ENHERTU® is an effective treatment options for patients with HER2+ mBC with treated/stable and untreated/active brain metastasis (BM)

Pooled exploratory analysis of DESTINY-Breast01, DESTINY-Breast02 and DESTINY-Breast03 in HER2+ mBC

Intracranial ORR[a]



Exploratory best IC response, ORR and DoR by BICR

	Treated/stable BMs (n = 104)	Untreated/active BMs (n = 44)	Treated/stable BMs (n = 58)	Untreated/active BMs (n = 25)
Best overall IC response, n (%)				
Stable disease	48 (46.2)	15 (34.1)	28 (48.3)	15 (60.0)
Progressive disease	3 (2.9)	1 (2.3)	7 (12.1)	5 (20.0)
Not evaluable/Missing	6 (5.8)	8 (18.2)	7 (12.1)	2 (8.0)
IC-DoR, median, months (95% CI)	12.3 (9.1-17.9)	17.5 (13.6-31.6)	11.0 (5.6-16.0)	NA[b]

This table considers both target and non-target lesions at baseline. Lesions in previously irradiated areas were not considered measurable target lesions unless there was demonstrated progression in the lesion. [a] IC-ORR was assessed per RESIST v1.1. [b] IC-DoRNA due to small number of responders (n < 10).

- Demonstrated **robust intracranial (IC) responses** in patients with stable BMs (IC-ORR 45.2% vs 27.6%, median IC-DoR 12.3 vs 11.0 months) and active BMs (IC-ORR 45.5% vs 12.0%, median IC-DoR 17.5 vs NA)
- **Numerically longer median CNS-PFS** was observed in stable BMs (12.2 vs 8.7 months) and active BMs (18.5 vs 4.0 months)
- The safety profile in patients with BMs was acceptable, generally manageable and similar to the safety profile in the overall patient population

BM: brain metastasis, BICR: blinded independent central review, DoR: duration of response, IC: intracranial, mBC: metastatic breast cancer, NA: not available, ORR: objective response rate, T-DXd, trastuzumab deruxtecan (ENHERTU®)

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

DESTINY-Breast08 Study

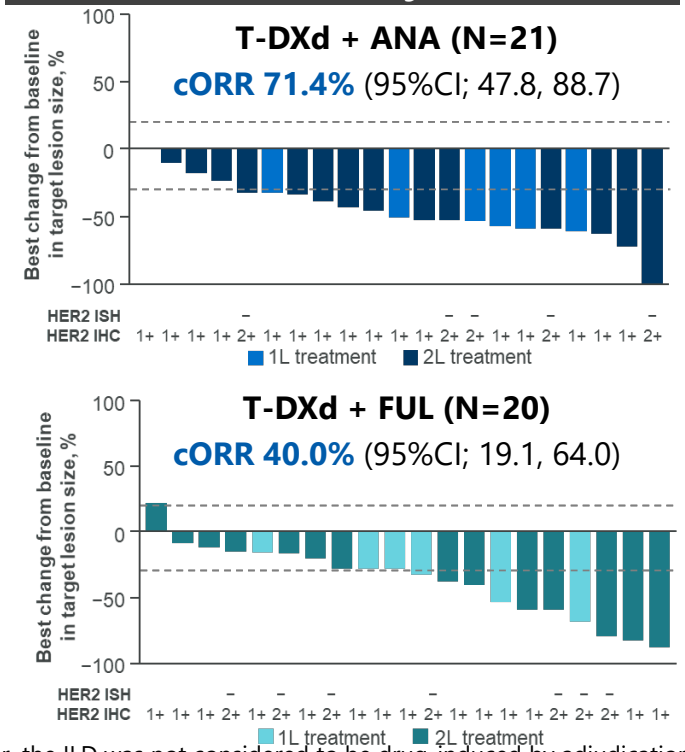
A Ph1b study to investigate safety, tolerability, PK and preliminary anti-tumor activity of ENHERTU® in combination with other therapeutics in patients with HER2 low mBC

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 Ejection fraction decreased‡ Pneumonitis (adjudicated as ILD related to any study drug)	1 (4.8) 0	1 (5.0) 5 (25.0), all grade 2

Data cutoff: Aug 16, 2023

Efficacy

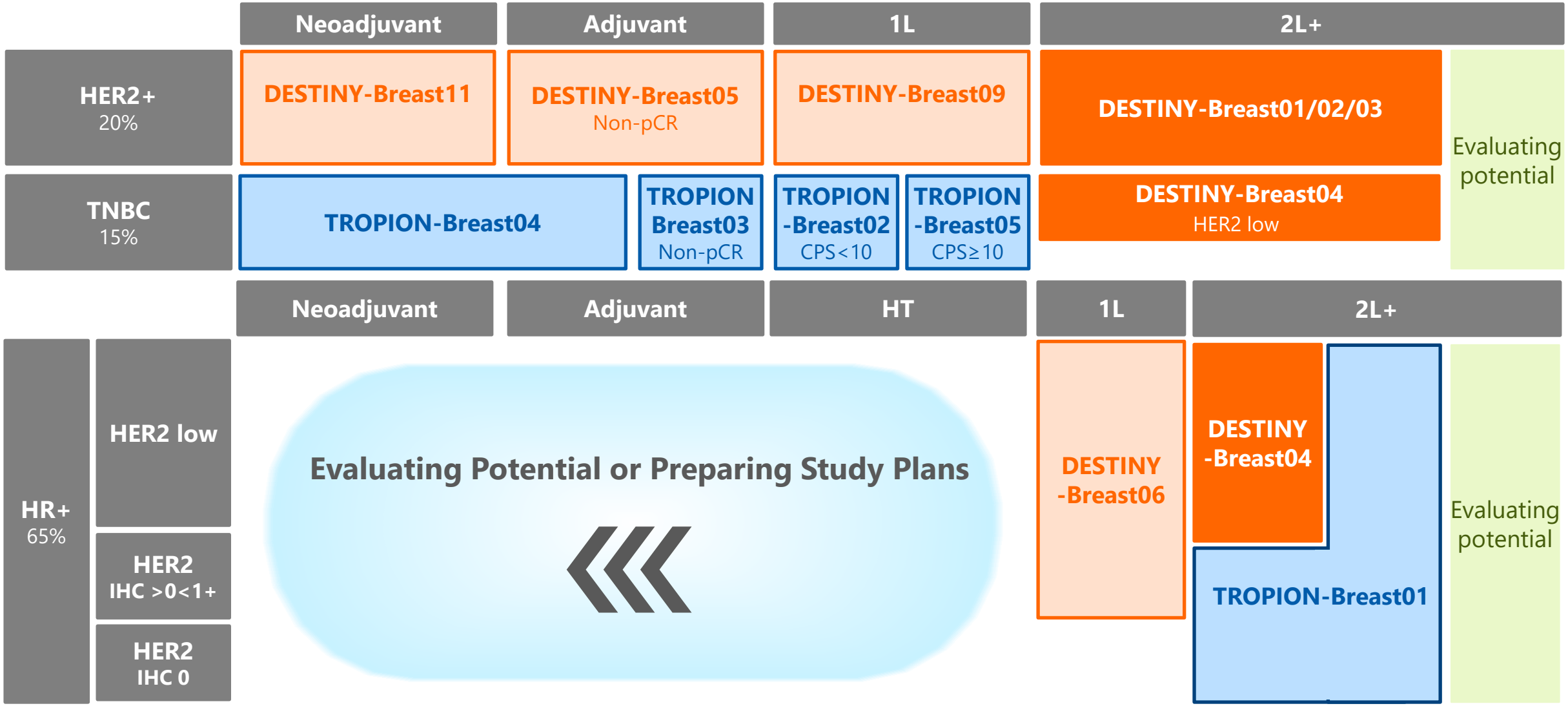


- For T-DXd+ ANA and T-DXd + FUL arms, 66.7% and 70.0% of patients received a prior line of treatment for mBC, respectively
- Safety profiles were generally consistent or comparable to the known safety profile
- No ILD in T-DXd + ANA arm, while 5 Grade 2 ILD/pneumonitis events in T-DXd + FUL arm
- Confirmed 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.

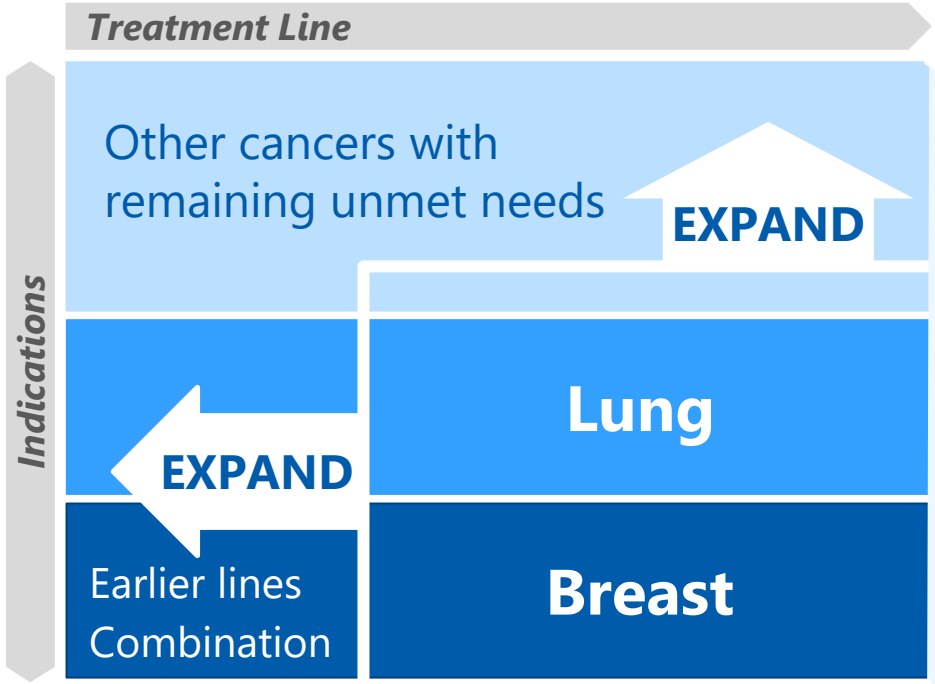
AE: adverse event, AESI: adverse event of special interest, ANA: anastrozole, CI: confidence interval, cORR: confirmed overall response rate, DOR: duration of response, ET: endocrine therapy, FUL: fulvestrant, IHC: immunohistochemistry, ISH: *in situ* hybridization, mBC: metastatic breast cancer, mPFS: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

Establish and expand DXd ADCs to address the broader spectrum of Breast Cancer



Pivotal studies only (not exhaustive). CPS, combined positive score; HT, Hormone therapy; HR, hormone receptor; IHC: immunohistochemistry, pCR: pathological complete response, TNBC, triple-negative breast cancer

EXPAND & EXTEND to deliver our technology to more patients



5DXd ADCs Progress and Future

- Breast cancer
- **Lung cancer**
- New disease areas

ADC: antibody-drug conjugate

Our Lung Cancer Strategy

Deliver practice-changing medicines to meet evolving unmet needs in lung cancer for a broad set of distinct patient types by harnessing the depth of the Daiichi Sankyo portfolio

- Provide superior 2L+ treatments and differentiated combinations in **metastatic NSCLC with DXd ADCs as the foundational treatment**
- Leverage the innovation in DXd ADCs **to move into early-stage NSCLC**
- Identify **novel therapeutic approaches for extensive-stage SCLC** to address significant unmet need

ADC: antibody-drug conjugate, NSCLC: non-small cell lung cancer; SCLC: small cell lung cancer

ENHERTU®

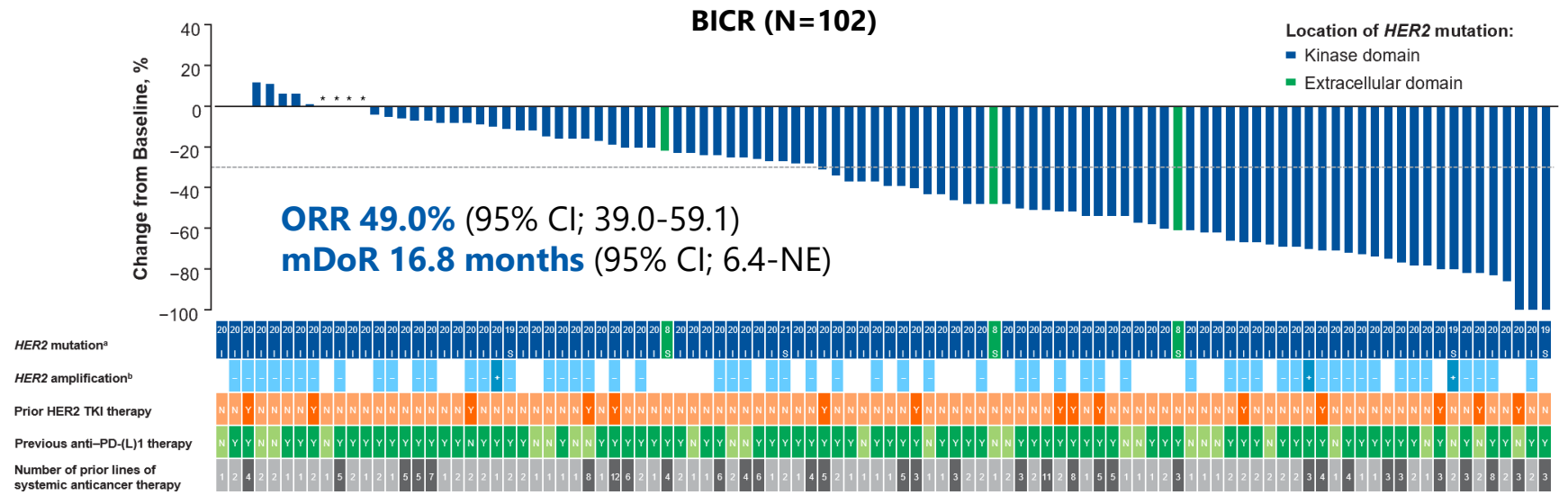
DESTINY-Lung02 Primary Analysis

WCLC 2023

Daiichi-Sankyo

ENHERTU® 5.4mg/kg is supported as the standard of care in previously treated *HER2mut* NSCLC population

Objective Response in 5.4 mg/kg



- ENHERTU® demonstrated **deep and durable responses** at both the 5.4 mg/kg and 6.4 mg/kg doses
- Responses were **consistent** regardless of HER2 mutation type, HER2 amplification status, and prior systemic anticancer therapy
- The safety profile was **acceptable and generally manageable** at both doses and favored the 5.4 mg/kg dose in terms of lower incidence of TEAEs and ILD

DESTINY-Lung02 Study

A Ph2 study assessed he efficacy and safety of ENHERTU® 5.4 mg/kg and 6.4 mg/kg in patients with *HER2m* metastatic NSCLC

Approval of ENHERTU® for HER2 mutant NSCLC was expanded to Japan (Aug) and EU (Oct) in 2023 based on the DESTINY-Lung02 results*

*Approved in US in Aug 2022

*Indicates the patient had 0 best percentage change from baseline in the sum of diameters for all target lesions. Numbers in the HER2 mutation row indicate in which exon the mutation occurred (8, 19, or 20). HER2 amplification was only assessed in patients who received T-DXd 5.4 mg/kg. [a]Activating HER2 mutation documented from an archival or fresh tumor tissue sample by certified local laboratory assessment. [b]HER2 amplification status was evaluated using an exploratory Oncomine DX Target test copy number algorithm on NSCLC formalin formalin-fixed paraffin paraffin-embedded tissue samples.
BICR: blinded independent central review; CI: confidence interval, I: insertion, ILD: interstitial lung disease, mDoR: median duration of response, NE: not estimable, NSCLC: non-small cell lung cancer, S: substitution, T-DXd: trastuzumab deruxtecan (ENHERTU®), TEAE: treatment emergent adverse events.

