Passion for Innovation.
Compassion for Patients.™

Daiichi-Sankyo

FY2018
R&D Day

DAIICHI SANKYO CO., LTD

George Nakayama
Chairman and CEO

December 12, 2018

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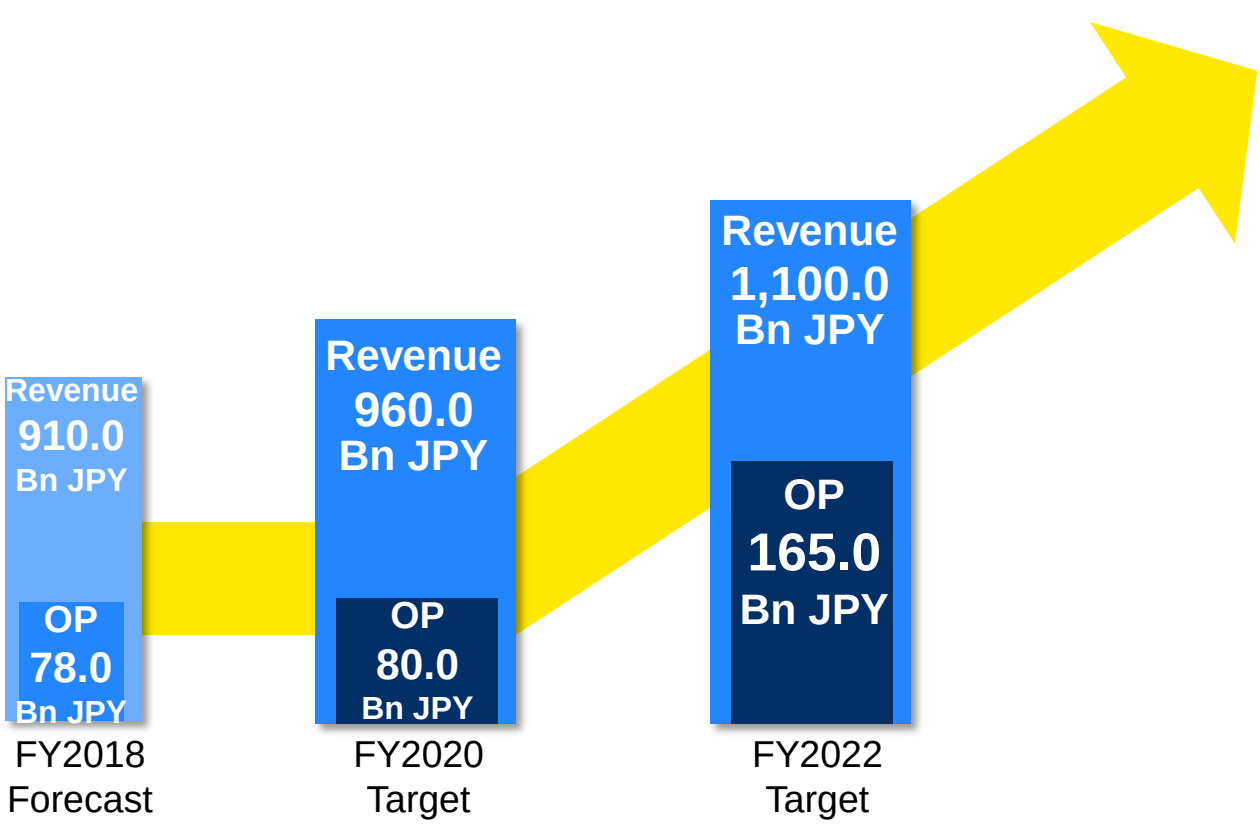
Toward 2025 Vision & 5-Year Business Plan



2025 Vision

Global Pharma Innovator with Competitive Advantage in Oncology

Establish a Foundation of Sustainable Growth: Six Strategic Targets

- Grow Edoxaban
- Grow as No.1 Company in Japan
- Expand US Businesses
- Establish Oncology Business
- Continuously Generate Innovative Medicine Changing SOC
- Enhance Profit Generation Capabilities

Establish Oncology Business
Continuously Generate Innovative Medicine Changing SOC

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Increase R&D investments

- ✓1.1 Tn JPY (increased by 200 Bn JPY) in 5 Years
- ✓May consider shifts of a part of BD funds, 500 Bn JPY, to R&D

Realize optimal balance between Oncology and SM*

- ✓Focus on LCMs & new products in SM to generate near-term profits
- ✓Continue discovery activities in SM to see beyond 2025 Vision

SM: Specialty Medicine Area: Cardiovascular-metabolics, pain, central nervous system diseases, heart and kidney diseases, and rare diseases

