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cancerenterprise

Care. Compassion. Science.
It's Our Obligation.

Daiichi Sankyo Cancer Enterprise

Cowen 39th Annual Health Care Conference

March 11, 2019

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Forward-Looking Statements

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Daiichi Sankyo Cancer Enterprise 2025

7 in **8**

A Delivery Machine:
Submissions & Data

Scale Up the Enterprise:
Meeting the Challenge

Secure World-class Leadership in **Science**

Cancer Enterprise 2025 <Multiple Opportunities for 7 New Drugs>

Cancer Enterprise | Major Clinical Pipeline

As of Mar 2019

Daiichi-Sankyo

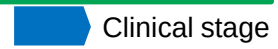
Franchise	Project Code	Potential Indications	Preclinical / Ph 1 / Pivotal	Designation
ADC	DS-8201 (HER2)	Breast, Gastric IO combo, other HER2+	Pivotal	BTD, Fast Track (BC) SAKIGAKE (GC)
	U3-1402 (HER3)	NSCLC, Breast	Ph 1	
	DS-1062 (TROP2)	NSCLC	Ph 1	
AML/Hematology	Quizartinib (FLT3)	AML 1st/ Relapsed/Refractory	Pivotal	BTD, Priority, Fast Track, ODD (US); Accel Assess, ODD (EU); ODD (JP) (NDA under review)
	DS-3032 (MDM2)	AML, Solid	Ph 1	
	DS-3201 (EZH1/2)	AML, ALL, ATL, PTCL	Ph 1	
	PLX2853 (BRD4)	AML	Ph 1	
	DS-1001 (IDH1m)	AML, Glioma	Ph 1	
	Axi-Cel® (CD19 CAR-T)	BCL (Japan)	Pivotal	ODD (JP)
Breakthrough	Pexidartinib (CSF-1R)	TGCT	Pivotal	BTD、Priority (NDA under review)
	DS-1205 (AXL)	NSCLC	Ph 1	
	DS-1647 (Oncolytic virus)	GBM (Japan)	Pivotal	SAKIGAKE, ODD (JP)

ALL: acute lymphoblastic leukemia, AML: acute myeloid leukemia, ATL/L: adult T-cell leukemia/lymphoma, BCL: B-cell lymphoma,
BTD: Breakthrough Therapy Designation. GBM: glioblastoma multiforme, NSCLC: non-small cell lung cancer,
ODD: Orphan Drug Designation, PTCL: peripheral T-cell lymphoma, TGCT: tenosynovial giant cell tumor