Dato-DXd

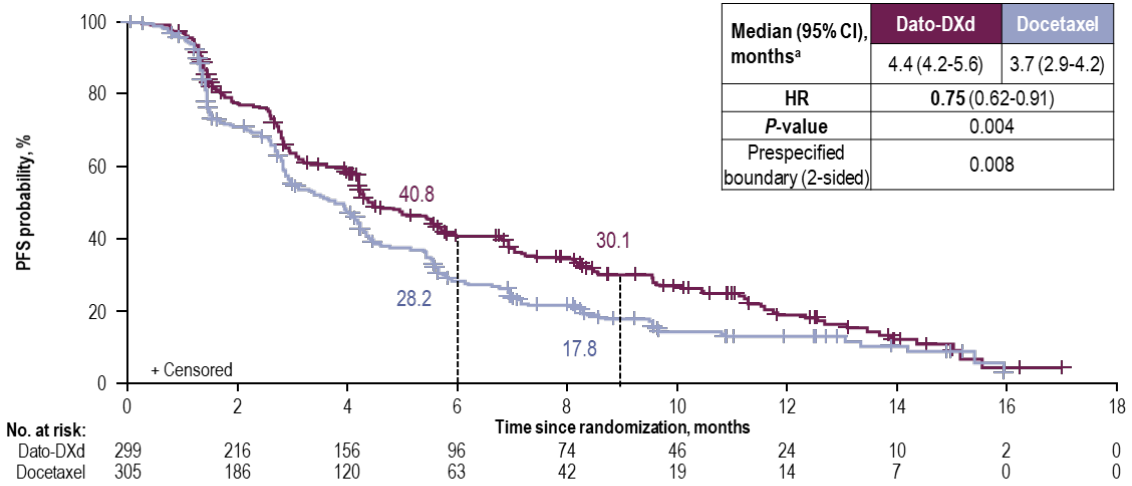
TROPION-Lung01 overall efficacy in NSCLC 2/3L

ESMO 2023

Daiichi-Sankyo

Dato-DXd is the first ADC to demonstrate a statistically significant improvement in PFS over docetaxel in NSCLC

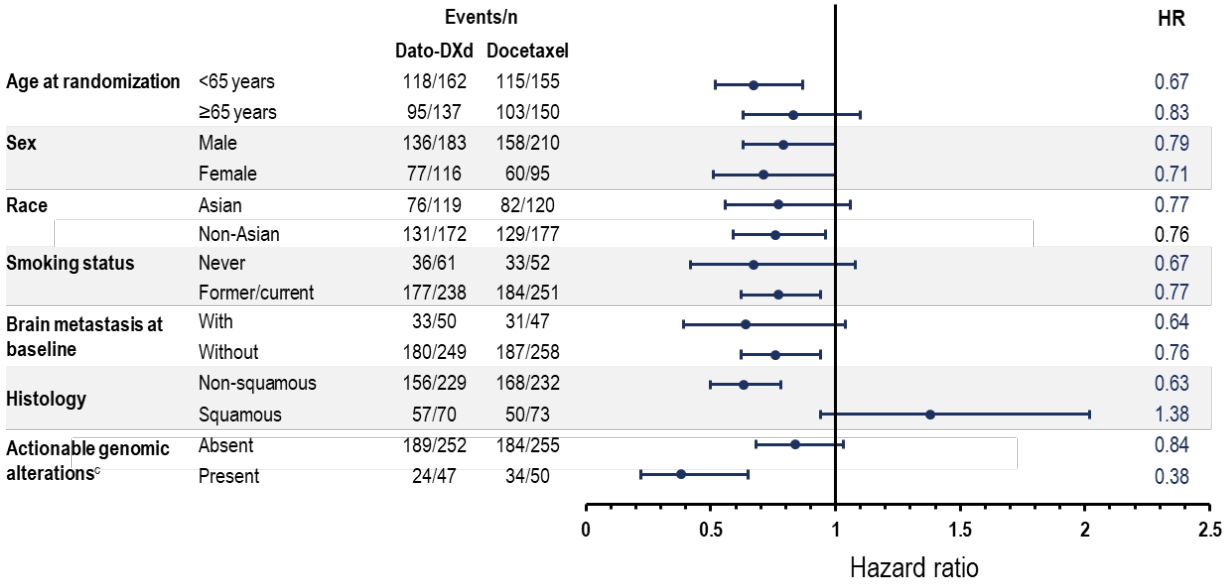
PFS for ITT



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)

PFS in Key Subgroups



Data cutoff: Mar 2023

- **Met dual primary endpoint of PFS**
- Hazard Ratio: 0.75 (95% CI, 0.62-0.91)
- ORR: Dato-DXd; 26.4%, Docetaxel; 12.8%
- Median PFS: Dato-DXd; 4.4 months, Docetaxel; 3.7 months
- The interim OS favors Dato-DXd, and the trial is continuing to final analysis

- Hazard ratio for non-squamous: 0.63, and for squamous:1.38
- Hazard ratio for patients without AGA: 0.84, and for patients with AGA: 0.38

[a]Median PFS follow-up time 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 four CRs and 75 PRs for Dato-DXd and 39 PRs for docetaxel. [c]Regardless of histology.
ADC: antibody-drug conjugate, AGA: actionable genomic alteration, CI: confidence interval, DOR: duration of response, DTX: docetaxel, HR: hazard ratio, ITT: intention-to-treat, mo: months, NSCLC: non-small cell lung cancer, ORR: objective response rate, OS: overall survival, PFS: progression-free survival

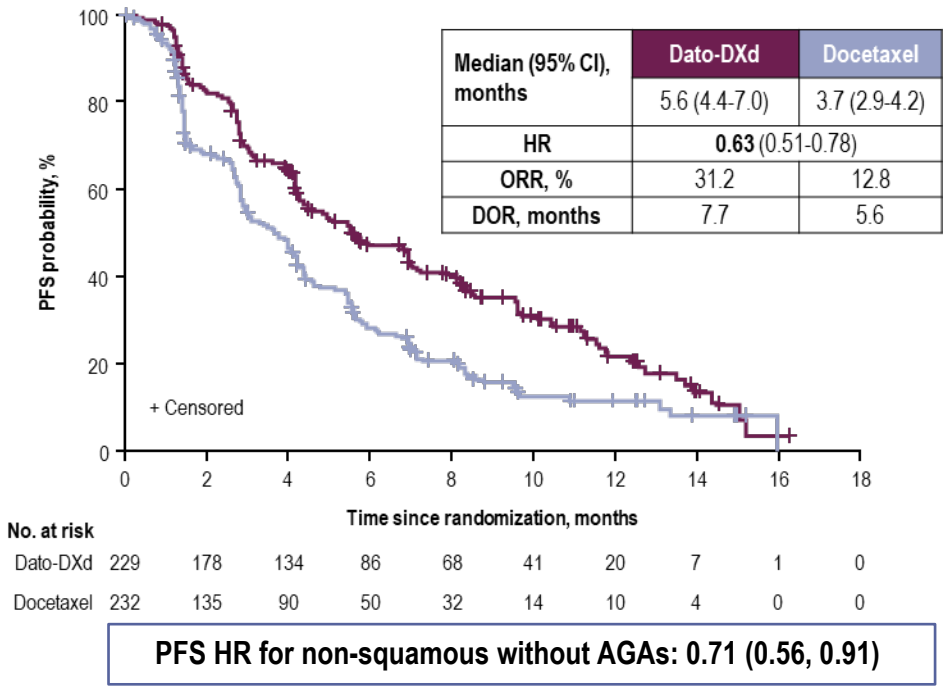
TROPION-Lung01 efficacy in non-sq and sq NSCLC

ESMO 2023

Daiichi-Sankyo

Dato-DXd is potentially practice-changing in non-squamous 2L+ NSCLC

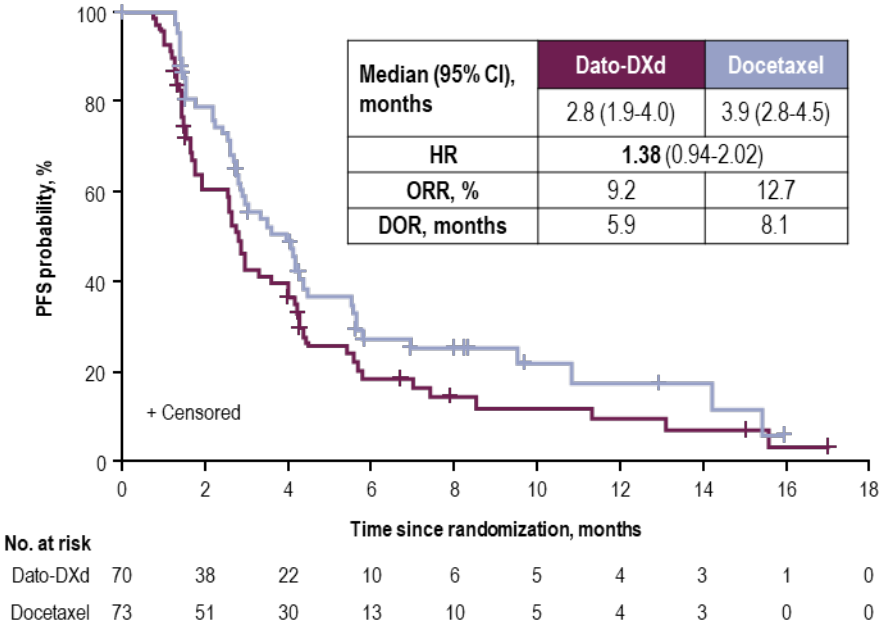
PFS in Non-squamous (with and without AGAs)



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

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

PFS in 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

- Longer median PFS was observed in prespecified subgroups including non-squamous histology (Nsq; 5.6 vs 3.7 months).
- Plan to amend TROPION-Lung08 study protocol to cap the squamous population
- **Plan to file in the US** with TROPION-Lung01 study data **within FY2023**

Squamous subset included 3 patients with AGAs.
AGA: actionable genomic alterations, CI: confidence interval, DOR: duration of response, HR: hazard ratio, NSCLC: non-small cell lung cancer, Nsq: non-squamous, ORR: objective response rate, PFS: progression-free survival. sq: squamous

TROPION-Lung01 Safety

ESMO 2023

Daiichi-Sankyo

Favorable tolerability against chemotherapy, careful monitoring is required for ILD management

TRAEs, n (%)	Dato-DXd N=297	Docetaxel N=290
All grades	257 (87)	252 (87)
Grade ≥3	73 (25)	120 (41)
Associated with dose reduction	58 (20)	85 (29)
Associated with dose delay	49 (17)	31 (11)
Associated with discontinuation	23 (8)	34 (12)
Associated with death[a]	3 (1)	2 (1)
Serious TRAEs	30 (10)	36 (12)
Grade ≥3	25 (8)	33 (11)

[a]Investigator assessed. Dato-DXd: 2 cases of ILD/pneumonitis and 1 case of sepsis; docetaxel: 1 case of ILD/pneumonitis and 1 case of septic shock.
The safety analysis set included all randomized patients who received ≥1 dose of the study drug.

- Fewer grade ≥3 TRAEs were observed with Dato-DXd compared with docetaxel
- Fewer TRAEs leading to dose reductions or discontinuations were seen with Dato-DXd compared with docetaxel

AESI, n (%)	Dato-DXd N=297	Docetaxel N=290
Stomatitis/oral mucositis[a]		
All grades	160 (54)	59 (20)
Grade ≥3	19 (6)	4 (1)
Ocular events[b]		
All grades	57 (19)	27 (9)
Grade ≥3	5 (2)[c]	0
Adjudicated drug-related ILD[d]		
All grades	25 (8)	12 (4)
Grade ≥3	10 (3)	4 (1)
Grade 5	7 (2)	1 (0.3)

[a]Events included the selected PTs oral mucositis/stomatitis, oropharyngeal pain, mouth ulceration, odynophagia, dysphagia, oral pain, glossitis, pharyngeal inflammation, aphthous ulcer, and oral mucosa erosion. [b]Ocular events included selected PTs from the corneal disorder SMQ and selected relevant PTs from the eye disorder SOC. [c]Included 4 cases of keratitis and 1 case of ulcerative keratitis. [d]ILD includes events that were adjudicated as ILD and related to use of Dato-DXd or docetaxel (includes cases of potential ILD/pneumonitis based on MedDRA v26.0 for the narrow ILD SMQ, selected terms from the broad ILD SMQ, and PTs of respiratory failure and acute respiratory failure). [e]Among treated patients, histology information per the case report form.

