

# **Conference Call Highlight from ASCO 2017**

## **DAIICHI SANKYO CO., LTD**

**Antoine Yver**

**Global Head of Daiichi Sankyo Cancer Enterprise**

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# Today's Agenda

1. Opening remark
2. Cancer Enterprise
3. Key highlight from ASCO 2017
4. Q&A

## Past

- Daiichi Sankyo has a **history of strong science and innovation**
- In April 2016, we shared our **2025 vision** – to become a **Global Pharma Innovator with a Competitive Advantage in Oncology**



## Present

- In process of launching **Cancer Enterprise** and **accelerating our most promising assets**
- Today, we are excited to **share our vision and progress to date**



## Future

- Cancer Enterprise is on track to support Daiichi Sankyo **5-Year Business Plan**
  - FY2020: 40+ Bn JPY
  - FY2025: ~300 Bn JPY
- We will **deliver our portfolio for patients** and our **2025 vision**



- **DS-8201: Flagship asset**, HER2 ADC, key to Daiichi Sankyo strength in oncology

- Broad opportunity
- Partnership implications



- **Emerging franchises**

- Acute Myeloid Leukemia (**AML**)
- Antibody Drug Conjugate (**ADC**) technology



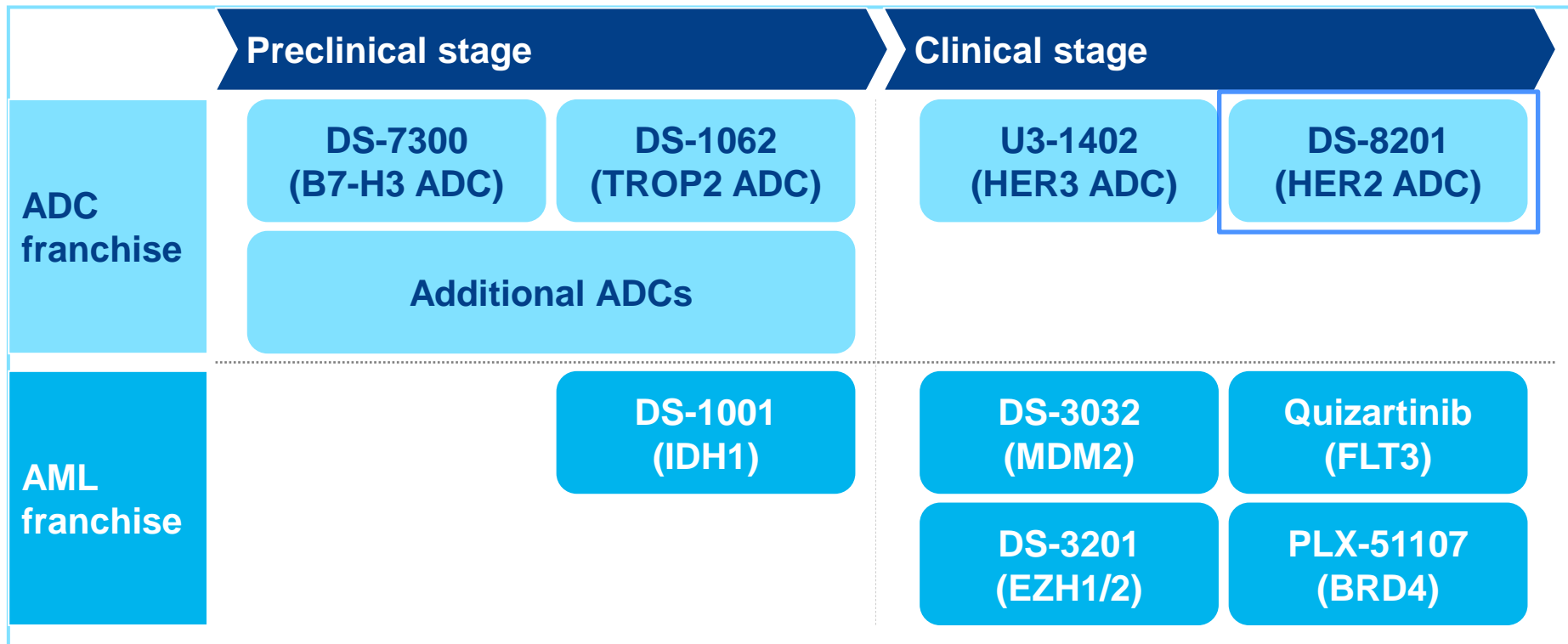
- Powerful **research engines**
  - Japan research labs, combining chemistry and biology expertise
  - Plexxikon discovery platform, enabling efficient candidate identification



- **Strategic investments** in enhanced capabilities
  - Align capabilities to aspirations
  - Strategic BD&L

# Cancer Enterprise two emerging franchises

Slide from  
R&D Day  
Dec 2016



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# Single agent activity of DS-8201a, a HER2-targeting antibody-drug conjugate, in heavily pretreated HER2 expressing solid tumors (Abstract No: 108)