Daiichi Sankyo ADC Franchise

As of Mar 2019

ADC Franchise

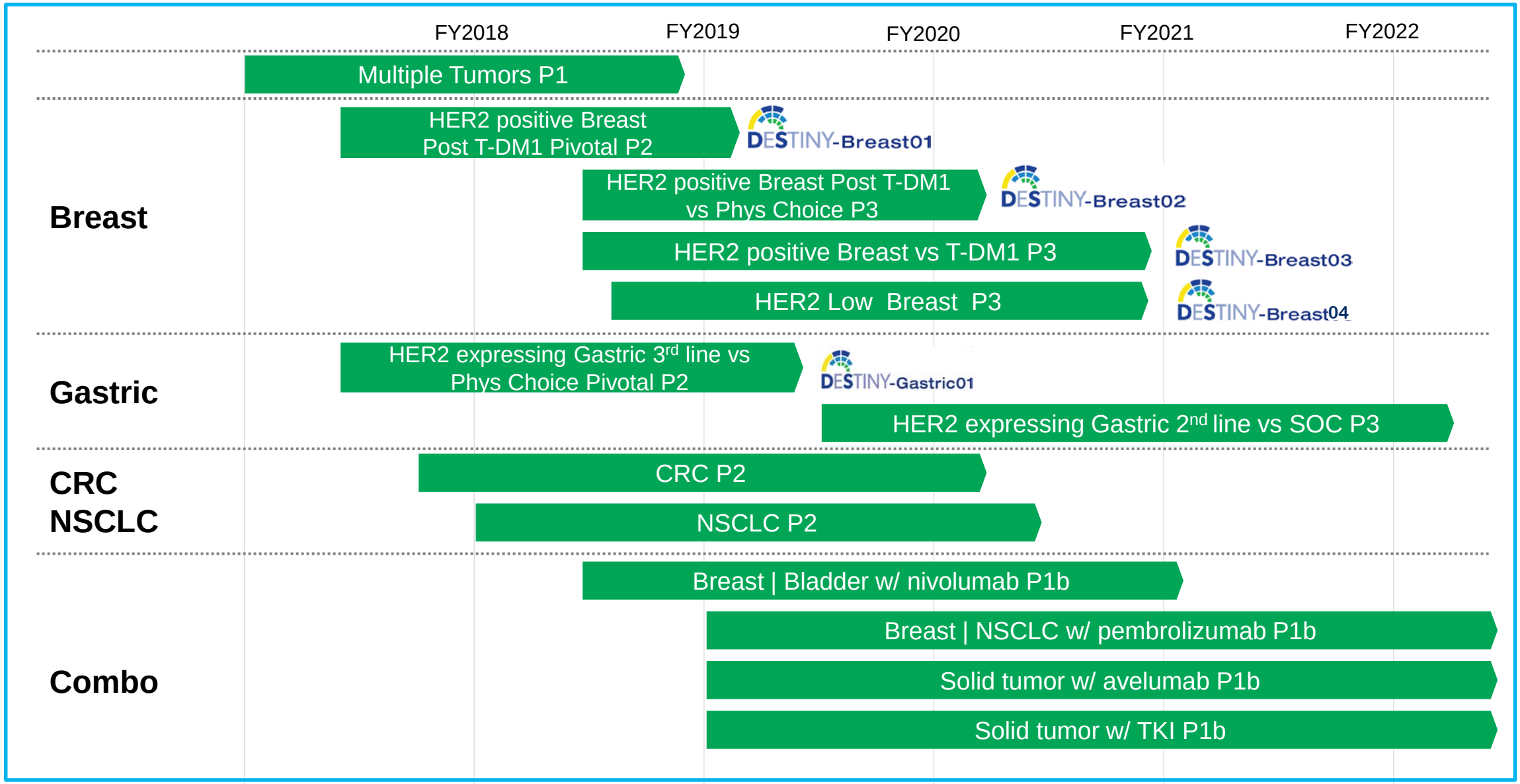


	Project (Target)	Potential Indications	Discovery	Pre-Clinical	Phase 1	Pivotal
1	DS-8201 (HER2)	Breast, Gastric, CRC, NSCLC				
2	U3-1402 (HER3)	NSCLC, Breast				
3	DS-1062 (TROP2)	NSCLC				
4	DS-7300 (B7-H3)	Solid tumors				
5	DS-6157 (GPR20)	GIST				
6	DS-6000 (undisclosed)	Renal, Ovarian				
7	(TA-MUC1)	Solid tumors				

CRC: colorectal cancer, NSCLC: non-small cell lung cancer, GIST: gastrointestinal stromal tumor

DS-8201: Clinical Program

As of Mar 2019



DS-8201: Clinical Program

As of Mar 2019

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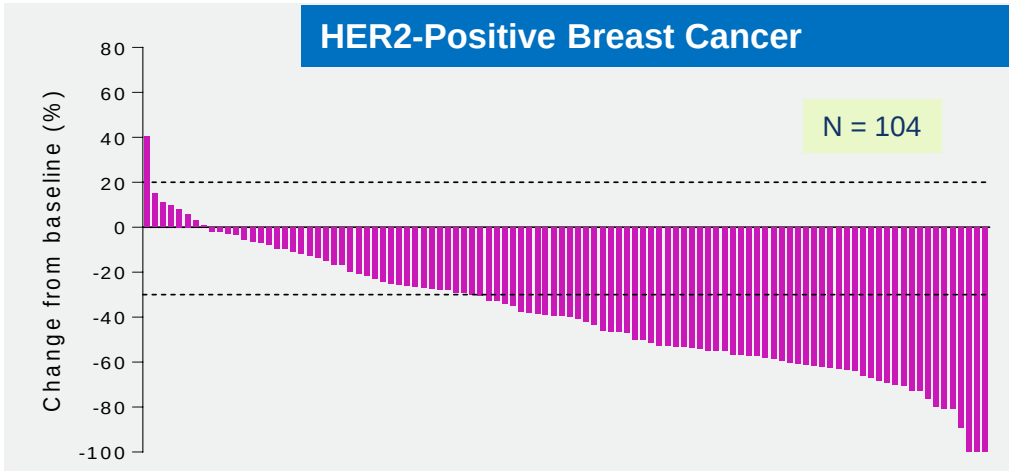
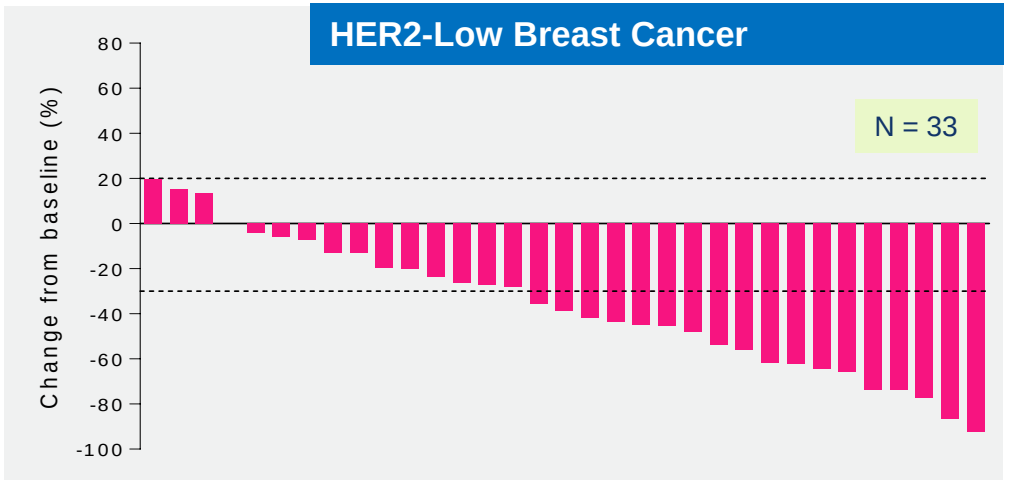
Current/future trials for further data-gated development