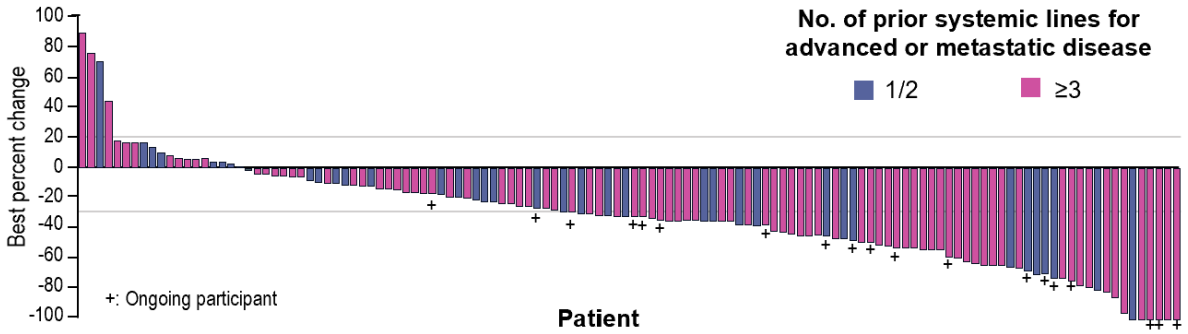
- Seven adjudicated drug-related grade 5 ILD events
  - Primary cause of death in 4 out of 7 was attributed to disease progression by investigator
  - Non-squamous: 4 of 232 patients (1.7%); Squamous: 3 of 65 patients (4.6%)[e]

AESI: adverse event of special interest, ILD: interstitial lung disease, MedDRA: Medical Dictionary for Regulatory Activities, PT: preferred term, SMQ: standard MedDRA queries, TRAE: treatment-related adverse events

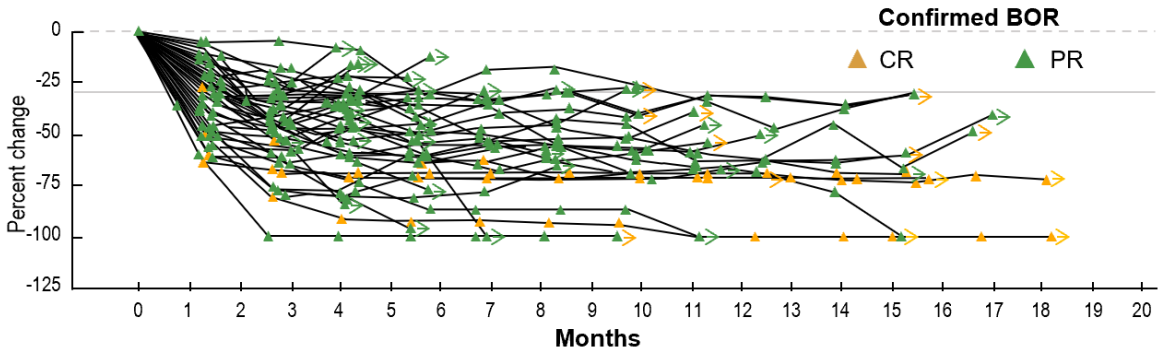
Encouraging antitumor activity was observed with Dato-DXd treatment in a heavily pretreated NSCLC population with AGAs

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

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

HERTHENA-Lung01 study – Efficacy in Brain Met

ESMO 2023

Daiichi-Sankyo

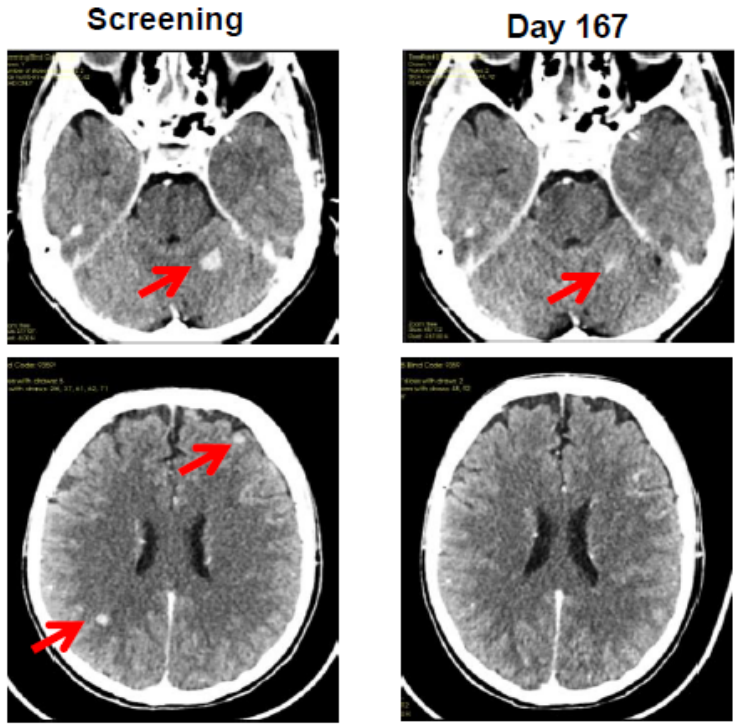
HER3-DXd demonstrated clinically meaningful and durable intracranial responses in patients with no prior radiotherapy

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.

Partial CNS Response in a Patient With a Measurable CNS BICR Target Lesion



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.

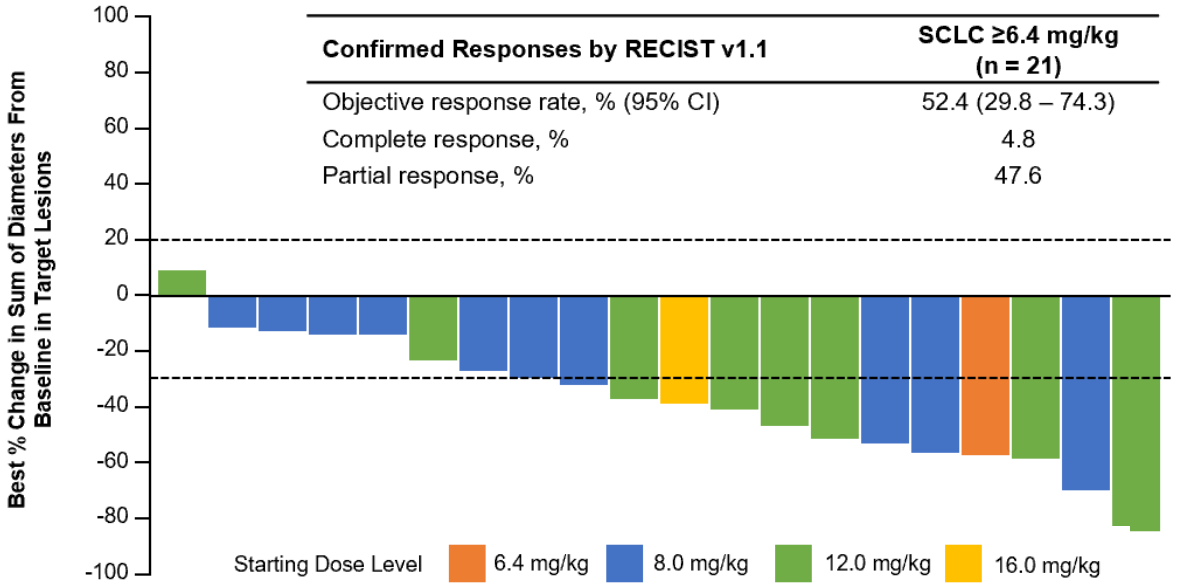
Ph1/2 Study: SCLC subgroup analysis

WCLC 2023

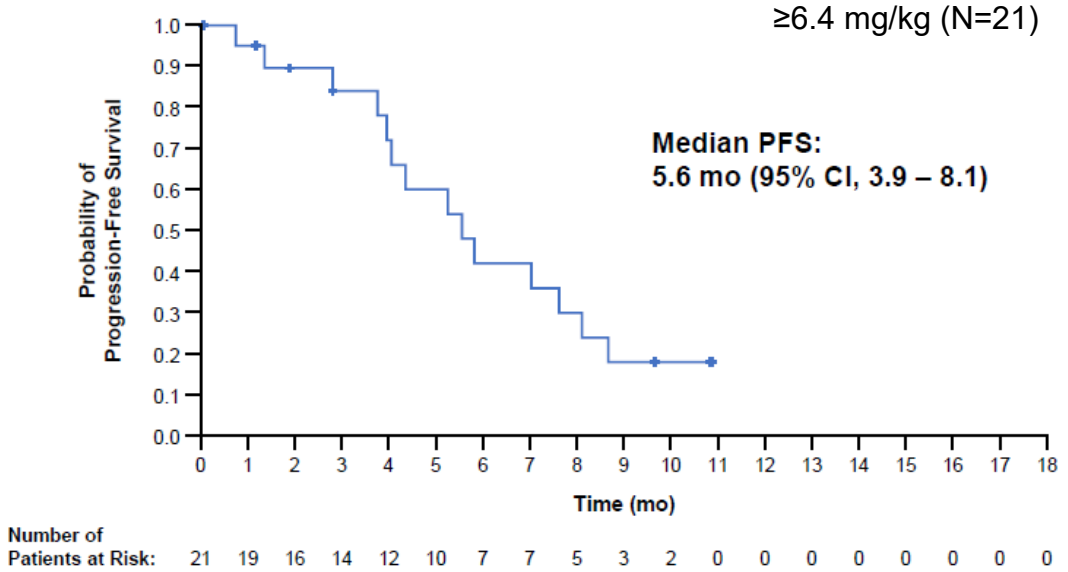
Daiichi-Sankyo

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

ORR



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)

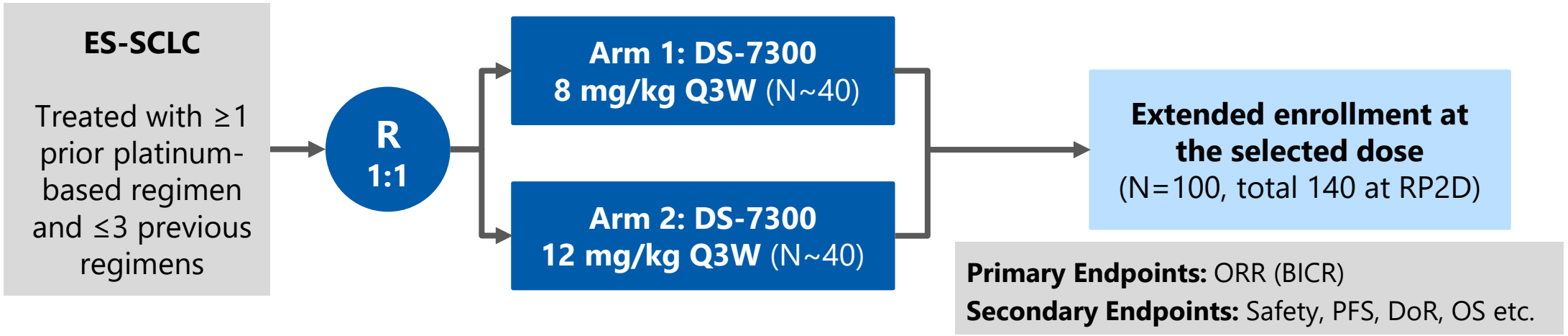
ADC: antibody-drug conjugate, CI: confidence interval, RECIST: response evaluation criteria in solid tumors, mDOR: median duration od response, mo: months, mOS: median overall survival, mPFS: median progression free survival, ORR,: objective response rate, SCLC: small cell lung cancer

DS-7300 (I-DXd)

IDeate-1: ES-SCLC Ph2 study

- **A Ph2 dose-optimization study evaluating DS-7300 in patients with previously treated ES-SCLC is ongoing (IDeate-1)**
- **Dose-optimization was completed, and preparing for extended enrollment**

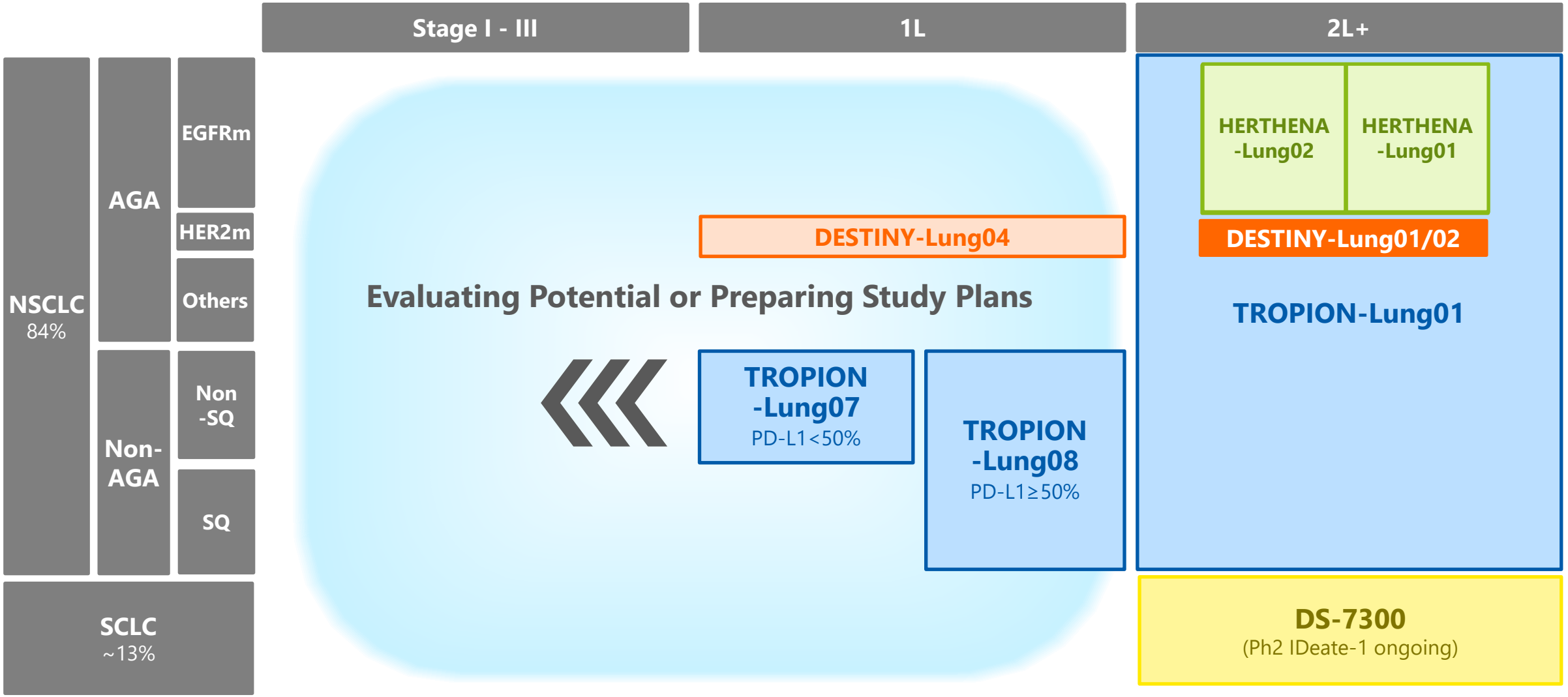
Study Design of Ongoing Ph2 study in ES-SCLC (IDeate-1)



- **A Ph3 study will be initiated in FY2024**

BICR: blinded independent central review, DOR: duration od response, ES-SCLC: extensive-stage small cell lung cancer, ORR: objective response rate, OS: overall survival, PFS: progression free survival, Q3W: every 3 weeks, RP2D: recommended Ph2 dose