Toshihiko Doi<sup>1</sup>, Hiroji Iwata<sup>2</sup>, Junji Tsurutani<sup>3</sup>, Shunji Takahashi<sup>4</sup>, Haeseong Park<sup>5</sup>, Charles H. Redfern<sup>6</sup>, Kohei Shitara<sup>1</sup>, Chikako Shimizu<sup>7</sup>, Hiroya Taniguchi<sup>2</sup>, Tsutomu Iwasa<sup>3</sup>, Shinichiro Taira<sup>4</sup>, Albert C. Lockhart<sup>5</sup>, Jennifer M. Fisher<sup>6</sup>, Takahiro Jikoh<sup>8</sup>, Yoshihiko Fujisaki<sup>8</sup>, Caleb Lee<sup>9</sup>, Antoine Yver<sup>9</sup>, Kenji Tamura<sup>7</sup>

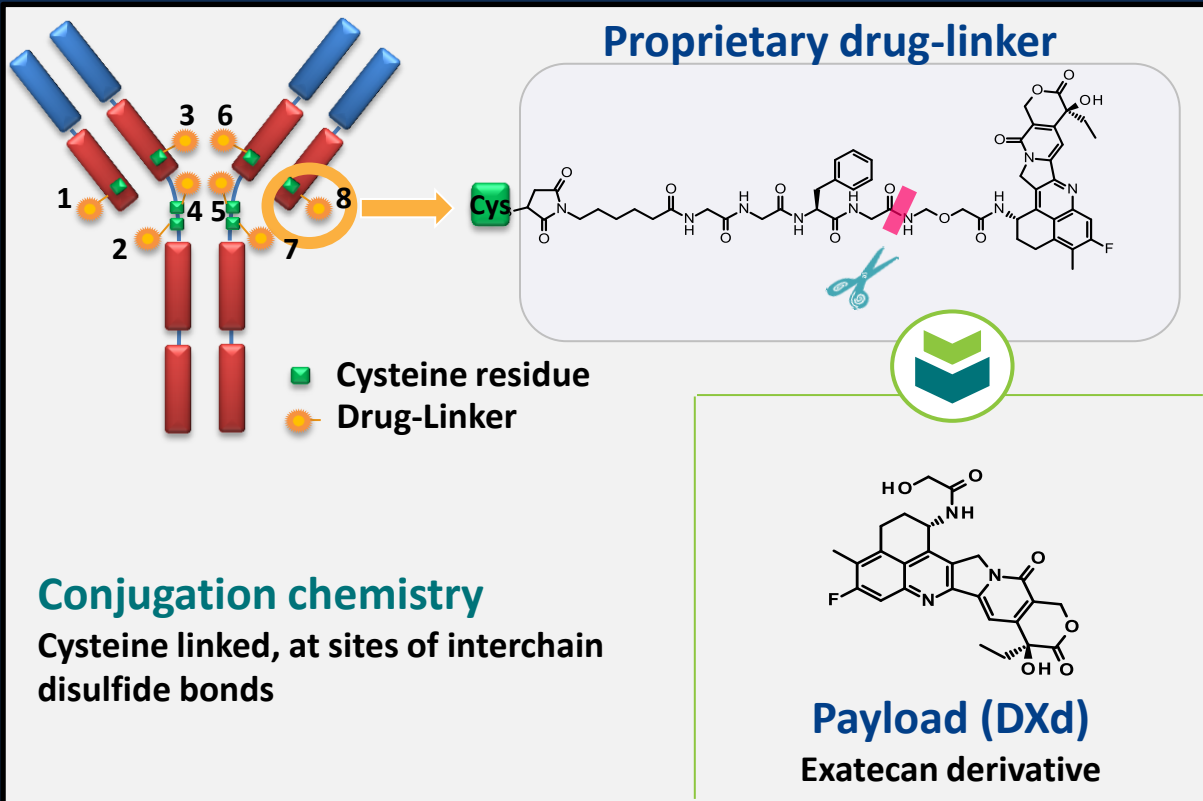
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# Disclosure

- Toshihiko Doi - Consulting or Advisory Role; Amgen, Chugai Pharma, Daiichi Sankyo, Kyowa Hakko Kirin, Lilly Japan, MSD, Nippon Boehringer Ingelheim, Novartis. Research Funding; Astellas Pharma, Bayer, Boehringer Ingelheim, Celgene, Chugai Pharma, Daiichi Sankyo, Janssen, Kyowa Hakko Kirin, Lilly Japan, Merck Serono, MSD, Novartis, Pfizer, Sumitomo Group, Taiho Pharmaceutical, Takeda.
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# DS-8201a