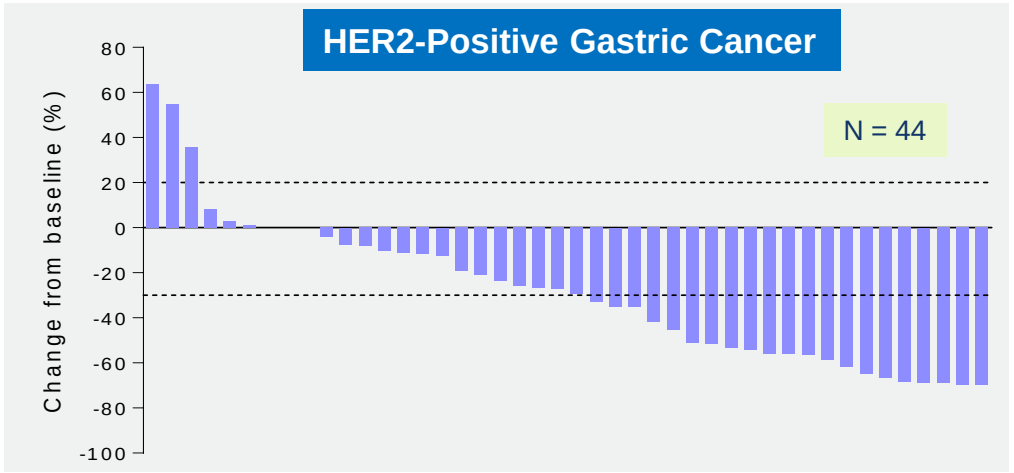
		Directions (Ph 1-3)
Breast	Move to 1st Line Metastatic Early Breast Cancer	• Neo-adjuvant • Adjuvant • Ph 3 in 1st Line HER2 positive • IO combinations • Hormonal therapy combinations • CDK4/6i combinations • PARPi combinations • Dual anti-HER2 combinations
Gastric	West HER2 expressing Gastric 2nd Line P2	• VEGFi combinations • Chemo combinations • IO combinations • HER2 Low • Early disease Gastric cancer
CRC **NSCLC**	CRC P2 NSCLC P2	• VEGFi combinations • Chemo combinations • IO combinations • HER2 Low
Other Combo	Other Tumor Types P2	• HER2 gene amplified basket • HER2 mutant basket • Ovarian • Uterine • Salivary • Bladder • Novel IO combos

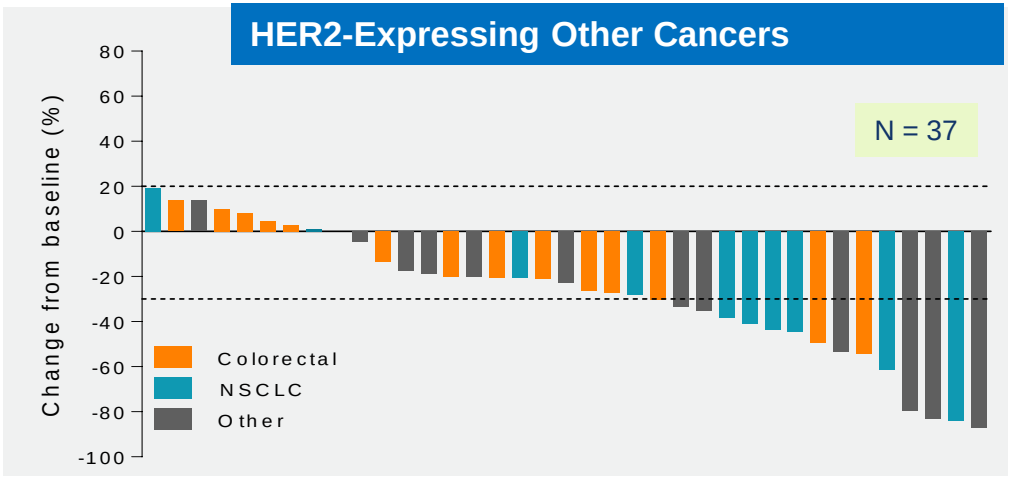
DS-8201: Phase 1 Study All Cancer Types

Tumor Shrinkage by Tumor Types: (5.4 or 6.4 mg/kg)