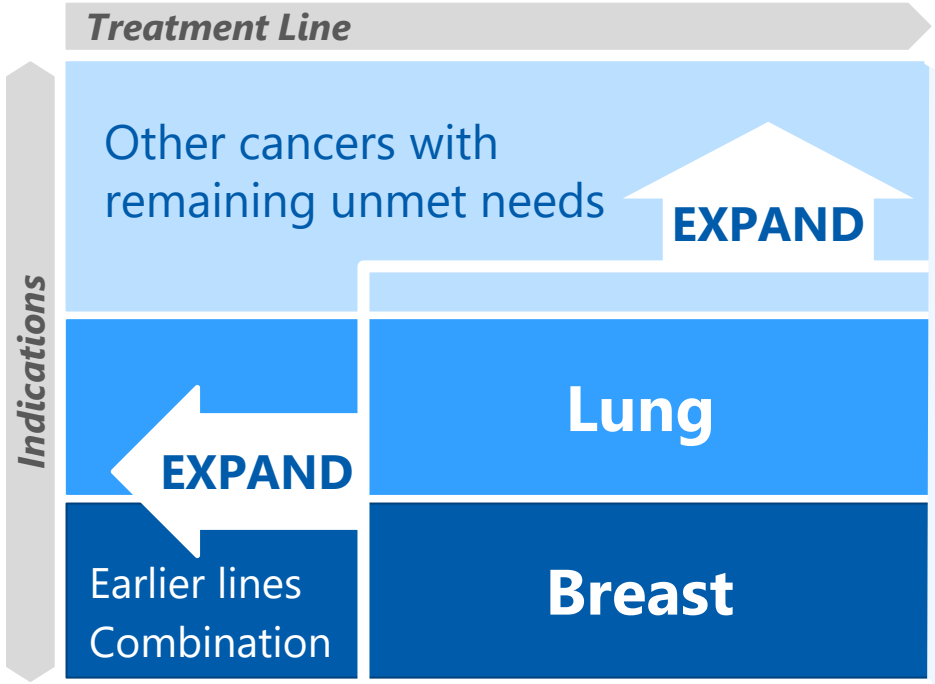
Establish and expand DXd ADCs as new treatment options in Lung Cancer



Pivotal studies and major Ph2 only, not exhaustive

ADC: antibody-drug conjugate, AGA: actionable genomic alteration, Non-SQ: non- squamous, NSCLC: non-small cell lung cancer, SCLC: small cell lung cancer, SQ: squamous

EXPAND & EXTEND to deliver our technology to more patients



5DXd ADCs Progress and Future

- Breast cancer
- Lung cancer
- **New disease areas**

ADC: antibody-drug conjugate

DXd ADCs expanding into new disease areas beyond Breast and Lung

Build upon the success of our DXd ADC platform and harness the potential of our full portfolio to extend the benefit of practice-changing medicines to more patients, including Gynecological, Genitourinary, and Gastro-Intestinal cancers

ADC: antibody-drug conjugate

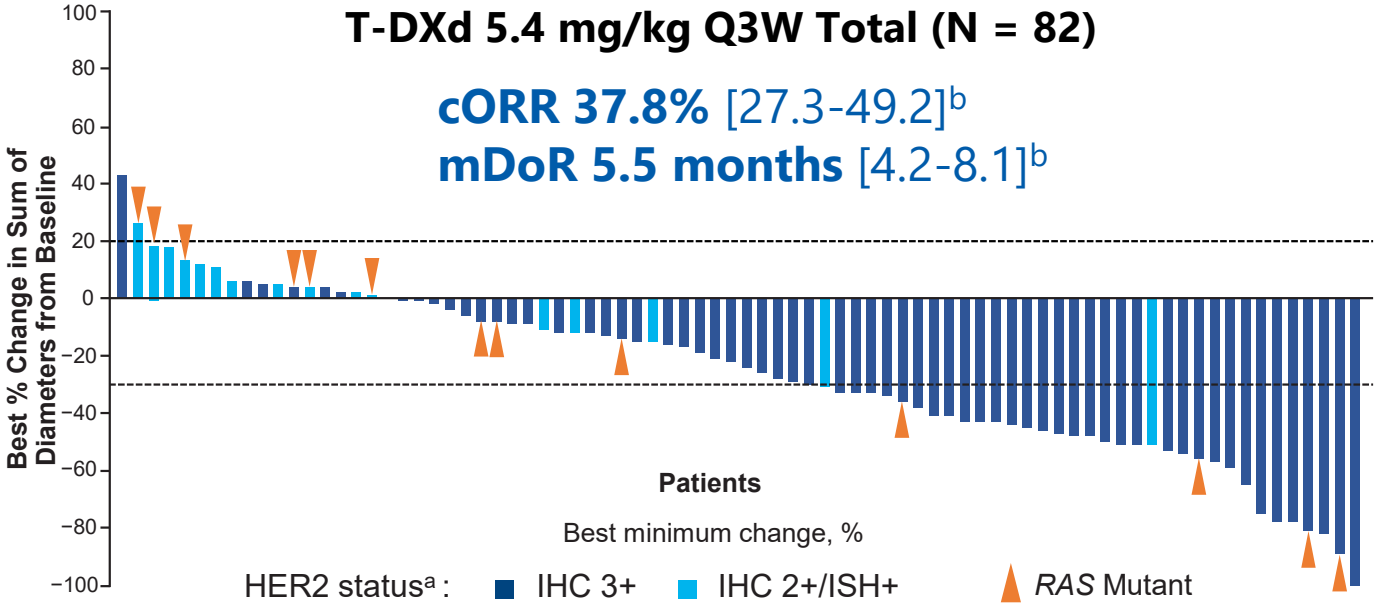
DESTINY-CRC02 Ph2 Primary Analysis

ASCO 2023

Daiichi-Sankyo

ENHERTU® showed promising efficacy and manageable safety in HER2+ mCRC

Objective Response

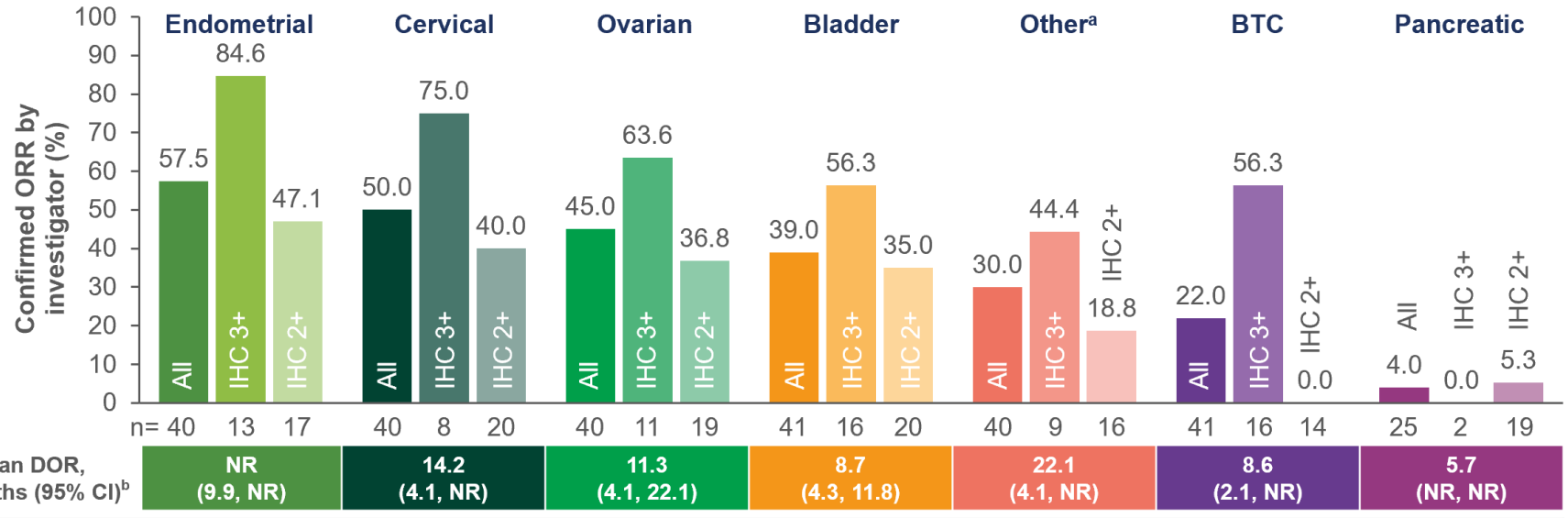


- Promising antitumor activity was observed at both 5.4 mg/kg and 6.4 mg/kg doses
- Antitumor efficacy was observed **irrespective of RAS mutation status** at 5.4 mg/kg dose
- The safety profile was consistent with the known profile of ENHERTU® and favored the 5.4 mg/kg
- All-grade adjudicated ILD/pneumonitis rates were 8.4% with 5.4 mg/kg and 12.8% with 6.4 mg/kg
- No grade ≥3 ILD/pneumonitis in 5.4 mg/kg arm, while 1 grade 5 case in 6.4 mg/kg arm
- The results support ENHERTU® 5.4 mg/kg as the optimal dose with positive benefit-risk profile

Only patients with measurable disease at baseline and at least one postbaseline tumor assessment were included in the waterfall graphs.
[a] HER2 status was assessed by central laboratory. [b] 95% confidence interval.
cORR: confirmed objective response rate, IHC: immunohistochemistry, ILD: interstitial lung disease, ISH: *in situ* hybridization, mCRC: metastatic colorectal cancer, mDoR: median duration of response, Q3W: every 3 weeks, T-DXd: trastuzumab deruxtecan (ENHERTU®).

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

ORR



	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®)

Ph1/2 Study Data Update

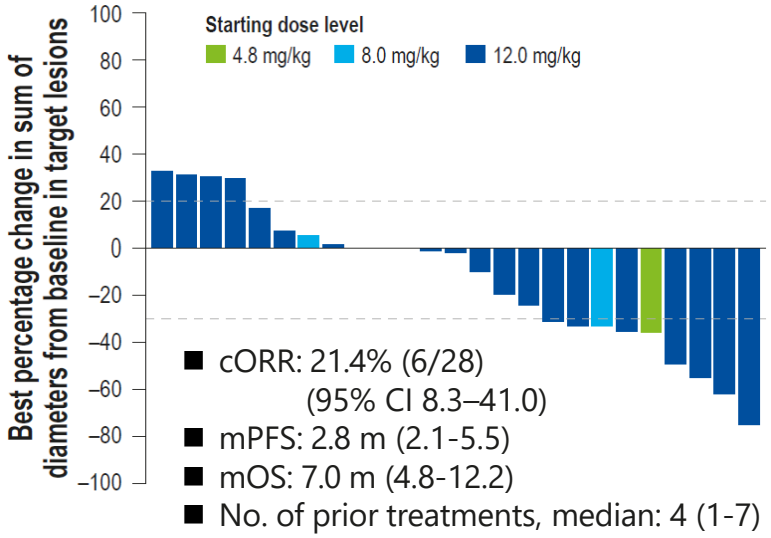
ESMO 2023

Daiichi-Sankyo

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

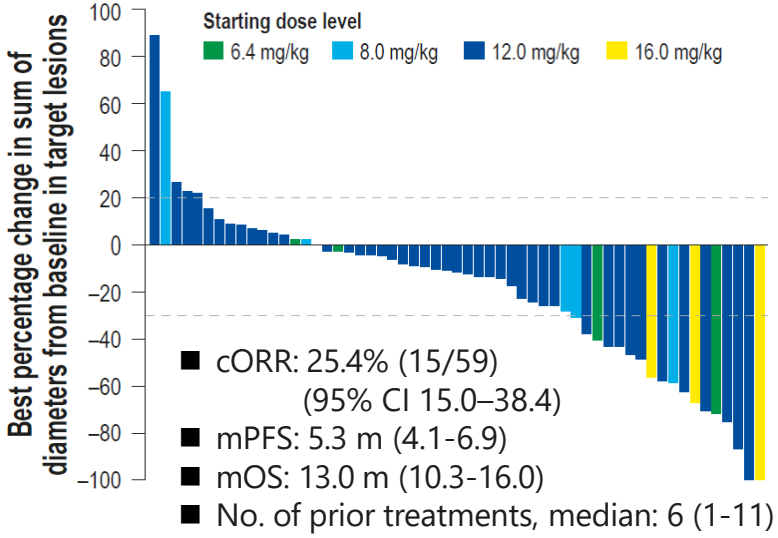
Efficacy in selected tumor types

ESCC



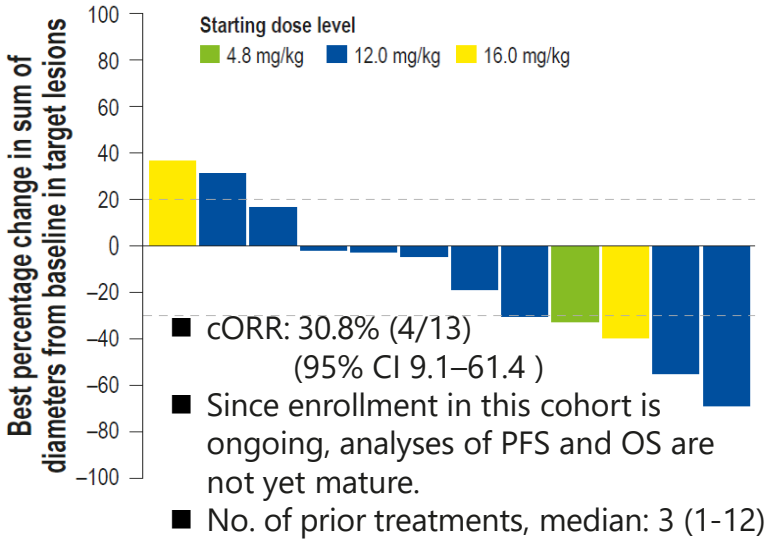
- cORR: 21.4% (6/28)
  (95% CI 8.3–41.0)
- mPFS: 2.8 m (2.1-5.5)
- mOS: 7.0 m (4.8-12.2)
- No. of prior treatments, median: 4 (1-7)