R&D 2025 Vision

CE 2025 Vision

ADC Franchise	AML Franchise	Breakthrough Science
3	3	1

Deliver 7 NMEs in 8 years

SM 2025 Vision

Maximize near-term revenue	Grow future franchises
2 NMEs in 2018-20	3 NMEs 2021-25

R&D 2025 Vision

CE 2025 Vision

R&D Day 2018
Main Topics

SM 2025 Vision

Maximize near-term revenue

2 NMEs in 2018-20

NDA submissions
Mirogabalin
Esaxerenone

Grow future franchises

3 NMEs 2021-25

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

Daiichi Sankyo Cancer Enterprise

Deliver, Scale Up and Lead in Science

December 12, 2018

Antoine Yver MD MSc
Exec VP & Global Head R&D Oncology

Today's Agenda

1 Cancer Enterprise 2025

- A Delivery Machine
- Scaling up the Enterprise
- Secure World-class Leadership in Science

2 DS-8201

- BLA FY2020 (upside 1H FY2019) on track
- Expanding program scope
- ILD well characterized
- Breast cancer: duration of response in Ph 1

3 U3-1402

- Breast cancer data at SABCS
- NSCLC EGFRm program progress
- Fast to market strategy and program scope

4 Next DXd ADCs

- DS-1062: Ph 1
- Others

5 Quizartinib

- Global US EU JP NDA submissions completed
- Biology and differentiation – the key role of QuANTUM First

6 Pexidartinib

- Submission status
- ENLIVEN

7 Recap

- DS is a science & technology company / future news flows

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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

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7 NMEs **in** **8** years

Lead in Smart-Treatment with BIC & FIC ADC	Establish a Competitive Hematology Franchise	Lead with Breakthrough Science
3	**3**	**1**

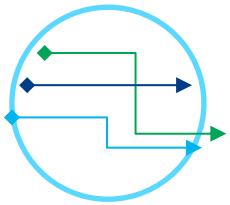
FY2018 → **2025**

Quizartinib	DS-8201	DS-3201	U3-1402	DS-1062	DS-7300
Pexidartinib	DS-1647			DS-3032	DS-1001
	Axi-Cel®			DS-1205	PLX2853

CE is a Virtual Organization that Delivers

3 NDA/BLA within ~12 months

- Quizartinib US EU JP NDA achieved in less than a month
- Pexidartinib US NDA submission confirmed for 2H FY2018
- Potential to submit DS-8201 in 1H FY2019 continues to be present



Flow of data: delivering evidence of high potential and beating expectations

- DS-8201 HER2 Low Breast cancer
- DS-8201 Duration of Response in HER2 positive Breast cancer post trastuzumab, T-DM1 ± pertuzumab
- DS-8201 activity in NSCLC and CRC
- U3-1402 (HER3 ADC) activity
- DS-1062 (TROP2 ADC) in lung cancer