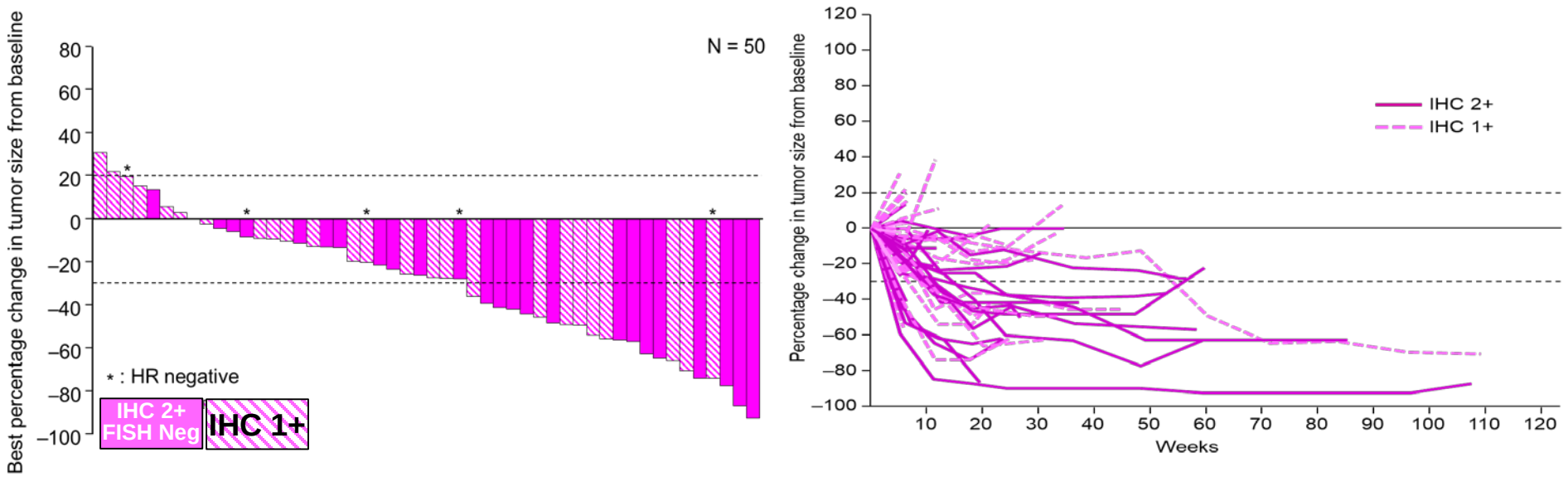




Includes subjects who had ≥1 postbaseline scan. Dotted lines denote 20% increase and 30% reduction in tumor size, respectively.
*Confirmed response includes subjects who had ≥2 postbaseline scans, progressive disease, or discontinued treatment for any reason prior to second postbaseline scan.
Data cutoff is April 18, 2018.

Iwata et al, ASCO, 2018; Abstract #2501

DS-8201: Phase 1 Study HER2 Low Breast Cancer



Dotted lines denote 30% decrease and 20% increase in tumor size cutoffs for partial response and progressive disease, respectively.
HR, hormone receptor; IHC, immunohistochemistry.

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

Modi et al, SABCS, 2018; Poster # P6-17-02, Abstract #486

TEAEs (≥20%) in All Breast Cancer Subjects, Regardless of HER2 Status, Who Received 5.4 or 6.4 mg/kg Doses of DS=8201 (N = 170)

Preferred Term	All Grades	Grade ≥3
Hematologic		
Anemia	68 (40.0)	25 (14.7)
White blood cell count decreased	43 (25.3)	16 (9.4)
Neutrophil count decreased	42 (24.7)	19 (11.2)
Platelet count decreased	41 (24.1)	11 (6.5)
Gastrointestinal		
Nausea	135 (79.4)	6 (3.5)
Vomiting	78 (45.9)	5 (2.9)
Diarrhea	65 (38.2)	5 (2.9)
Constipation	65 (38.2)	1 (0.6)
Stomatitis	65 (38.2)	1 (0.6)
Other		
Decreased appetite	92 (54.1)	5 (2.9)
Alopecia	79 (46.5)	0
Fatigue	72 (42.4)	7 (4.1)
AST increased	43 (25.3)	3 (1.8)
Malaise	40 (23.5)	0
Pyrexia	35 (20.6)	2 (1.2)
ALT increased	34 (20.0)	1 (0.6)

All values are n (%). Data cutoff October 12, 2018.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; HER2, human epidermal growth factor receptor 2; TEAEs, treatment-emergent adverse events..

Modi et al, SABCS, 2018; Poster # P6-17-02, Abstract #486

Drug-related ILD (Interstitial lung disease)

- More than 380 medications known to induce respiratory disease, mostly ILD[1]
- Probability remains largely **unpredictable and idiosyncratic**
- **Diagnosis made on signs/symptoms** (e.g., fever, cough, shortness breath) and **excluding other causes**
- **Treatment is high dose steroids and withdrawal of causing agent**
- Benchmark example: TAGRISSO [US Label]
  - ILD in 3.9% of 1,142 cases
  - 0.4% fatal