Novel payload

High potency

Bystander effect

Short systemic half-life payload

Stable linker-payload

Tumor selective cleavable-linker

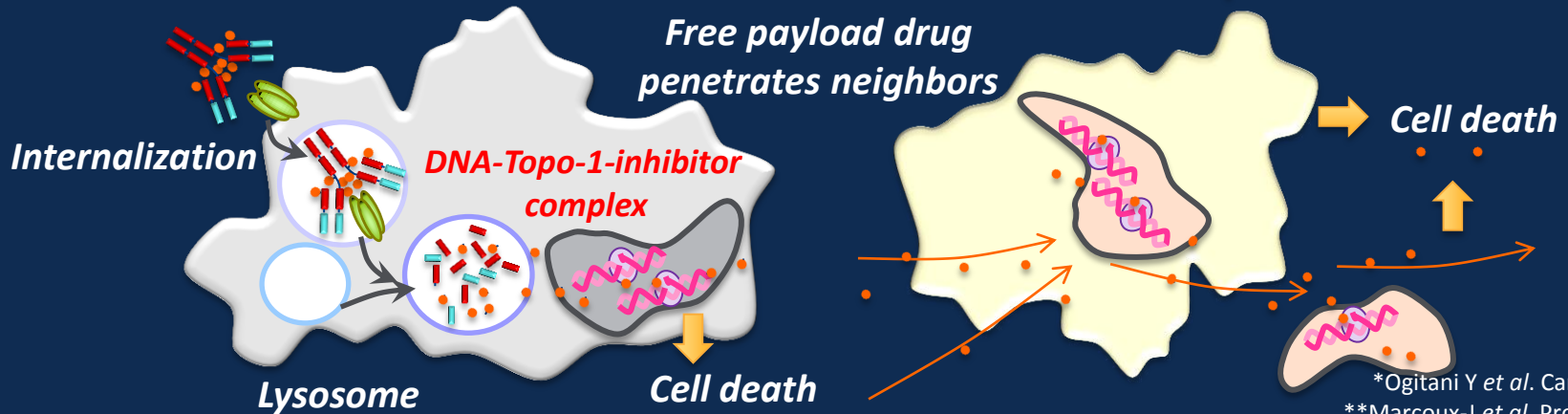
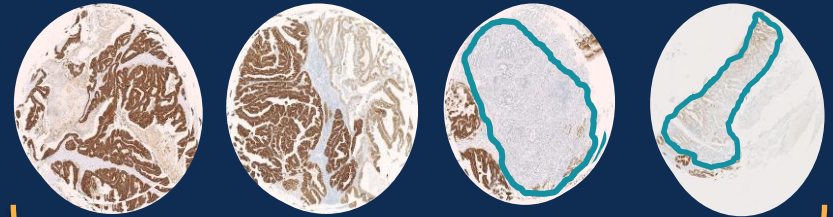
High drug-to-antibody ratio

# MoA of DS-8201a

	DS-8201a	T-DM1
Antibody	Anti-HER2 Ab	Trastuzumab
MOA	<b>Topoisomerase I</b> <b>Bystander effect*</b>	Tubulin
Drug-to-antibody ratio	7-8	3.5**

## Heterogeneity of IHC staining in gastric cancer

All cases classify into HER2 score 3+



\*Ogitani Y et al. Cancer Sci. 2016

\*\*Marcoux-J et al. Protein Sci. 2015

# Ph1 Evaluation & Key eligibility criteria

## Endpoint

DLT, Safety and tolerability, Efficacy, PK

## Key inclusion criteria

- ECOG PS 0-1     • LVEF  $\geq$  50%
- Adequate organ function including platelet  $\geq$  100,000 /mm<sup>3</sup>, Hb  $\geq$  8.5 g/dL, ANC 1,500/mm<sup>3</sup>