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

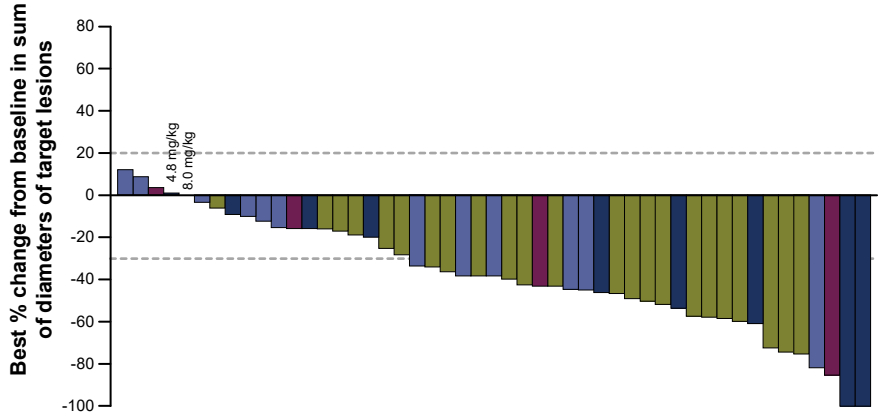
Ph1 Study OVC Cohort Data Update

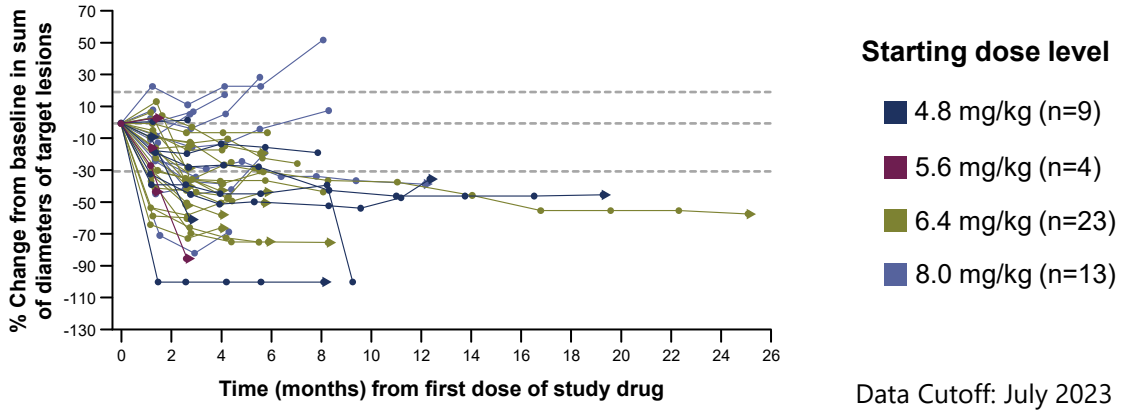
ESMO 2023

DS-6000 (CDH6 directed DXd ADC) continued to demonstrate strong clinical activity in patients with platinum resistant ovarian cancer

Efficacy*

- **Confirmed ORR: 46%** in the 4.8–8.0 mg/kg OVC cohort (23/50; 95% CI: 32–61)
- **DCR**: **98%**
- **Number of prior systemic regimens, median (range):** 4 (1-13)
- Median time to response: 6 weeks (95% CI: 5–11)
- Median **DOR**: **11.2 months** (95% CI: 3.0–NE)
- Median **PFS**: **7.9 months** (95% CI: 4.4–12.4)





Data Cutoff: July 2023

- Confirmed ORR: 46%, median DOR: 11.2 months and median PFS: 7.9 months
- Safety profile is manageable, and toxicities are consistent with those observed with other DXd ADCs
- 8.9% (4/45) of patients in 4.8-6.4 mg/kg cohort experienced ILD (all grade 2), of which 2 were adjudicated as treatment-related. 3.3% (2/60) of patients in 8.0 mg/kg cohort experienced grade 5 ILD
- Based on the accumulated overall safety, tolerability, PK and efficacy profile, the 8.0 mg/kg cohort was closed and further assessment is ongoing at three dose levels: 4.8, 5.6 and 6.4 mg/kg
- Ph2/3 study is under preparation

Two patients with no measurable lesions at baseline and one patient who discontinued and did not have a post-baseline tumor assessment were not included in the waterfall plot and spider plot.
CI: confidence interval, DCR: disease control rate, DOR: duration of response, ILD: interstitial lung disease, NE: not estimable, ORR: objective response rate, OVC: ovarian cancer, PFS: progression-free survival, PK: pharmacokinetics

5DXd ADCs are making steady progress toward the vision to deliver their benefits to more patients

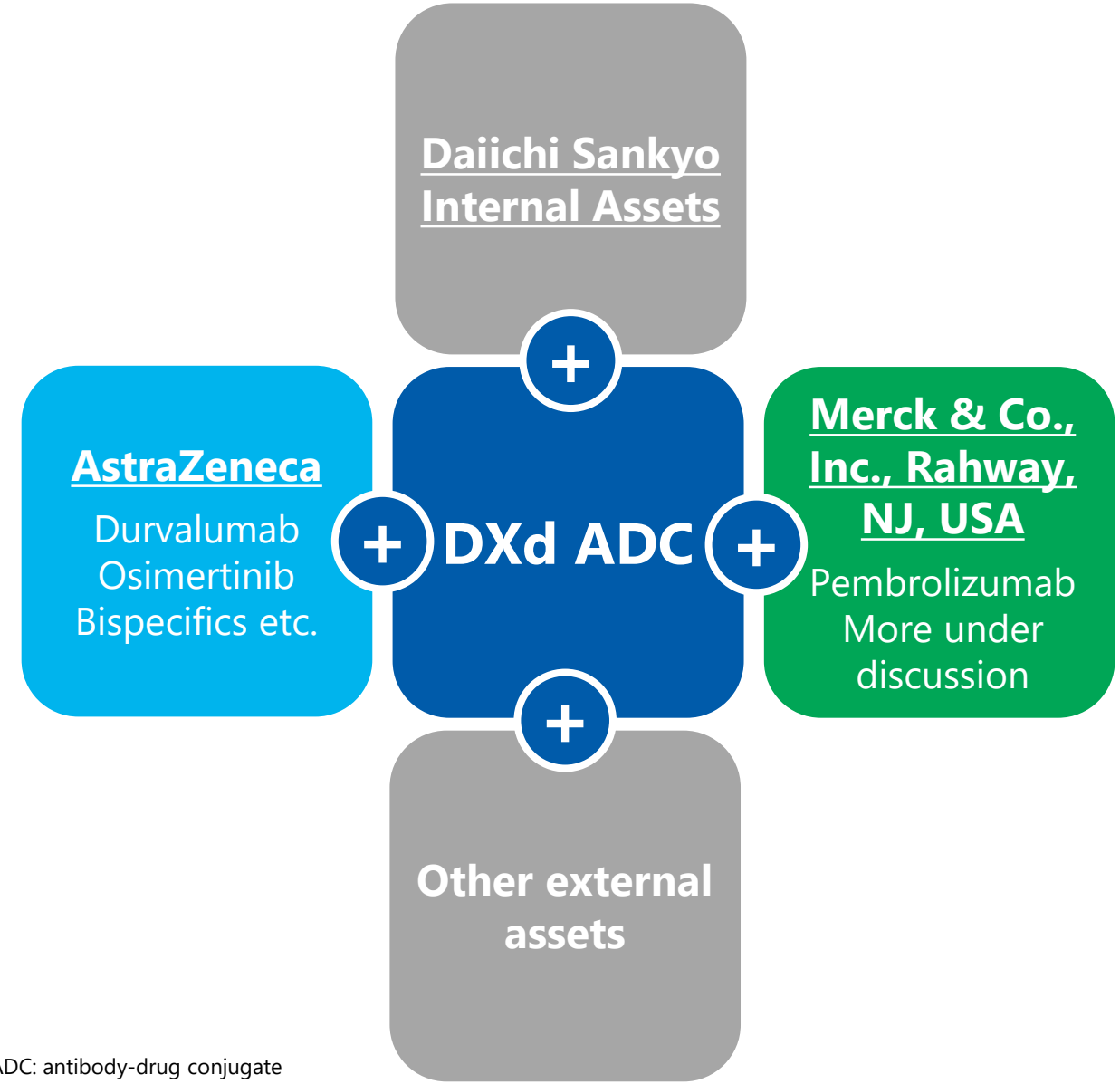
Daiichi-Sankyo

Strategic alliances further accelerate the programs

	Build the Foundation	Go Earlier	Go Wider	
ENHERTU®	Established in Breast, Gastric and HER2mut NSCLC	DESTINY-Breast09/05/11 DESTINY-Breast06 DESTINY-Lung04	DESTINY-PT02 Further planning	AstraZeneca
Dato-DXd	TROPION-Lung01 TROPION-Breast01	TROPION-Breast02/03/04/05 TROPION-Lung07/08	TROPION-PanTumor01/02/03	
HER3-DXd	HERTHENA-Lung01/02	Evaluating combinations	Plan in Progress	Merck & Co., Inc., Rahway, NJ, USA
DS-7300 (I-DXd)	Strong signal in SCLC Ph2 IDeate-1 ongoing	Plan in Progress	Signals in ESCC/mCRPC /sqNSCLC Further evaluation & planning	
DS-6000 (R-DXd)	Strong signal in OVC	Plan in Progress	Plan in Progress	

ADC: antibody-drug conjugate, ESCC: esophageal squamous cell carcinoma, mCRPC: metastatic castration-resistant prostate cancer, NSCLC: non-small cell lung cancer, OVC: ovarian cancer, SCLC: small cell lung cancer, sqNSCLC: squamous non-small cell lung cancer

Combinations further unlock the potential of DXd ADCs



- Combination is a key to realize our DXd ADC expansion strategy
- Pursuing unique combinations with our internal assets
  - Valametostat or DS-1103 combined with ENHERTU®
- **Strategic alliances expand combination opportunities for DXd ADCs**
  - Immune checkpoint inhibitors
  - Targeted therapies
- In addition to above, we actively work on combinations with other agents having promising new mechanisms of action

ADC: antibody-drug conjugate

5DXd ADCs Summary

5DXd ADCs are steadily progressing toward the vision to deliver the benefits to more patients

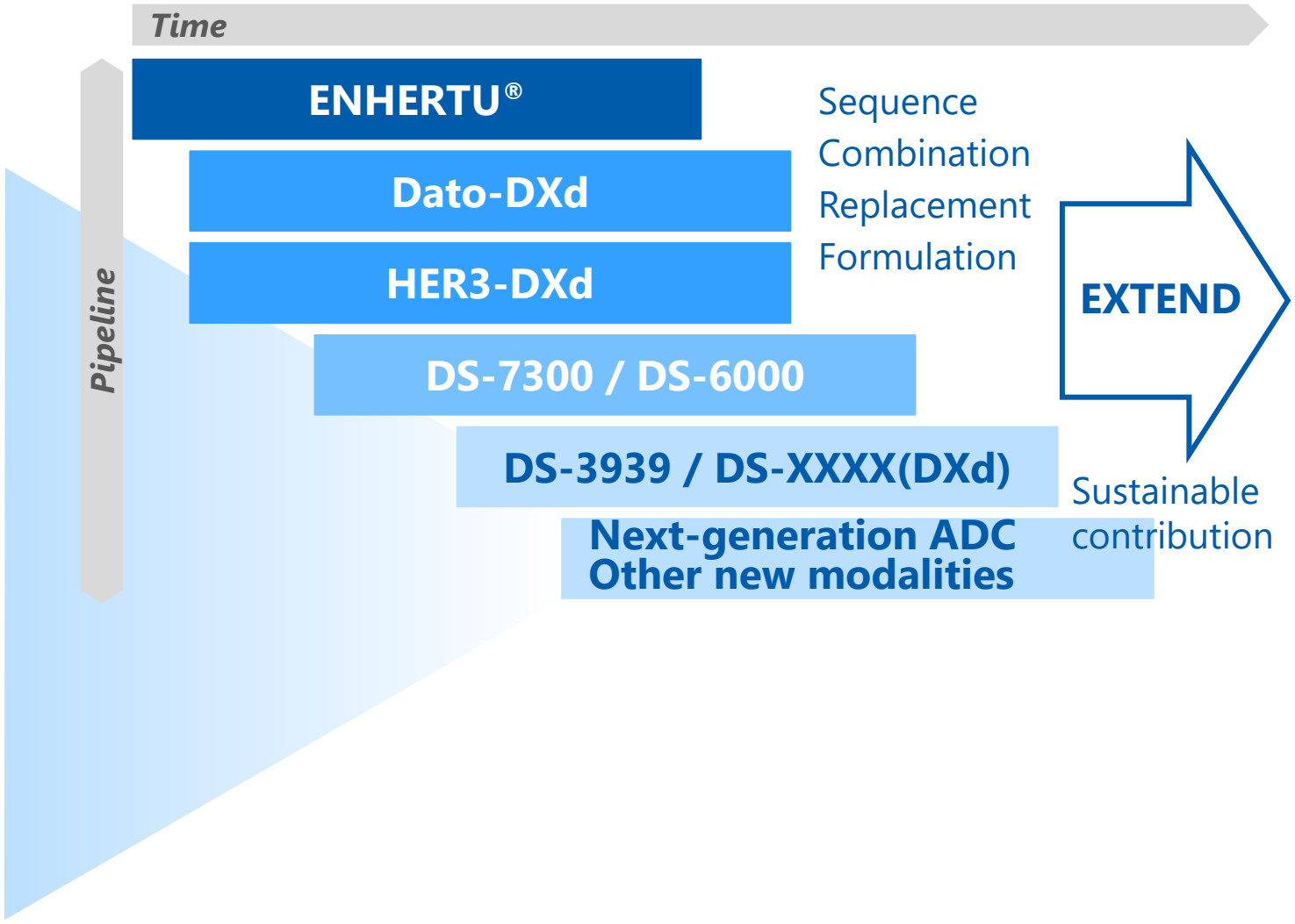
- **Breast**
  - **ENHERTU®** continues to solidify its position as standard of care in HER2+ and HER2 low BC
  - **Dato-DXd** provides potential new treatment option for HR+ mBC and is expanding into TNBC in early/front line
- **Lung**
  - **ENHERTU®** represents a new HER2-directed therapy globally
  - **HER3-DXd** and **Dato-DXd** are establishing foundation of DXd ADC therapy in various type of NSCLC
  - **DS-7300** pioneers a new treatment option for ES-SCLC
- **New disease areas**
  - **ENHERTU®** may represent a tumor-agnostic therapy in HER2-expressing solid tumors
  - **DS-7300** and all other DXd ADCs are exploring opportunities in other multiple tumor types
  - **DS-6000** goes into a potential new treatment of OVC

ADC: antibody-drug conjugate, BC: breast cancer, ES-SCLC: extensive-stage small cell lung cancer, HR: hormone receptor, mBC: metastatic breast cancer, NSCLC: non-small cell lung cancer, OVC: ovarian cancer, TNBC: triple-negative breast cancer

EXPAND & EXTEND to deliver our technology to more patients

Next Wave Update

- **The 6th DXd ADC in clinical stage**
- Combinations with DXd ADC
- Unique and innovative assets