[1]M Schwaiblmair Open Respir Med 2012;6:63-74

DS-8201 | Safety: ILD

Investigator-Reported and Adjudicated Cases of ILD

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

Data cutoff: October 15, 2018

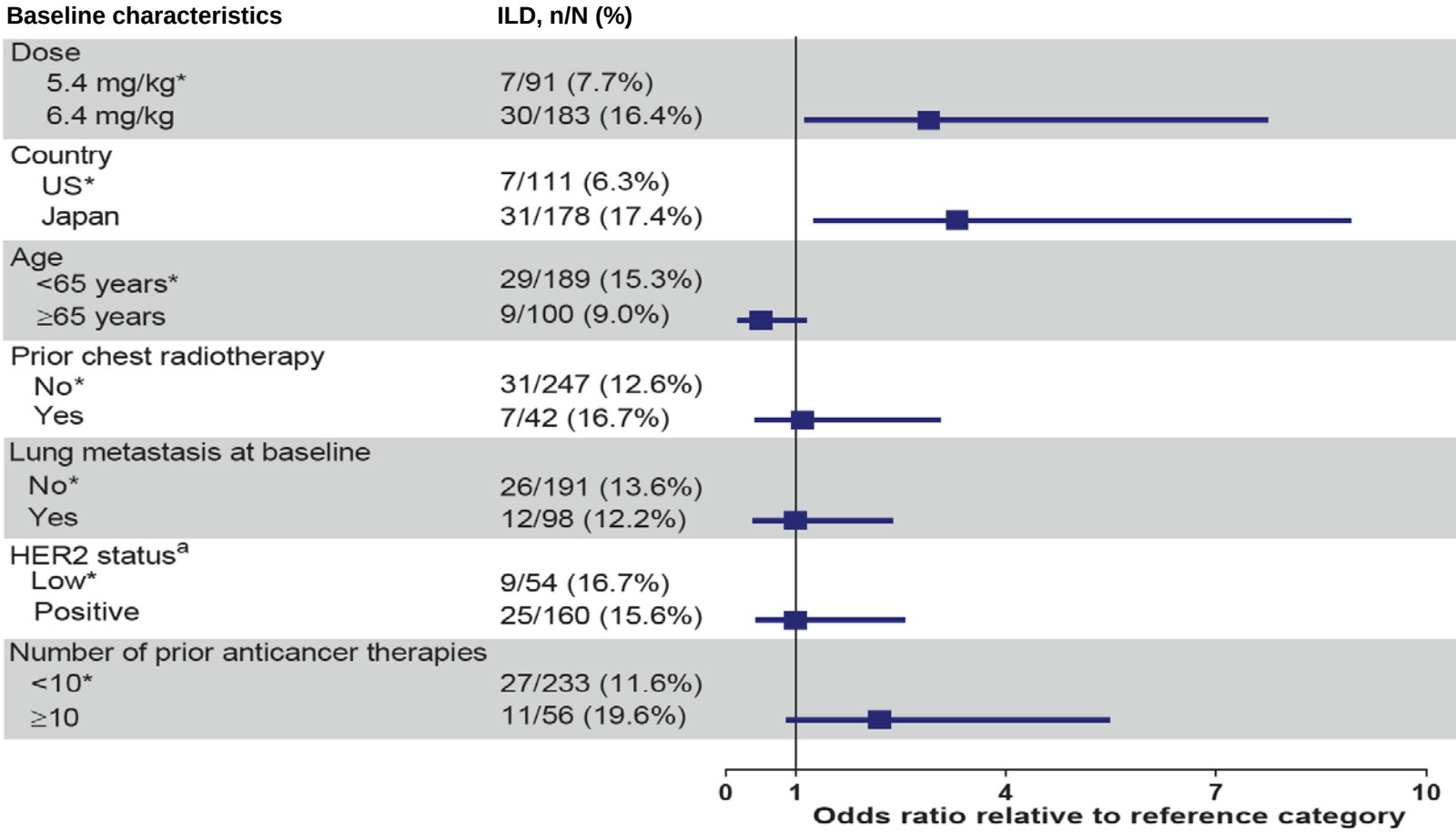
- Median duration of treatment 108 days
- 29.5% subjects on treatment for ≥180 days
  - Median time to onset of ILD 149 days

- **Feb-March 2018: ILD recognized as DS-8201 risk: key actions implemented**:
  - Proactive awareness of subjects thru consent, to report signs or symptoms of possible ILD
  - Active training of investigational sites on monitoring for, evaluation and treatment of suspected ILD cases

Powell et al, SABCS, 2018; Poster # P6-17-06, Abstract #979

DS-8201 | Safety: ILD

Odds Ratio (95% CI) for Association of Characteristics with Developing ILD (study J101)



A higher dose *and* ***Japanese origin*** *associated with* ***higher likelihood of developing ILD*** *after adjusting for the other factors*

Odd ratios and 95% confidence intervals were computed using a multivariate logistic regression model that included all variables shown.
*Reference category.
[a]HER2 status was only available for breast and gastric cancer.