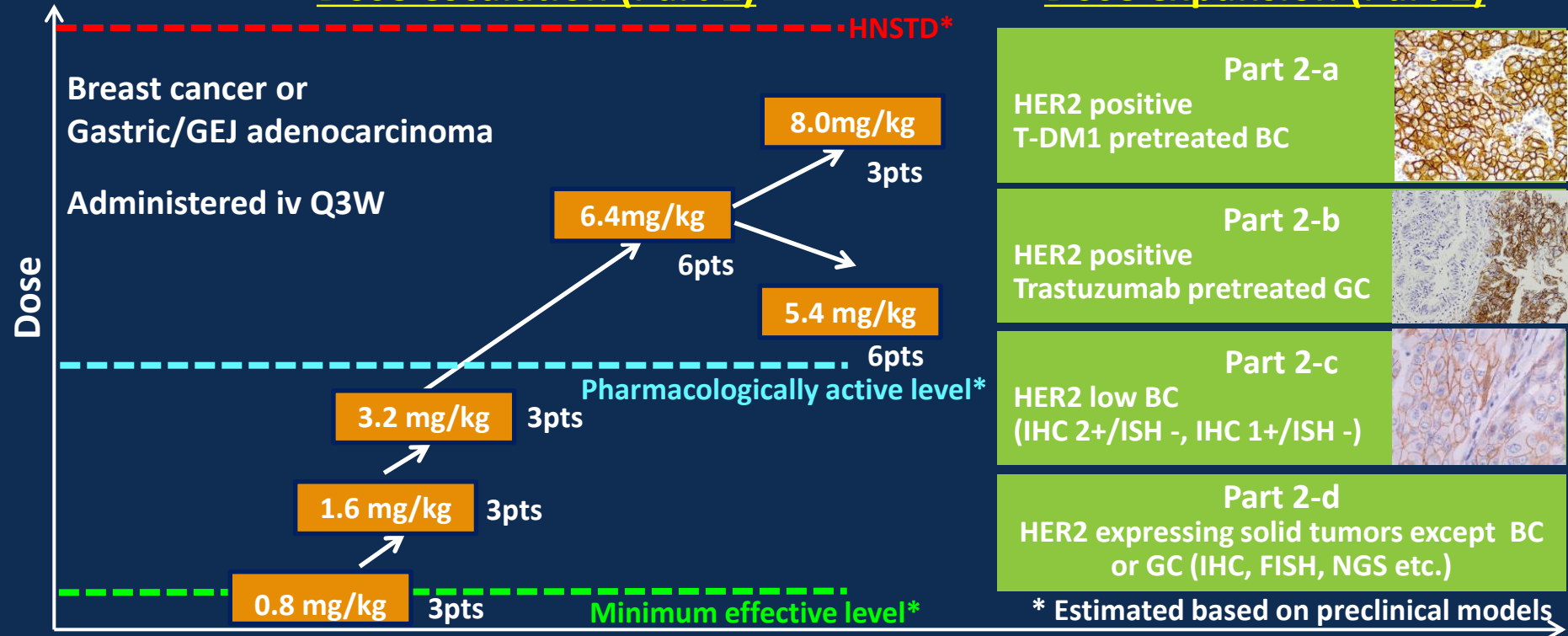
## Definition of key DLT criteria

- Gr4 neutrophil count decreased lasting > 7days
- Gr4 anemia
- Gr4 platelet count decreased or Gr $\geq$ 3 platelet count decreased lasting > 7days
- Gr4 AST or ALT increased
- Gr $\geq$ 3 non-hematologic, non-hepatic major organ toxicities including symptomatic CHF, LVEF decline to < 40% or 20 % drop from baseline

# Ph1 Dose escalation and expansion

## Dose escalation (Part 1)

## Dose expansion (Part 2)



# Demographics (Part 1+Part 2, 5.4 + 6.4 mg/kg, N=134)

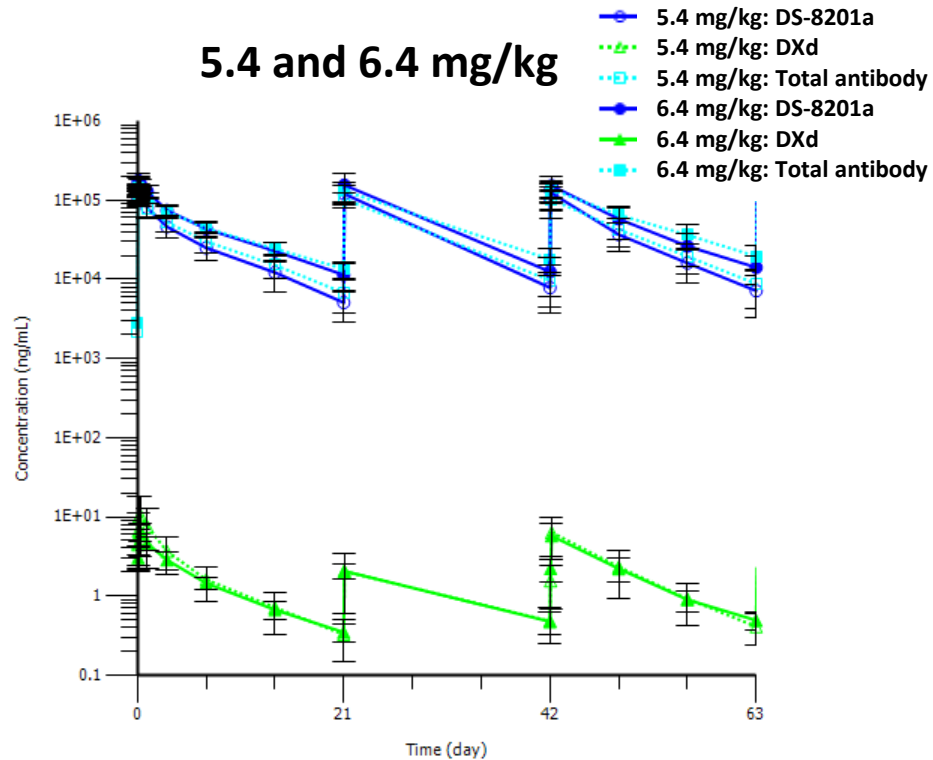
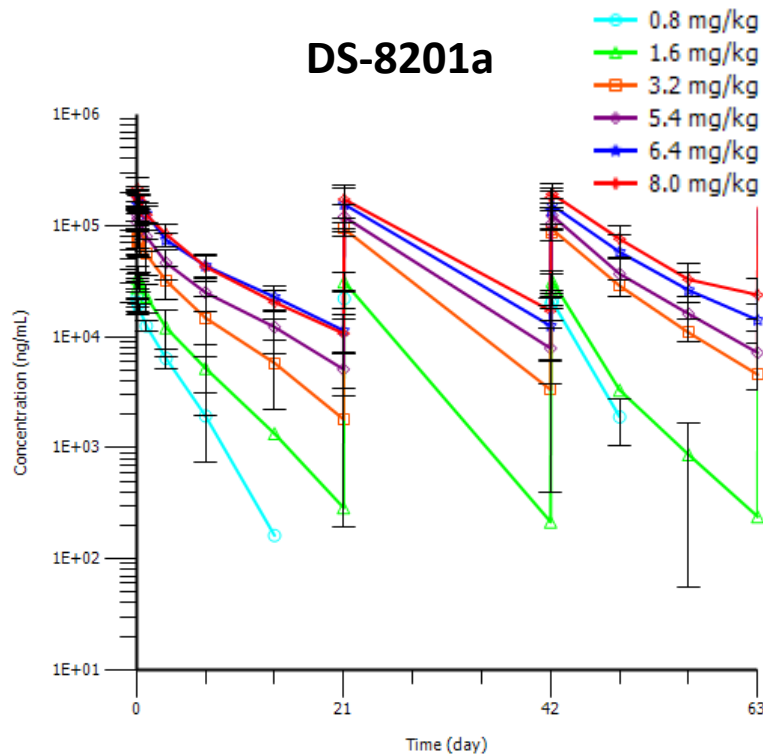
Breast cancer (N=64)	
HER2 status	
HER2 Positive	83%
HER2 Low	17%
# of prior regimen	
Median: 5.0	
Tumor size (Median: 5.1 cm)	
≤ 5cm	49%
5 – 10 cm	32%
≥ 10 cm	19%