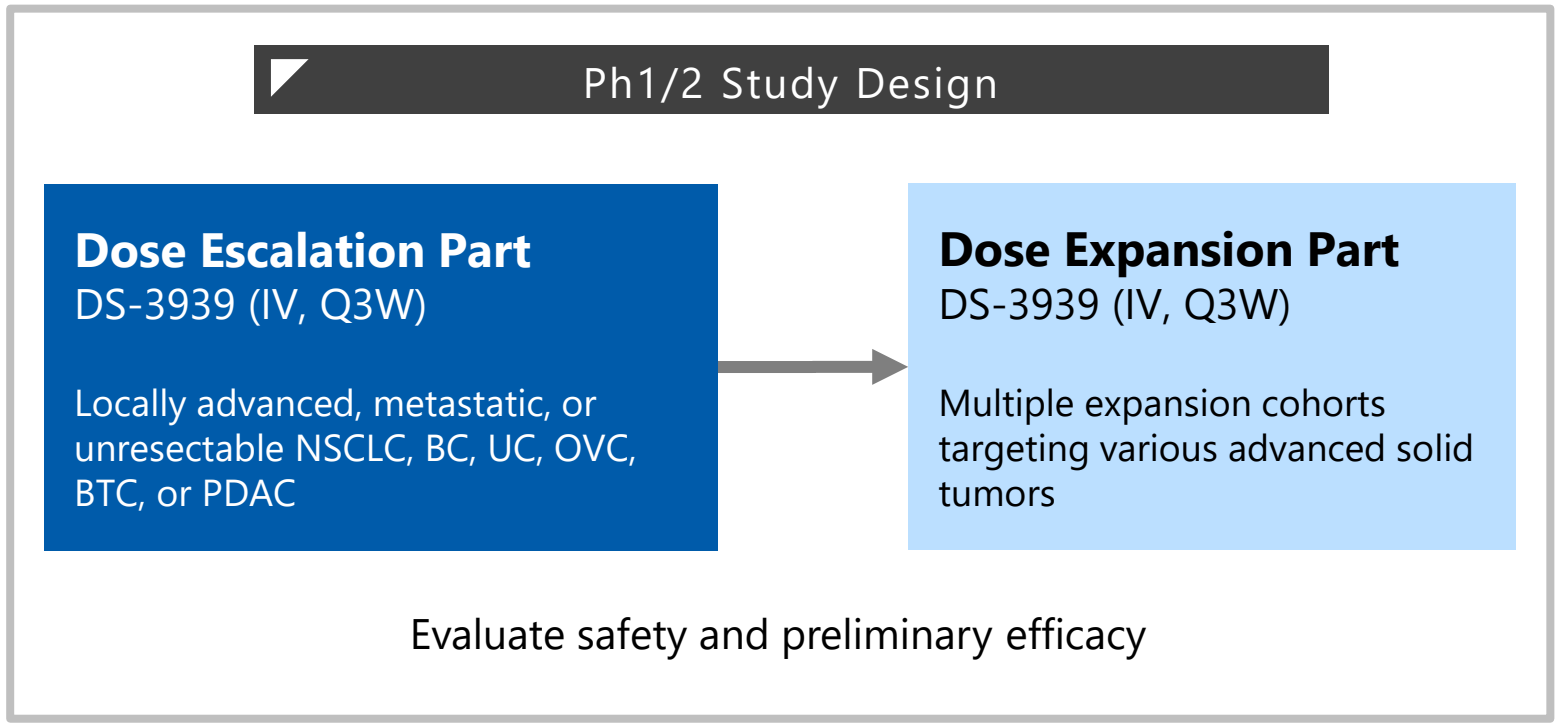


ADC: antibody-drug conjugate

DS-3939

The 6th DXd ADC with broad potential

A Ph1/2 study is ongoing in solid tumors



- The 6th DXd ADC targeting tumor-associated mucin 1 (TA-MUC1), a transmembrane glycoprotein overexpressed in **broad range of tumors** including NSCLC, BC, UC, OVC, BTC and PDAC
- Combined DXd ADC technology (DAR 8) and an anti-TA-MUC1 antibody in-licensed from Glycotope GmbH (Berlin, Germany)
- Ph1 dose escalation part is ongoing

BC: breast cancer, BTC: biliary tract cancer, DAR: drug-antibody ratio, IV: intravenous, NSCLC: non-small cell lung cancer, OVC: ovarian cancer, PDAC: pancreatic ductal adenocarcinoma, Q3W: every 3 weeks, UC: urothelial cancer

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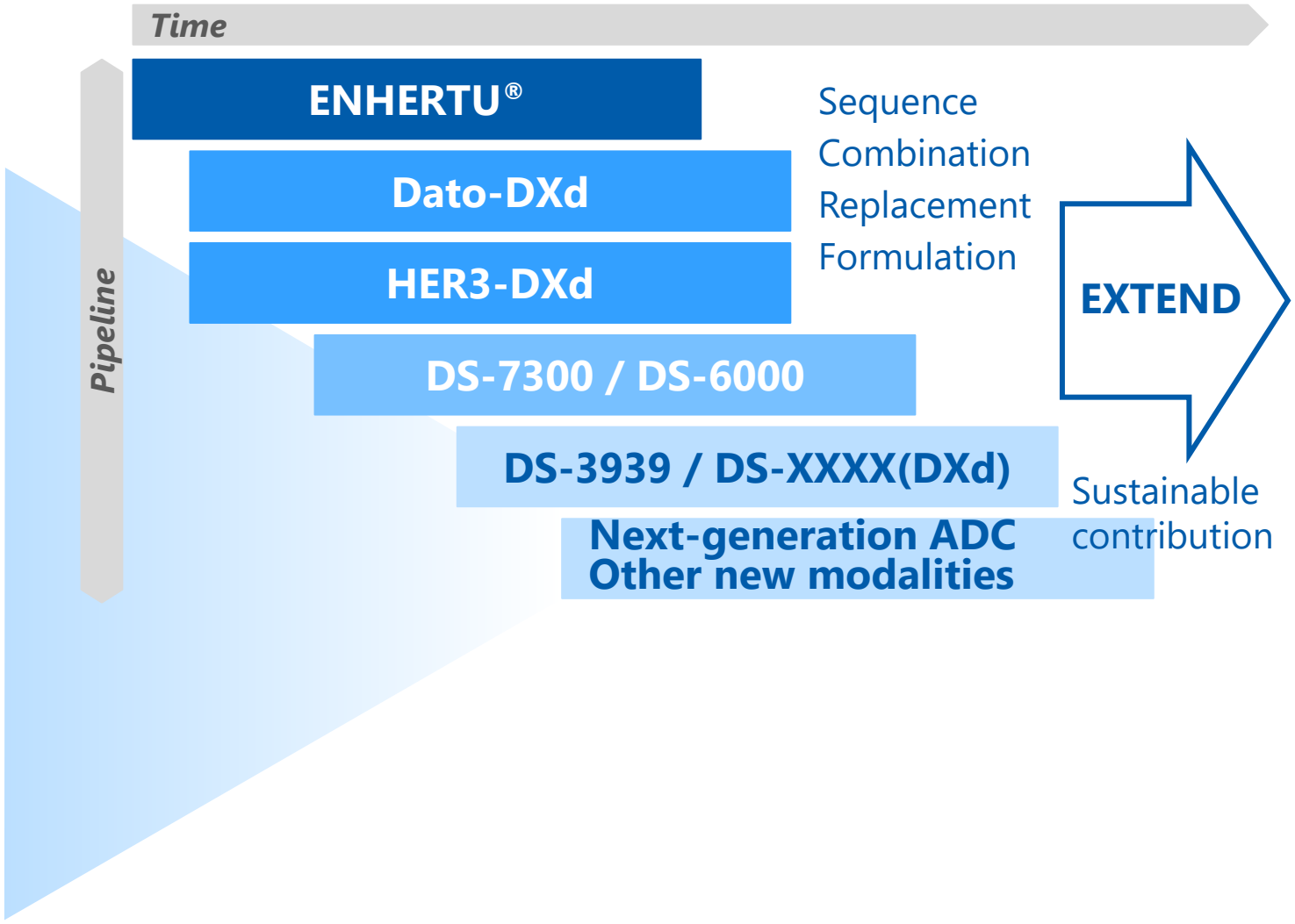
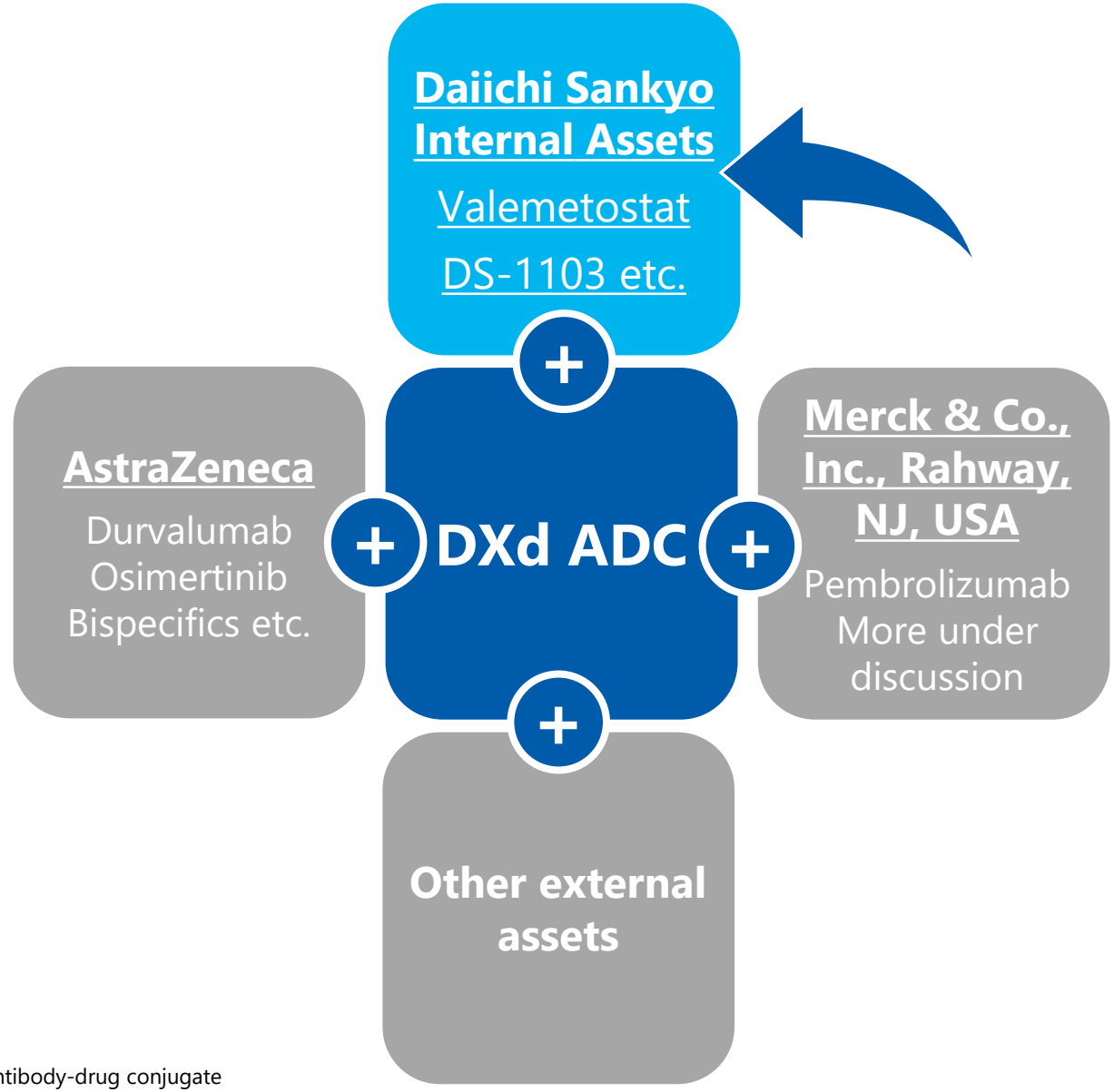


ADC: antibody-drug conjugate

Combinations further unlock the potential of DXd ADCs



- Combination is a key to realize our DXd ADC expansion strategy
- **Pursuing unique combinations with our internal assets**
  - **Valemetostat or DS-1103 combined with ENHERTU®**
- Strategic alliances expand combination opportunities for DXd ADCs
  - Immune checkpoint inhibitors
  - Targeted therapies
- In addition to above, we actively work on combinations with other agents having promising new mechanisms of action

ADC: antibody-drug conjugate

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

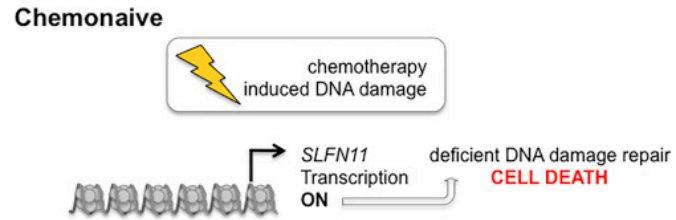
↓

Increase SLFN11 expression

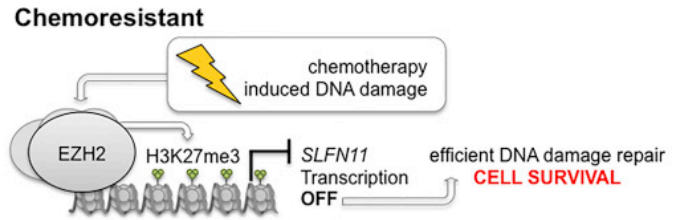
↓

Increase sensitivity to DXd payload

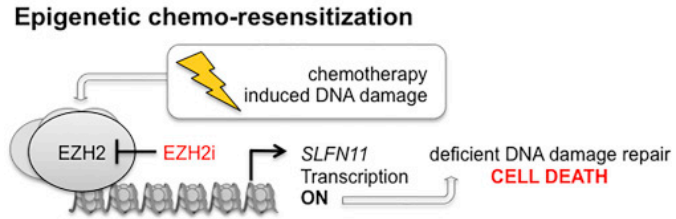
- SLFN11 is a dominant determinant of sensitivity to DNA-damaging agents



- 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

Daiichi-Sankyo

■ **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

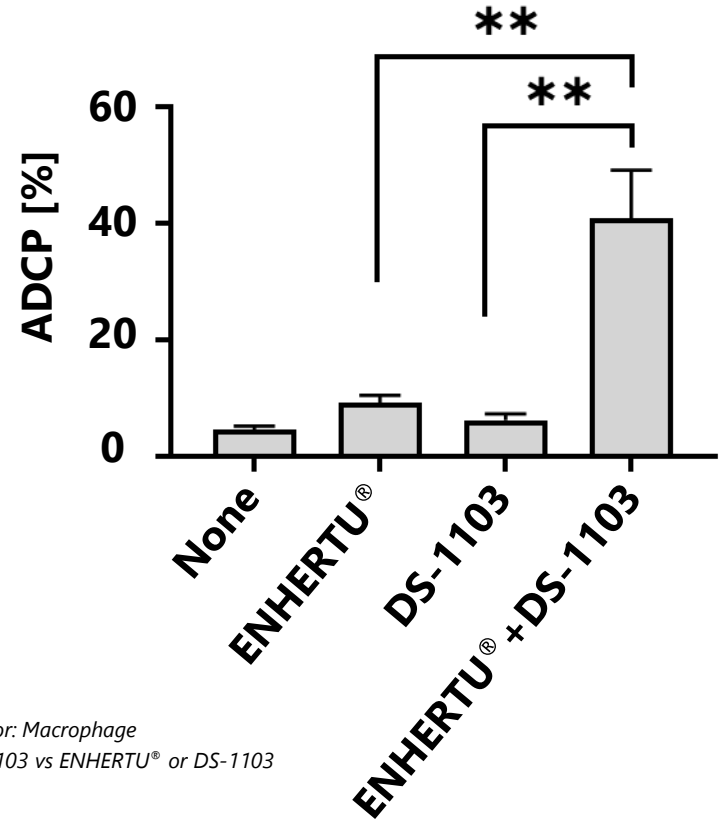
■ **Another combination study (company-sponsored) is under preparation to investigate valemetostat combinations with multiple DXd ADCs in multiple indications**