Manufacturing of development and commercial supplies

- Massive acceleration and scaling up is underway

ADC Manufacturing

Meeting Massive Increase in Demand

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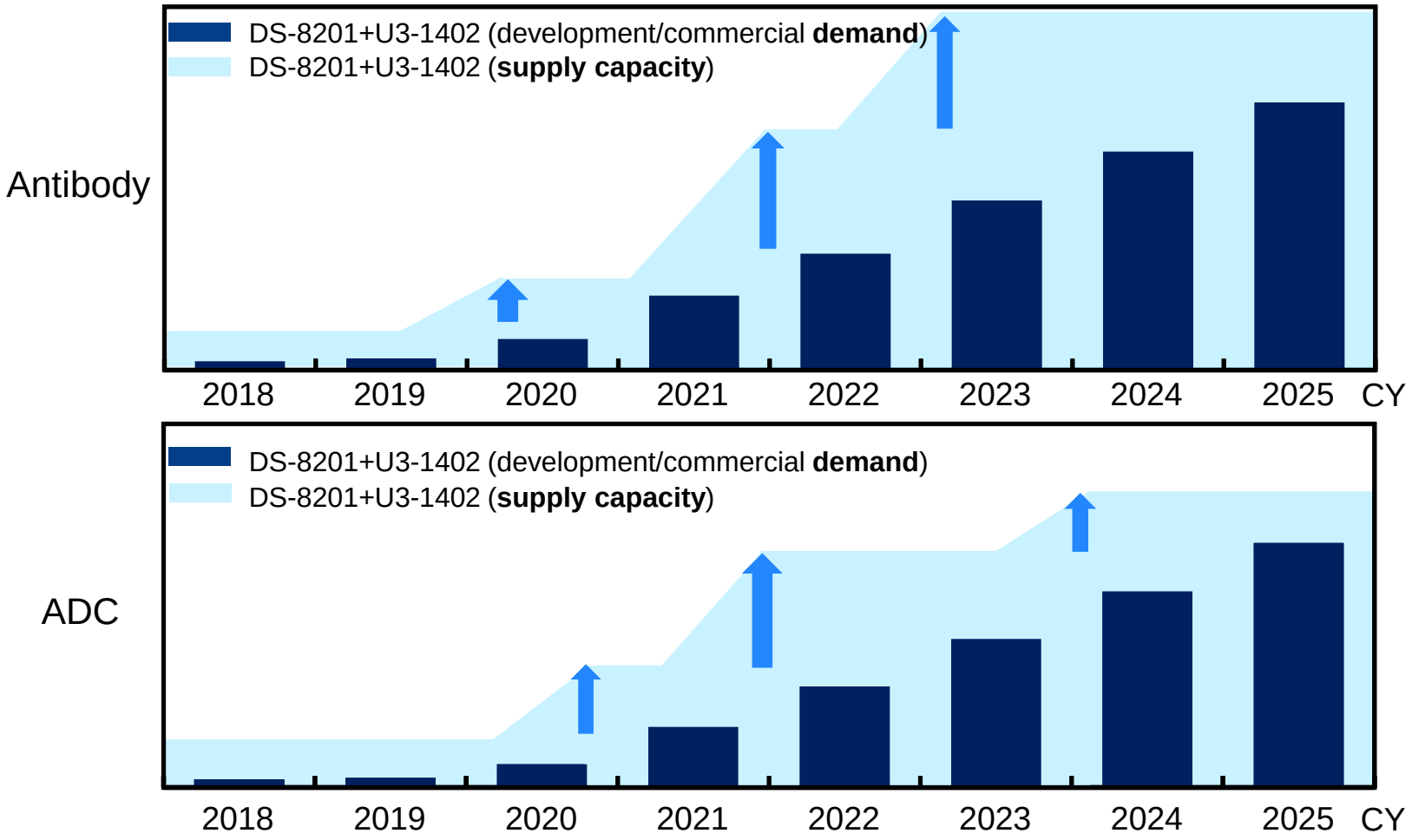
Ready for possible FY2019 submission of DS-8201 and for ADC programs scale-up



Each action includes in particular adding sites, tech transfer and network use of CMO, etc.

CE is Scaling Up the Enterprise

CE operates now at a resource level that was, in October 2016, predicted to be required for success

CE expects further increase due to better than anticipated portfolio scope

- ~ 70 to 80% of R&D, Pharmaceutical Technology and Global Medical Affairs resources are now CE focus
- Supported by the revision in 5-year Business Plan of R&D spend to 1,100 B JPY over 5 years
- Makes the case to consider R&D collaboration, especially for large scale operations, to maximize value

Daiichi Sankyo | A Traditional Japanese Company Transforming into a Global Power

Daiichi Sankyo

NOVARTIS
SANOFI
MERCK
Roche
Bristol-Myers Squibb
Lilly
Pfizer
AstraZeneca

New global operating model in place

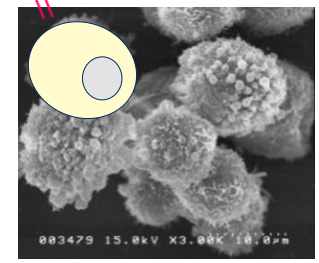
- **Japanese leadership** in critical domains, e.g.: Research, Protein engineering and production processes, Translational research, Development
- **West-based leadership** for translational and global development
  - Over the past 2 years, ~15 new senior leaders have joined DS from numerous top-tier global pharmaceutical companies
  - Collectively, these professionals represent over 250 years of oncology R&D experience, including more than 50 separate NDA / BLA submissions
- **Matrix-function organization led** by Global Teams, **from US or JP**
  - Innovative delivery (e.g. Sarah Cannon Research Institute collaboration)

CE Leadership in Science

- Healthy flow of **new drug candidates**, in ADC beyond DXd, in Hematology and in Breakthrough Science
- Establishing clinical analysis function in RD Novare to strengthen **translational science capability**
- Establishing a **state-of-the-art Bio-IT Omics platform**
- **CMC process and scale** mastery including business continuity planning
  - Enhanced ADC Technology