Gastric cancer (N=44)	
HER2 status	
HER2 Positive	98%
HER2 Low	2%
# of prior regimen	
Median: 3.0	
Tumor size (Median: 4.7 cm)	
≤ 5cm	54%
5 – 10 cm	17%
≥ 10 cm	29%

Others (N=26)	
# of prior regimen	
Median: 3.0	
Tumor size (Median: 7.2 cm)	
≤ 5cm	35%
5 – 10 cm	30%
≥ 10 cm	35%

Analysis set: Enrolled patients at 5.4 and 6.4 mg/kg  
Data cutoff on 11-May-2017

# Pharmacokinetics



Analysis set: PK evaluable patients in Part1  
Data cutoff on 11-May-2017

# TEAE, any grade, >20% (No DLT observed)

Preferred Term (N=133)	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)	All (%)
<b>Hematologic</b>					
Platelet count decreased	13.5	9.0	8.3	3.8	34.6
Anaemia	3.0	12.0	14.3	1.5	30.8
Neutrophil count decreased	0.8	9.8	12.0	3.0	25.6
White blood cell count decreased	0.8	12.8	9.0	1.5	24.1
<b>Gastrointestinal disorders</b>					
Nausea	51.9	13.5	1.5	0.0	66.9
Decreased appetite	33.8	20.3	3.8	0.0	57.9
Vomiting	31.6	3.8	1.5	0.0	36.8
Diarrhoea	19.5	5.3	0.8	0.0	25.6
Constipation	18.8	3.0	0.0	0.0	21.8
<b>Others</b>					
Alopecia	21.1	6.0	0.0	0.0	27.1
Malaise	18.0	4.5	0.8	0.0	24.1

**Any Grade 3/4 – 43.6%**

Analysis set: Safety evaluable patients who received at least one dose of DS-8201a  
Data cutoff on 11-May-2017