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-1103

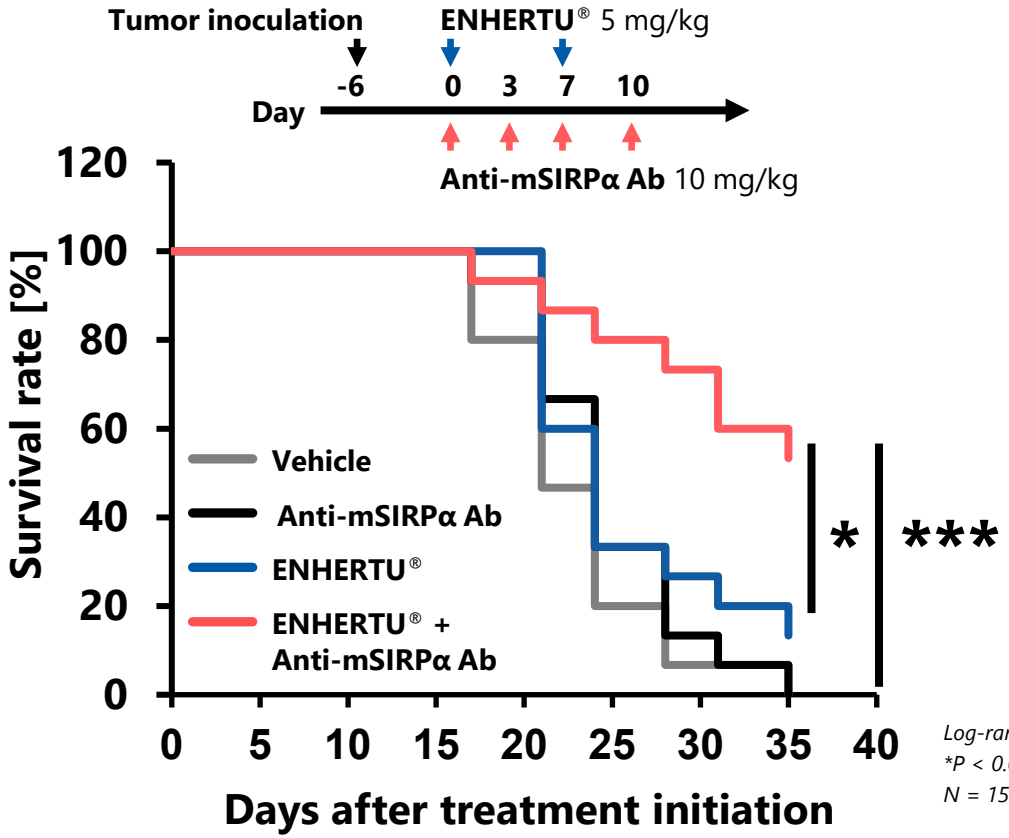
Preclinical data support the rationale for the combination of ENHERTU® and DS-1103

- 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-1103

Evaluating potential of combination with DXd ADC in clinical trial

Daiichi-Sankyo

- **A Ph1 first-in-human study of DS-1103 is ongoing in HER2-expressing solid tumors in combination with ENHERTU®**

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 (RDE) + ENHERTU® (5.4 mg/kg Q3W)
HER2 low BC

- **Further studies are under planning for combination with other DXd ADCs**

ADC: antibody-drug conjugate, BC: breast cancer; Q3W: once every 3 weeks, RDE: recommended dose for expansion

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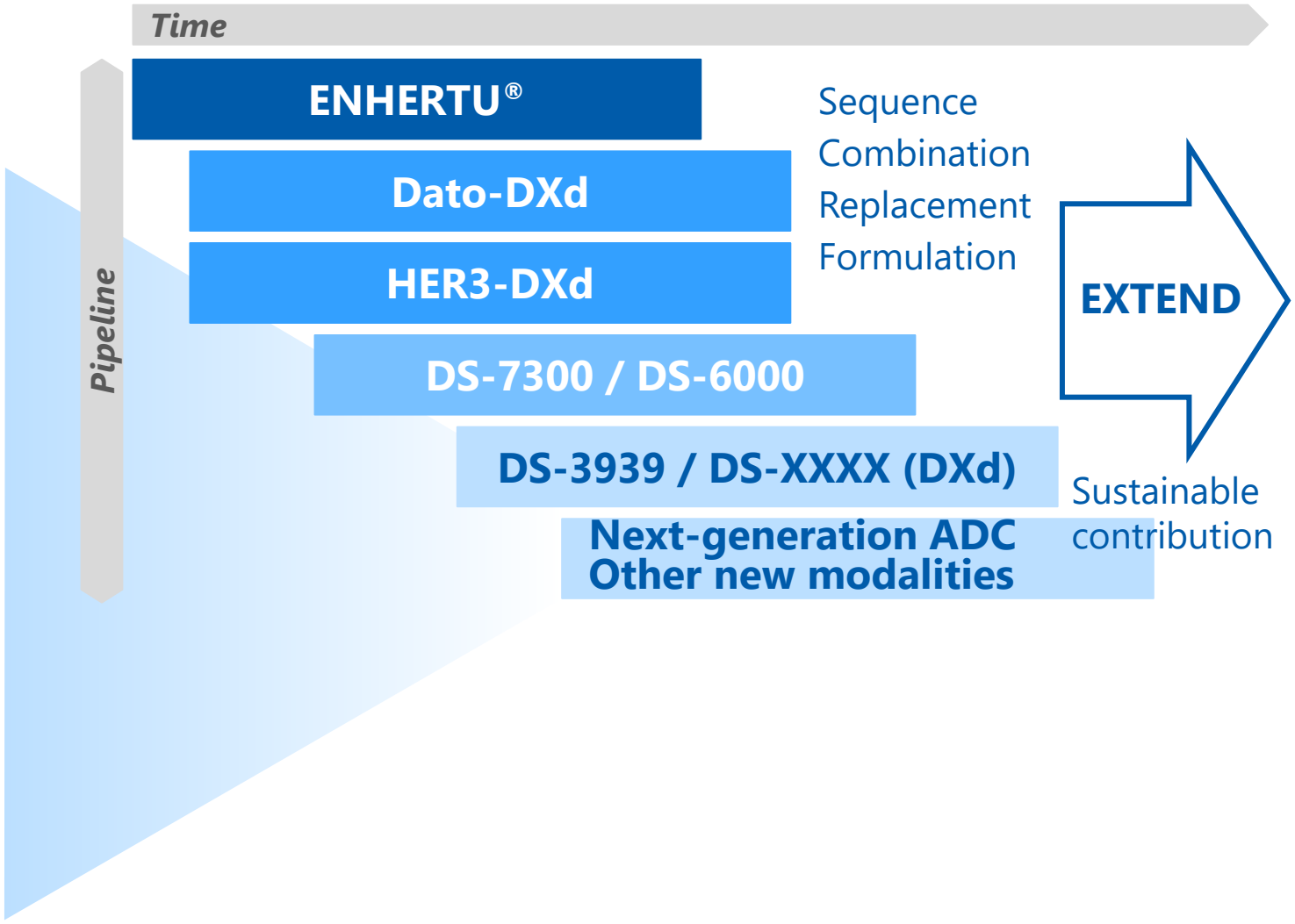
- **Unique and innovative assets**



ADC: antibody-drug conjugate

VALENTINE-PTCL01 Primary Results

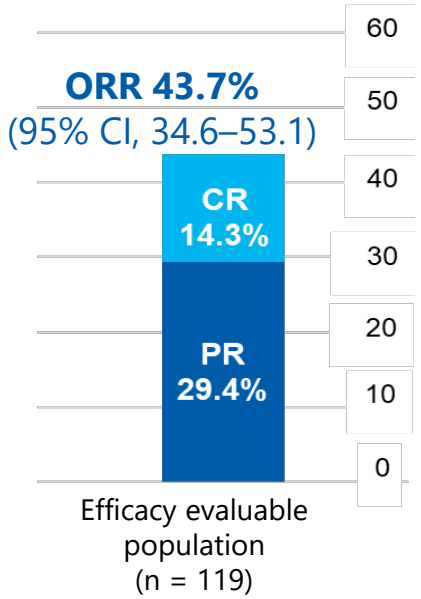
ASH 2023

Daiichi-Sankyo

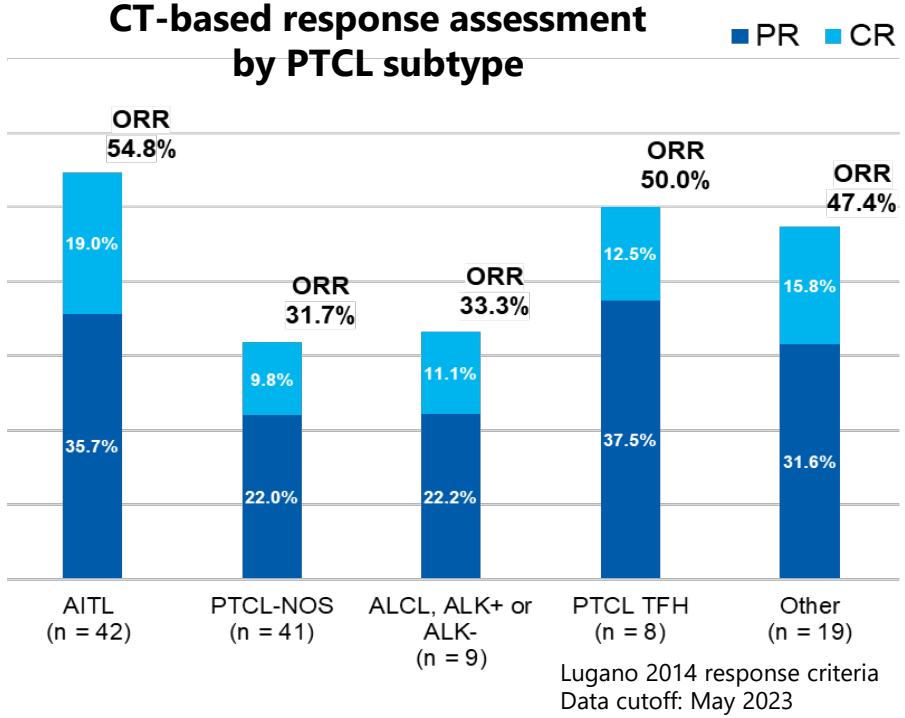
Valemetostat monotherapy provides a clinically meaningful benefit for patients with R/R PTCL

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

QuANTUM-First Approvals

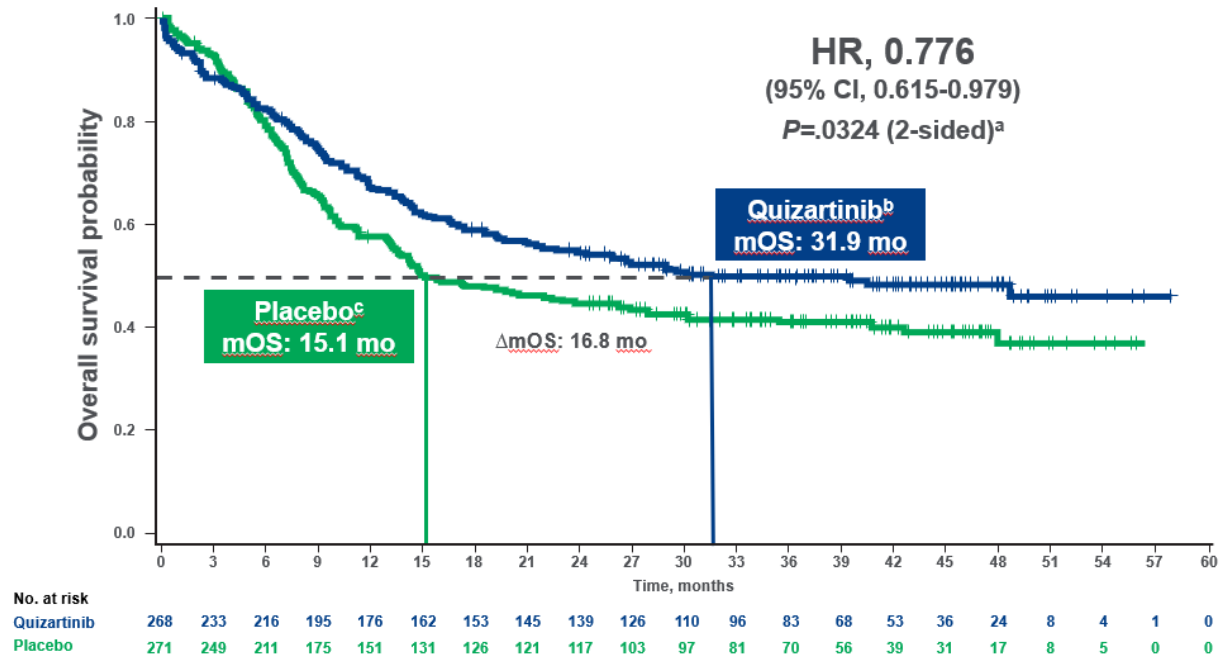
Quizartinib + Chemotherapy now globally approved in all three treatment phases* for patients with newly diagnosed *FLT3*-ITD (+) AML

QuANTUM-First Ph3 Newly Diagnosed AML *FLT3*-ITD (+):

- Multicenter, double-blind, randomized (1:1), placebo-controlled Ph3 trial (N=539)

Approved:

- Japan May 25, 2023
- US July 20, 2023
- EU November 6, 2023



[a]*P* value was calculated using a stratified log-rank test. [b, c] Median follow-up time for both arms was 39.2 months

Erba et al. EHA Abstract 2022
Erba HP, Montesinos P, Kim H-J, Patkowska E, Vrhovac R, Žák P, et al. Lancet. 2023;401(10388):1571–83.