Powell et al, SABCS, 2018; Poster # P6-17-06, Abstract #979

DS-8201 | ILD experience Breast Cancer at Recommended Dose

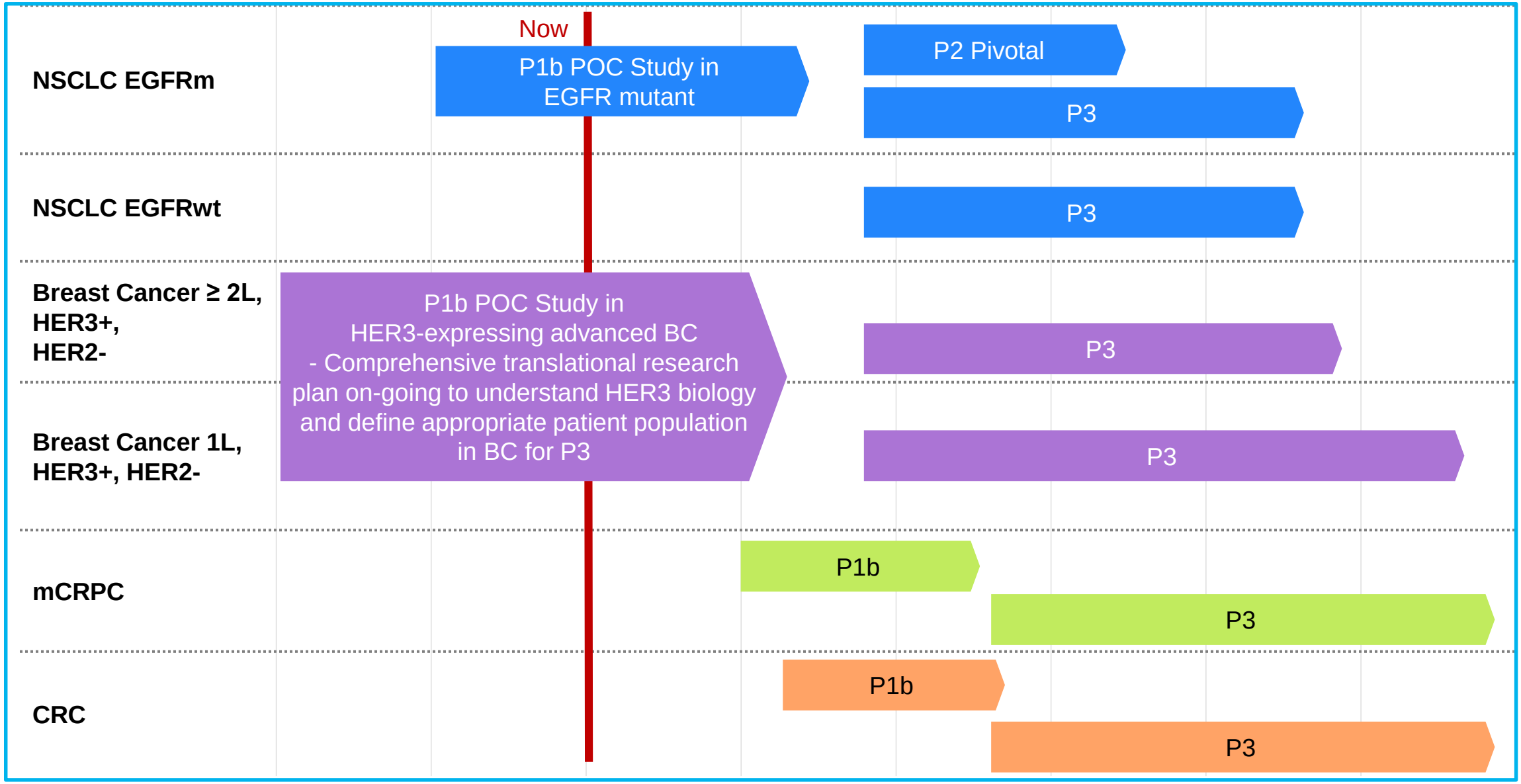
- Based on safety, efficacy and exposure data, 5.4 mg/kg was selected as the dose for pivotal development in breast cancer
- At 5.4mg/kg in breast cancer, ILD appears as a well characterized risk