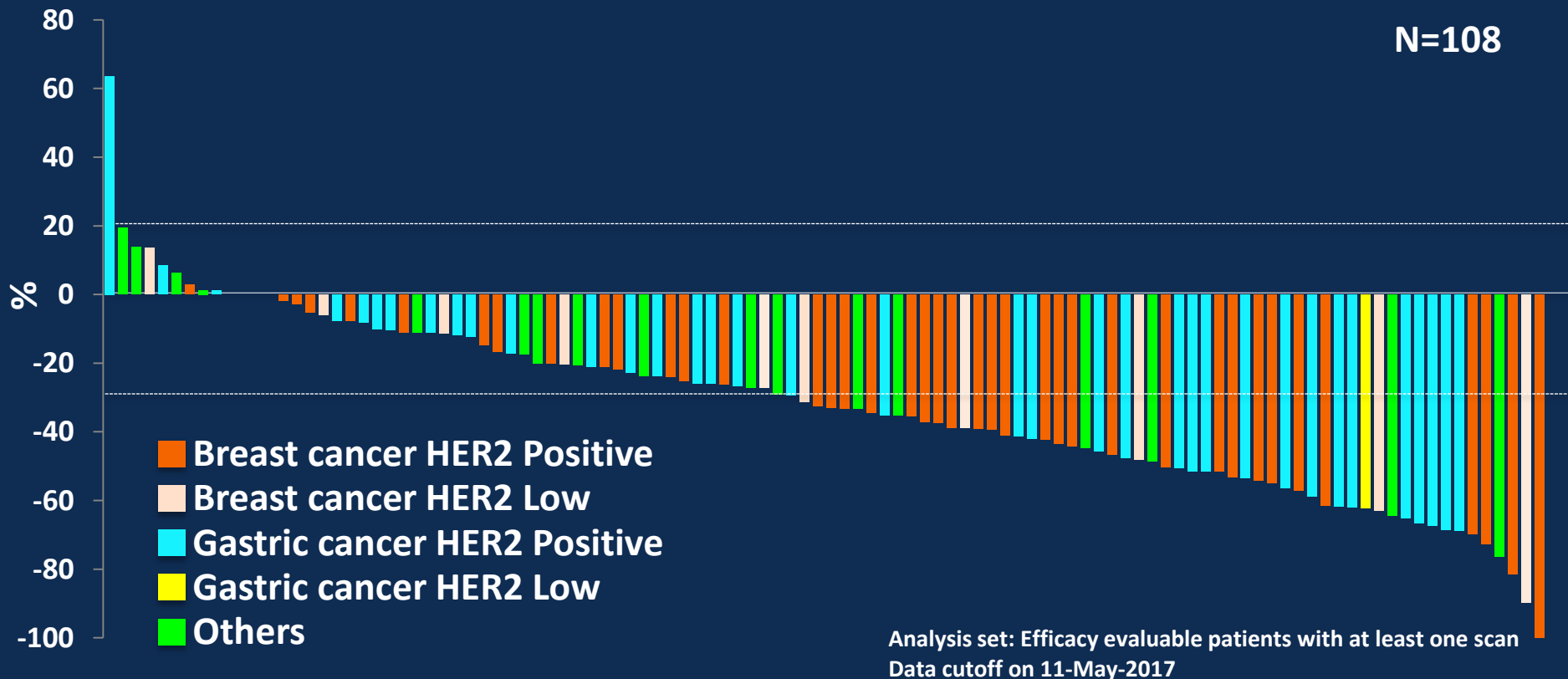
# Confirmed overall response rate (5.4+6.4 mg/kg)

	ORR n (%)	DCR n (%)
<b>Total</b>	<b>39/97 (40.2)</b>	<b>89/97 (91.8)</b>
<b>Breast Cancer</b>	<b>19/45 (42.2)</b>	<b>44/45 (97.8)</b>
<b>BC Prior T-DM1</b>	<b>16/35 (45.7)</b>	<b>35/35 (100.0)</b>
<b>BC Prior T-DM1+Pertuzumab</b>	<b>14/30 (46.7)</b>	<b>30/30 (100.0)</b>