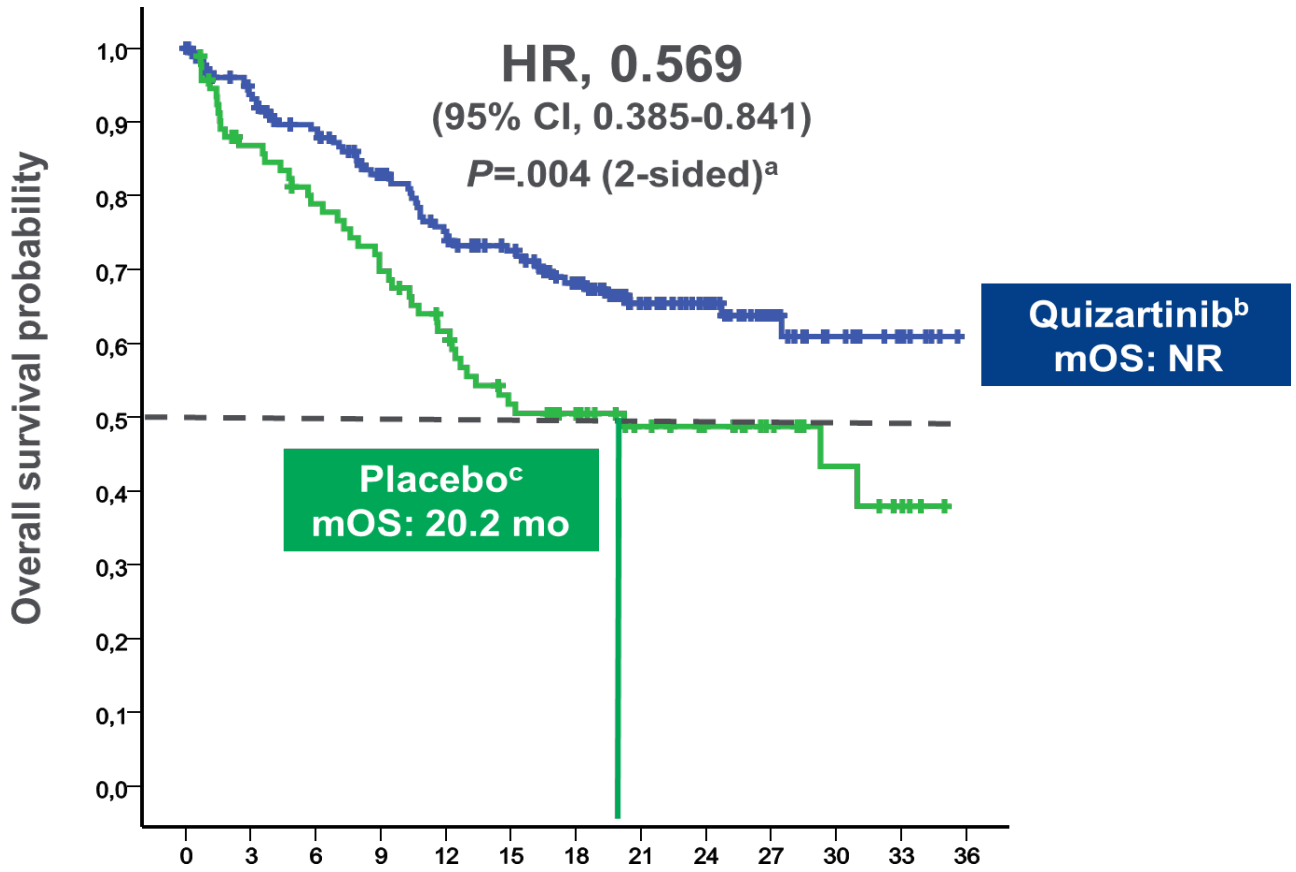
* three treatment phases: induction phase, consolidation phase, maintenance phase
AML: acute myeloid leukemia, CI: confidence interval, HR: hazard ratio, mo: months, mOS: median overall survival

QUIWI Ph2 Investigator-Initiated Study Interim Results

Daiichi-Sankyo

Preliminary evidence of efficacy of Quizartinib + Chemotherapy for patients with newly diagnosed *FLT3*-ITD (-) AML (collaboration with PETHEMA)

- Roughly 70-80% of Fit AML patients will have *FLT3*-WT[1-3]
- Multicenter, double-blind, randomized (2:1), placebo-controlled Ph2 trial (N=273)
- EFS primary endpoint did not reach statistical significance:
  - HR = 0.741 (95%CI, 0.535-1.026), p=0.059, (2-sided)
- OS secondary endpoint
  - HR = 0.569 (95%CI, 0.385-0.841), p=0.004, (2-sided)
  - 2-year OS was 63.5% with quizartinib vs 47% with placebo



[a] *P* value was calculated using a stratified log-rank test. [b] Median follow-up time for quizartinib arm, 21.5 months. [c] Median follow-up time for placebo arm, 20.3 months.

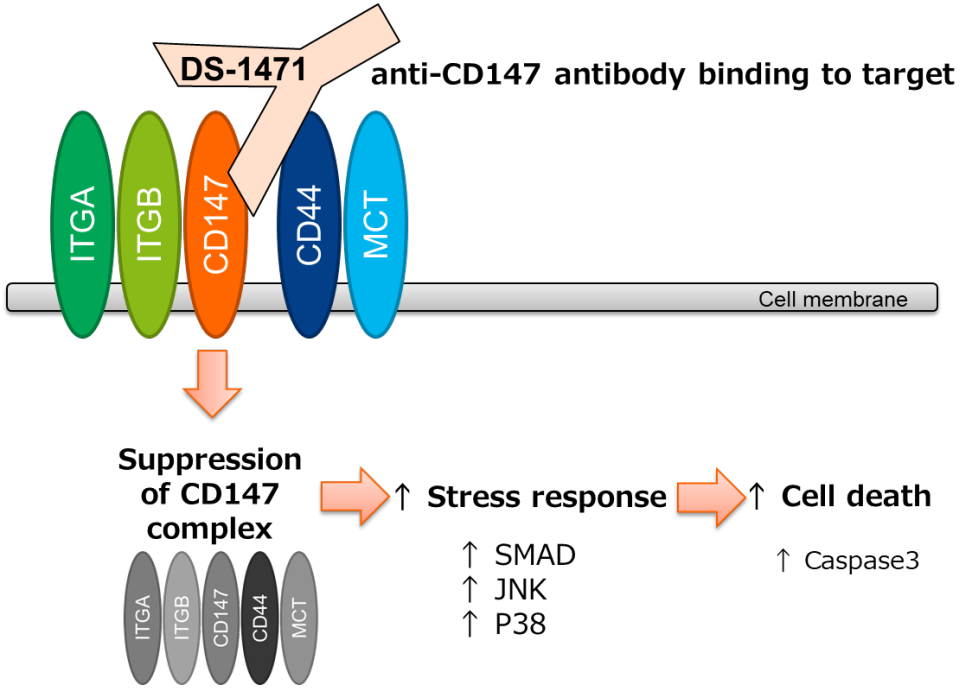
1. Levis M, et al. Hematology Am Soc Hematol Educ Program. 2013:220-226
2. Daver N, Schlenk RF, Russell NH, Levis MJ. Leukemia. 2019;33(2):299-312.
3. Juliusson G, Jädersten M, Deneberg S, et al. Blood Adv. 2020;4(6):1094-1101.
4. Montesinos P, Rodriguez-Veiga R, Burgues JMB, Algarra L, Botella C, Antonio PSJ, et al. EHA Abstract 2023

AML: acute myeloid leukemia, CI: confidence interval, EFS: event-free survival, HR, hazard ratio, mOS: median overall survival; NR: not reached, OS: overall survival, PETHEMA: Programa para el Estudio de la Terapéutica en Hemopatía Maligna

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



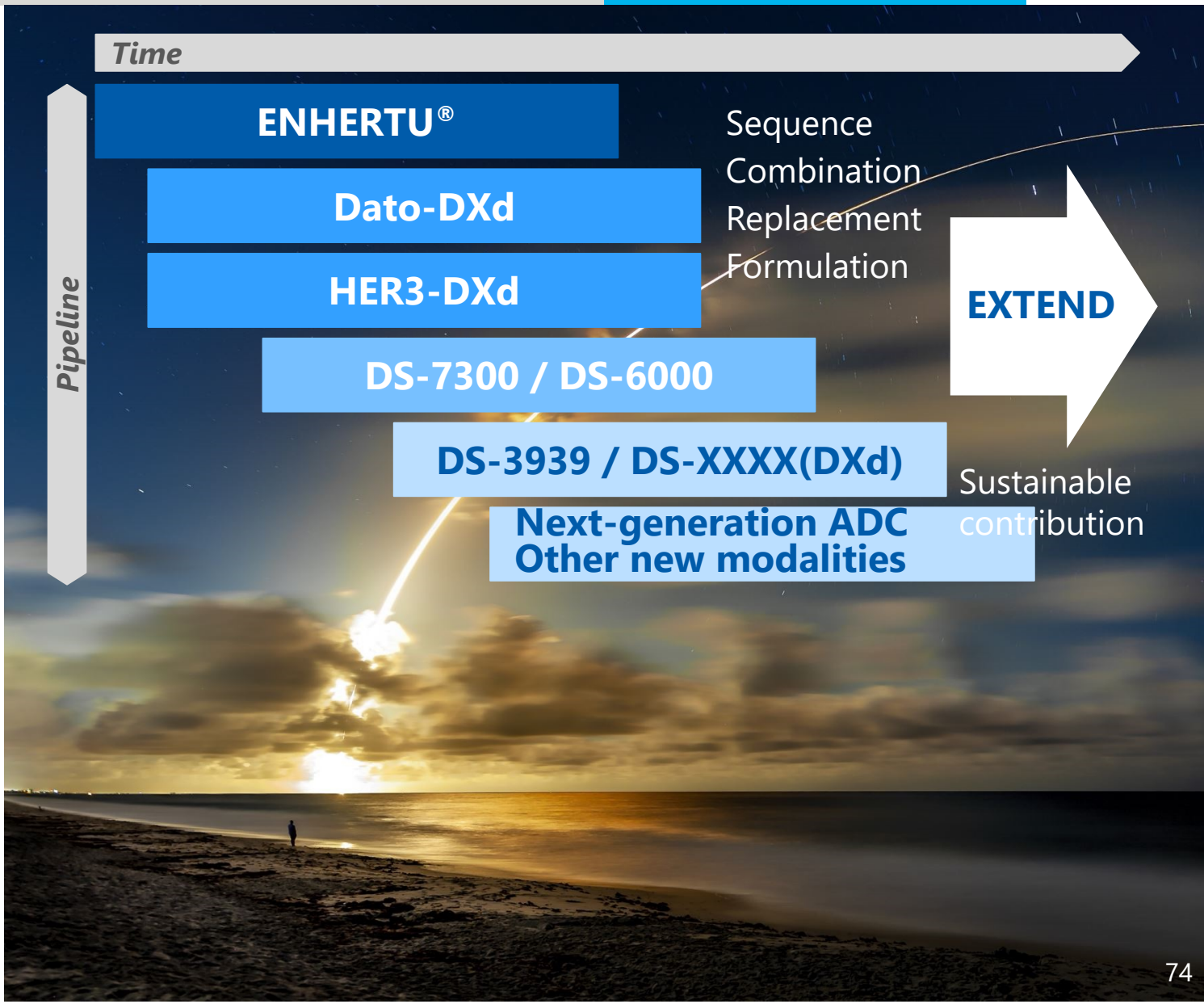
- CD147 is known as a potential prognostic biomarker for various types of cancer including HCC, CRC etc.
- CD147 complex is also reported to play important roles in survival, invasion and metastasis in cancer tissues
- DS-1471 exhibits **unique mechanism of action** by downregulating CD147 complex which leads to cellular stress response and apoptotic cell death
- Ph1 dose escalation part is ongoing

CRC: colorectal cancer, HCC: hepatocellular carcinoma

Next Wave Summary

Unique and innovative assets follow 5DXd ADCs to extend our contribution to future care

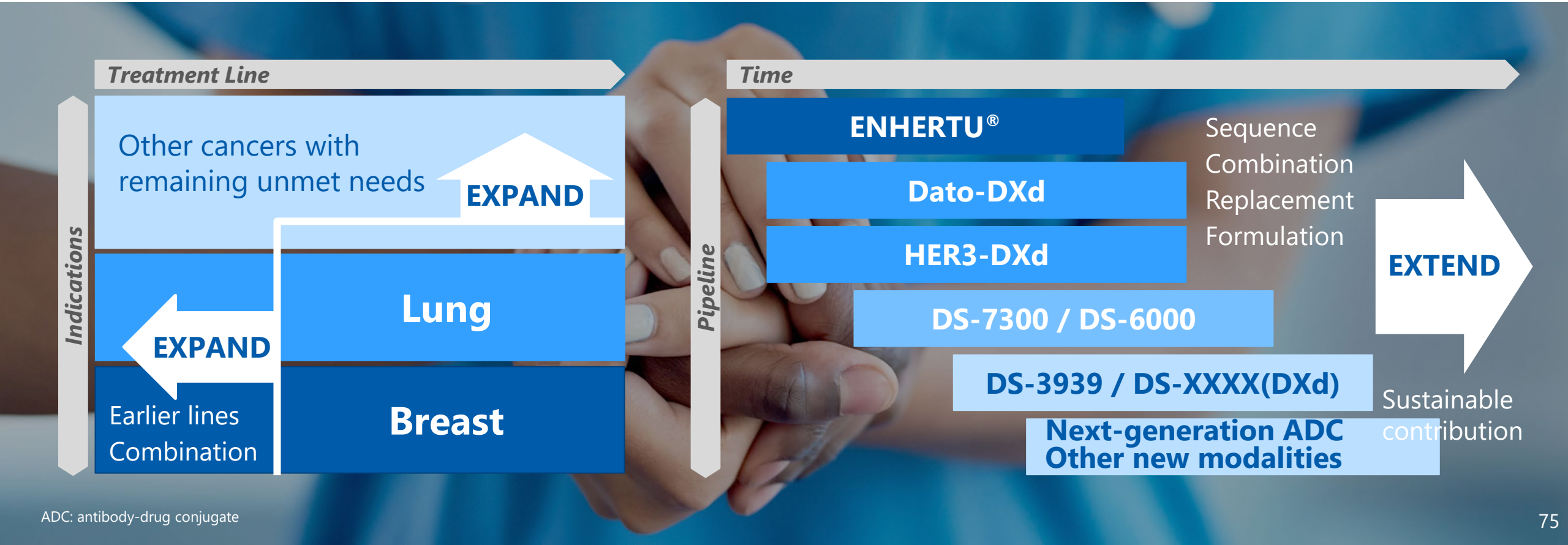
- Focus on combinations of selected next-wave assets with DXd ADC to maximize the potential of our assets
- Accelerate development of early clinical assets to bring new therapies to patients as quickly as possible
- Evaluating >20 candidates in IND-enabling stage in oncology, specialty medicine and vaccine areas



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

Clinical Summary

- **5DXd ADCs** establishes foundations, Go Earlier and Go Wider
- **Next Wave** pipeline continues to grow following the 5DXd ADCs



ADC: antibody-drug conjugate

Agenda

1. Opening
2. R&D Strategy
3. Research Capability
4. Clinical Progress
5. **Q&A**

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