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

Powell et al, SABCS, 2018; Poster # P6-17-06, Abstract #979

U3-1402 HER3-ADC: Directional Development Plan

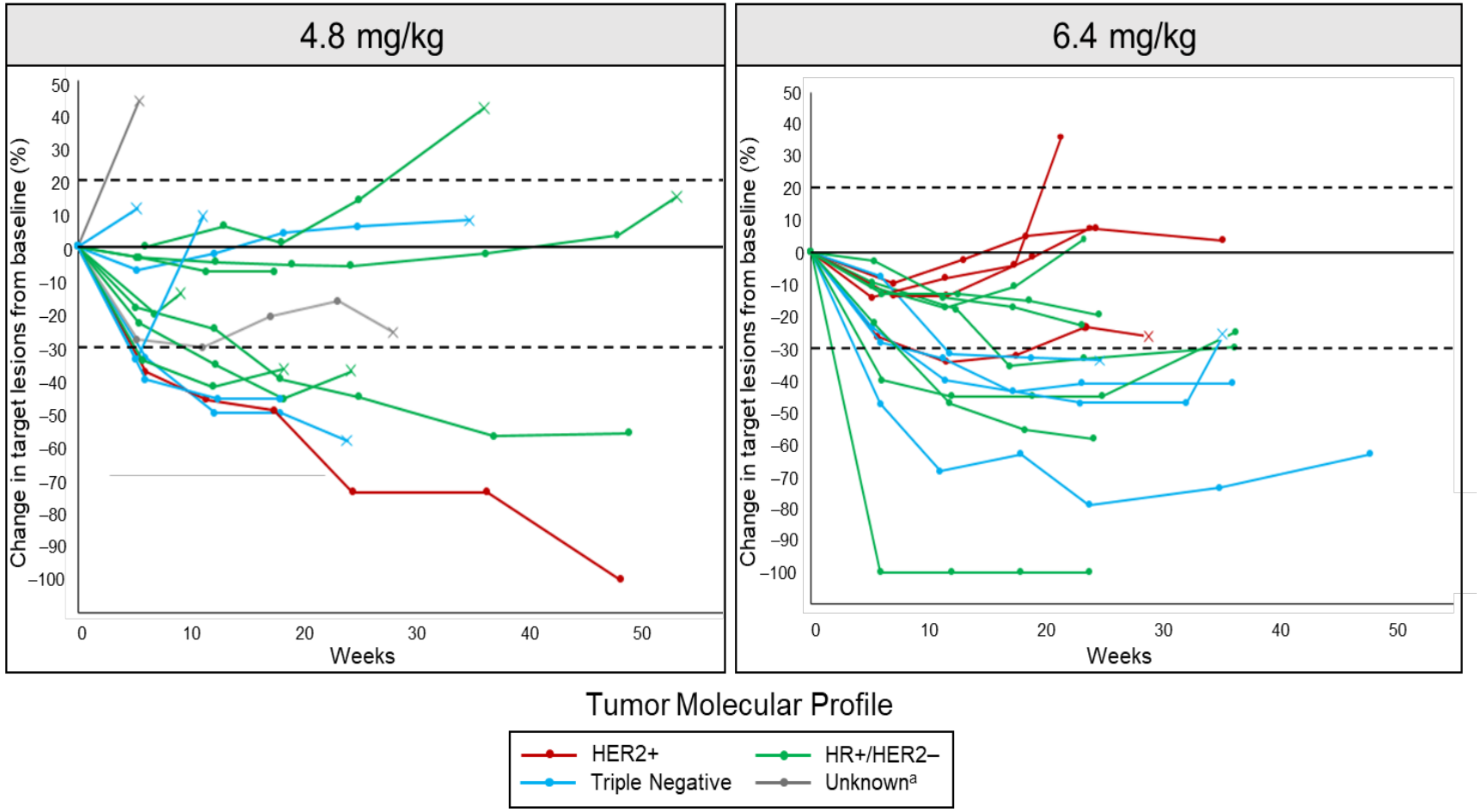
As of Mar 2019



mCRPC: metastatic castrate-resistant prostate cancer; CRC: colorectal cancer

U3-1402: Phase 1 Breast Cancer Study Efficacy by Dose Level

Percentage Change in Target Lesions from Baseline



Data cutoff date of November 6, 2018. X indicates patients who discontinued treatment.
[a]Unknown includes 2 patients with HR+ and HER2 IHC/FISH unknown; 1 patient with HR– and HER2 IHC/FISH unknown; and 1 patient HR+ and HER2 IHC 2+/FISH unknown.
Dotted lines denote 30% decrease and 20% increase in tumor size threshold for partial response and progressive disease, respectively.
Analysis set: efficacy-evaluable patients with at least 1 postbaseline tumor assessment.
FISH, fluorescent in situ hybridization; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IHC, immunohistochemistry.

Masuda et al, SABCS, 2018; Poster # PD1-03 , Abstract #1024

U3-1402: Phase 1 Study Safety Profile (Nov. 06, 2018)

Characteristics	Dose Escalation + Dose Finding (N = 42)
TEAEs regardless of causality	42 (100.0)
Serious TEAEs regardless of causality	14 (33.3)
Drug-related	7 (16.7)
TEAEs leading to drug withdrawal/ discontinuation	1 (2.4)
TEAEs leading to dose reduction	8 (19.0)
TEAEs leading to dose interruption	19 (45.2)
TEAEs associated with death as outcome	0

TEAEs, treatment-emergent adverse events

- Median **drug exposure 7.6 months** for 42 subjects, all breast cancer
- In Dose Escalation (n=34), **DLT** in 4 subjects: transient, reversible thrombocytopenia (grade 4) and AST and ALT increased (grade 3); none required discontinuation
- **A single subject had a TEAE leading to drug discontinuation** (grade 2 pneumonitis)
- **Pulmonary adverse events of special interest**, observed in 1 patient each:
  - grade 1 radiation fibrosis and grade 3 radiation pneumonitis, not drug related and recovered, treatment resumed
  - grade 2 pneumonitis, drug related, recovered after treatment discontinued
  - grade 2 interstitial pneumonitis, drug related, recovering after treatment withdrawn
- All cases are being adjudicated