<b>Gastric Cancer</b>	<b>16/36 (44.4)</b>	<b>32/36 (88.9)</b>
<b>GC Prior CPT-11</b>	<b>8/18 (44.4)</b>	<b>17/18 (94.4)</b>

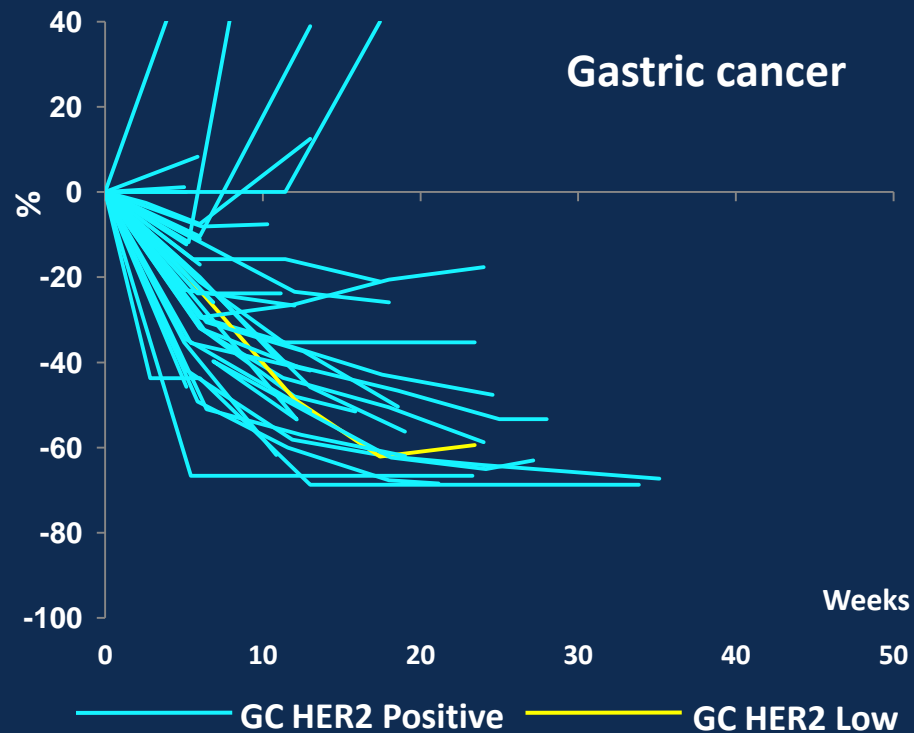
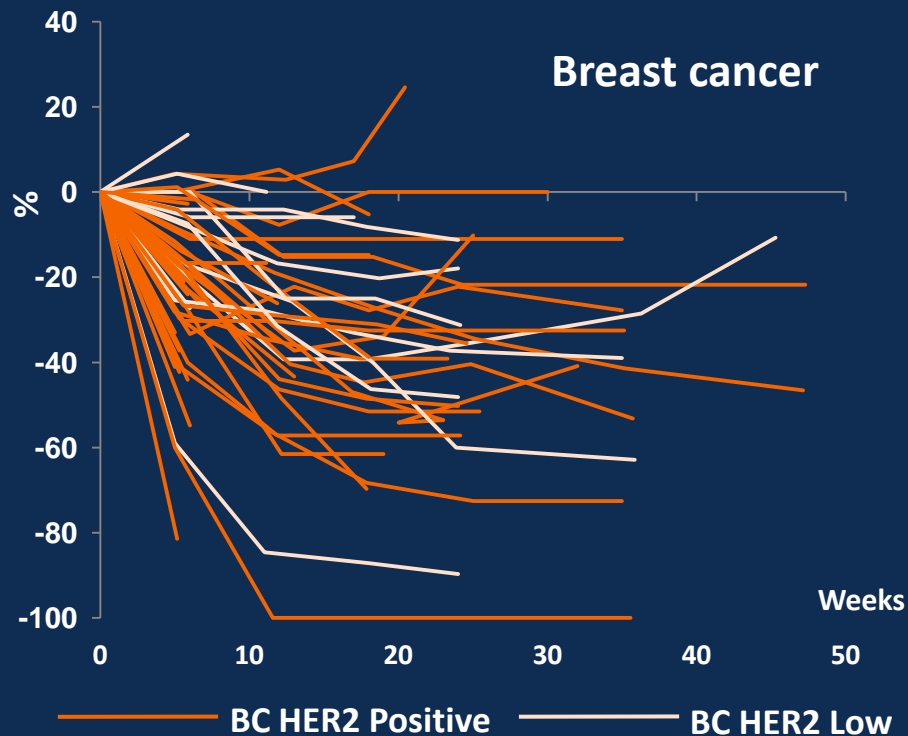
Analysis set: Efficacy evaluable patients for confirmed overall response  
Data cutoff on 11-May-2017

# Tumor size: best % change from baseline (5.4+6.4 mg/kg)

N=108

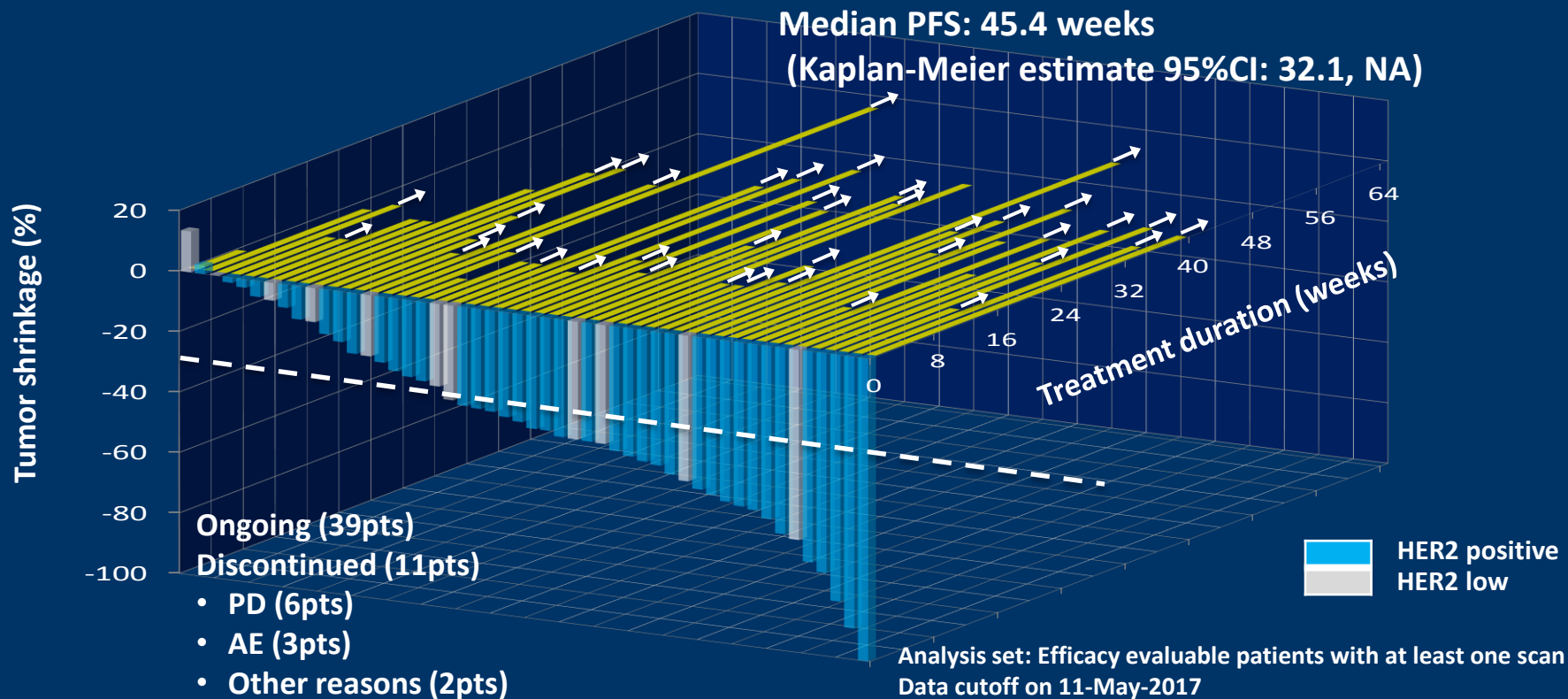


# Tumor size: % Change from baseline (5.4 + 6.4 mg/kg)

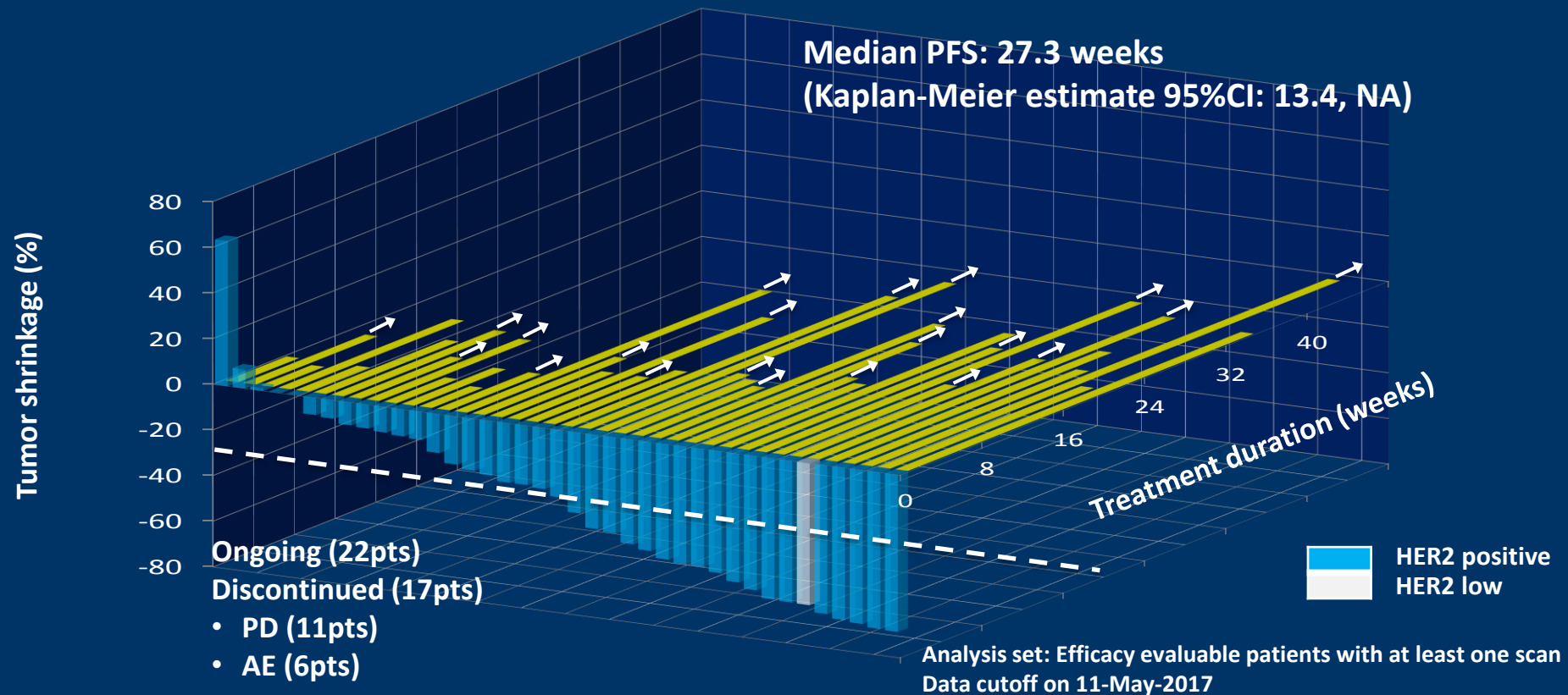


Analysis set: Efficacy evaluable patients with at least one scan  
Data cutoff on 11-May-2017

# Response and treatment duration (Breast cancer, 5.4 + 6.4 mg/kg)



# Response and treatment duration (Gastric cancer, 5.4 + 6.4 mg/kg)



# Conclusions

- **Preliminary results in first in human Phase 1 trial, DS-8201a demonstrated promising antitumor activity and favorable safety profile**
  - For HER2 + Breast cancer pts pretreated with T-DM1 and pertuzumab, ORR was 46.7 %
  - For HER2 + Gastric cancer pts pretreated with trastuzumab, ORR was 44.4%.
  - No DLT was observed and MTD was not reached
  - DS-8201a had few Gr 3 or more AEs or unexpected events, with low risk of cardiac toxicities
- **Based on these preliminary results, Phase 2 trials are planned in pts with HER2 + GC and BC**

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