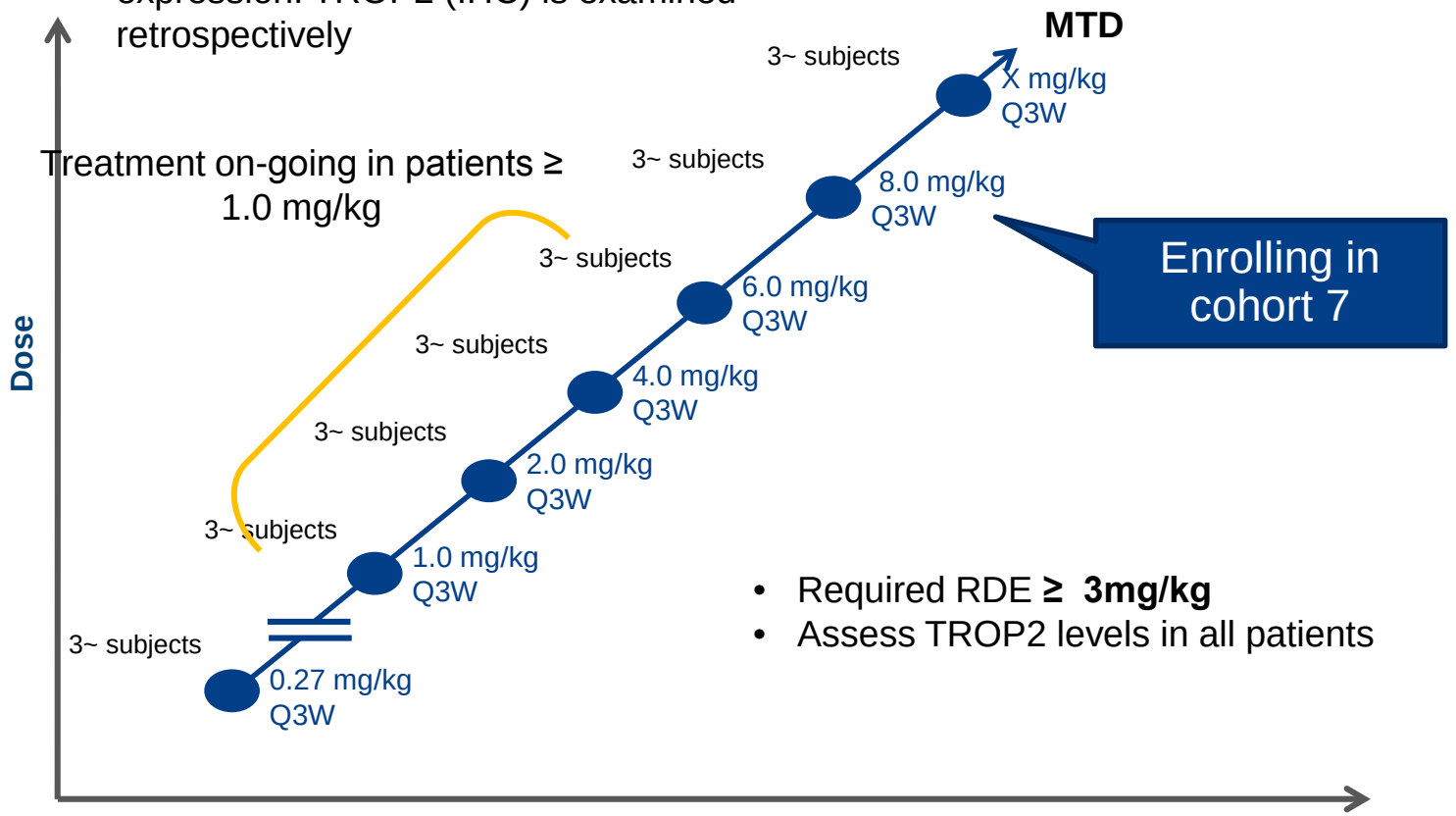
Masuda et al, SABCS, 2018; Poster # PD1-03 , Abstract #1024

DS-1062 TROP2 ADC | Ph 1 Study | Lean Plan to POC

NSCLC ≥ 3rd line

Dose Escalation

No selection based on TROP2 expression. TROP2 (IHC) is examined retrospectively



Enrolling in cohort 7

- Required RDE **≥ 3mg/kg**
- Assess TROP2 levels in all patients

Dose Expansion

n=40 in RDE* — POC

Assess efficacy and safety for GO/NO-GO decision

Following NSCLC POC

- Open 2 other expansion cohorts for other TROP2 positive tumors

POC

Expansion Indication A n=40

Expansion Indication B n=40

* RDE: Recommended Dose for Expansion

Tolerability of DS-1062 up to 6.0mg/kg warrants further evaluation of safety and efficacy signals in higher dose exposure
Dose escalation data to be presented at ASCO 2019

POC: Proof of Concept

Cancer Enterprise | Upcoming Milestones

ADC Franchise

- DS-8201: decision for early BLA submission in FY2018 Q4~
- Potential ASCO 2019 disclosures:
  - U3-1402 & DS-1062: first disclosures of data in NSCLC

AML/Hematology Franchise

- Quizartinib: marketing applications under expedited review in US/EU/Japan
  - FDA PDUFA: May 25, 2019
  - EU (Accelerated Assessment) and Japan actions anticipated 2H FY2019

Breakthrough Science

- Pexidartinib: marketing application under expedited review in US
  - FDA PDUFA: August 3, 2019

Cancer Enterprise | Deliver, Scale Up, Lead

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