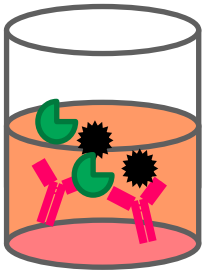
Enhanced ADC Technology

cell substrate



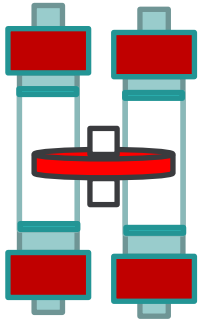
DS expression system
Cell cloning technology for high-producing cell isolation

cultivation



High performance medium
Scale-up technology

purification



High-performance flow-through purification

Original cell-vector system

Manufacturing efficiency
Productivity Improvement

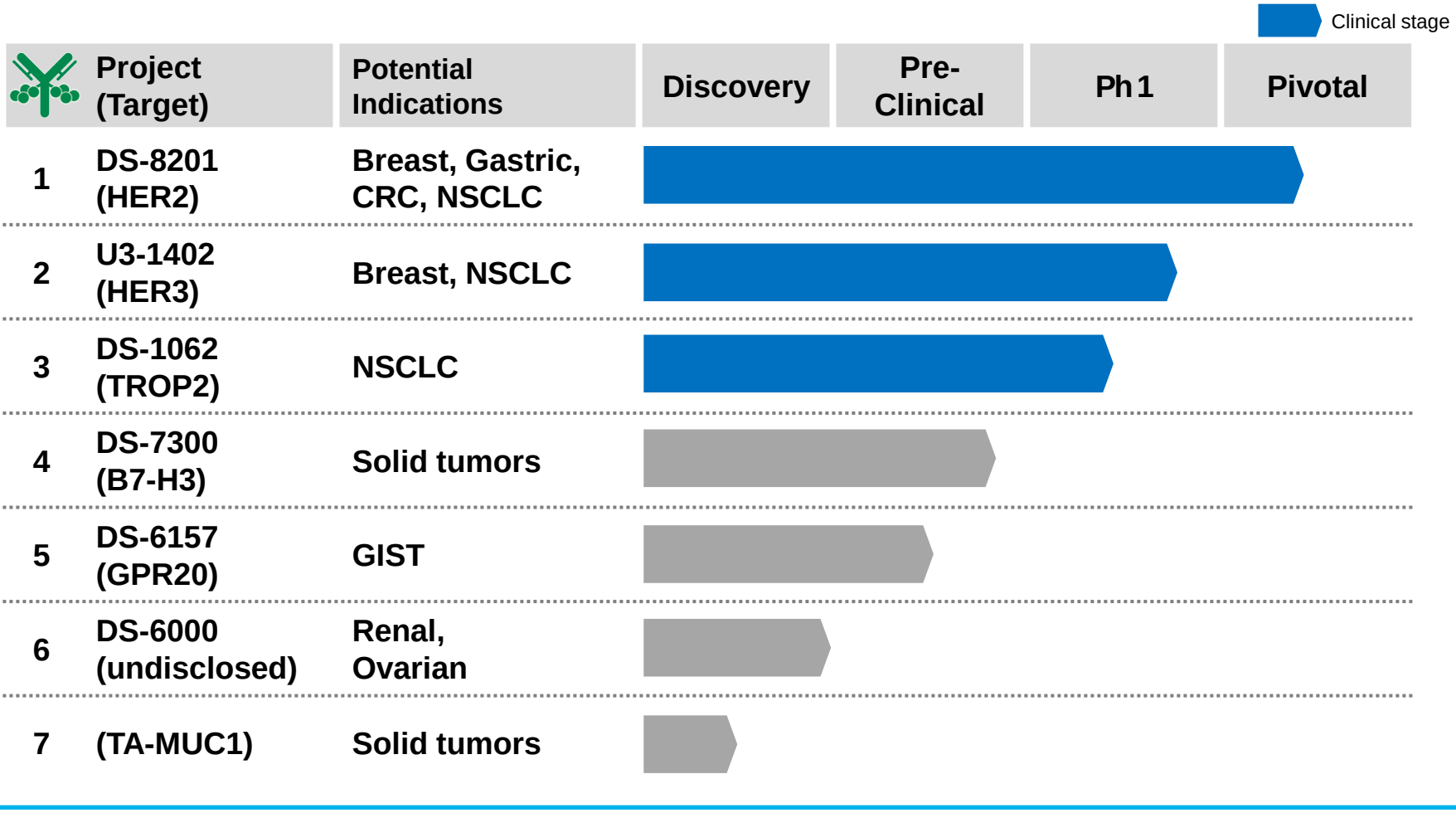
Labor-saving / efficient continuous process
Cost reduction of raw materials

Cost and time efficient, security of process by utilizing antibody manufacturing platform developed on DS proprietary technologies

Daiichi Sankyo ADC Franchise

As of Dec 2018

ADC Franchise



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

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ADC | DS-8201 (fam-trastuzumab deruxtecan) **Top News**

DS-8201 Flagship Asset

Breakthrough Therapy Designation (BTD)

厚生労働省 Ministry of Health, Labour and Welfare

Sakigake Designation

DESTINY

Ongoing pivotal development

- DESTINY-Breast01
- DESTINY-Gastric01
- Breast HER2 positive post T-DM1
- Breast HER2 positive vs T-DM1
- Breast HER2 Low

Planned further development

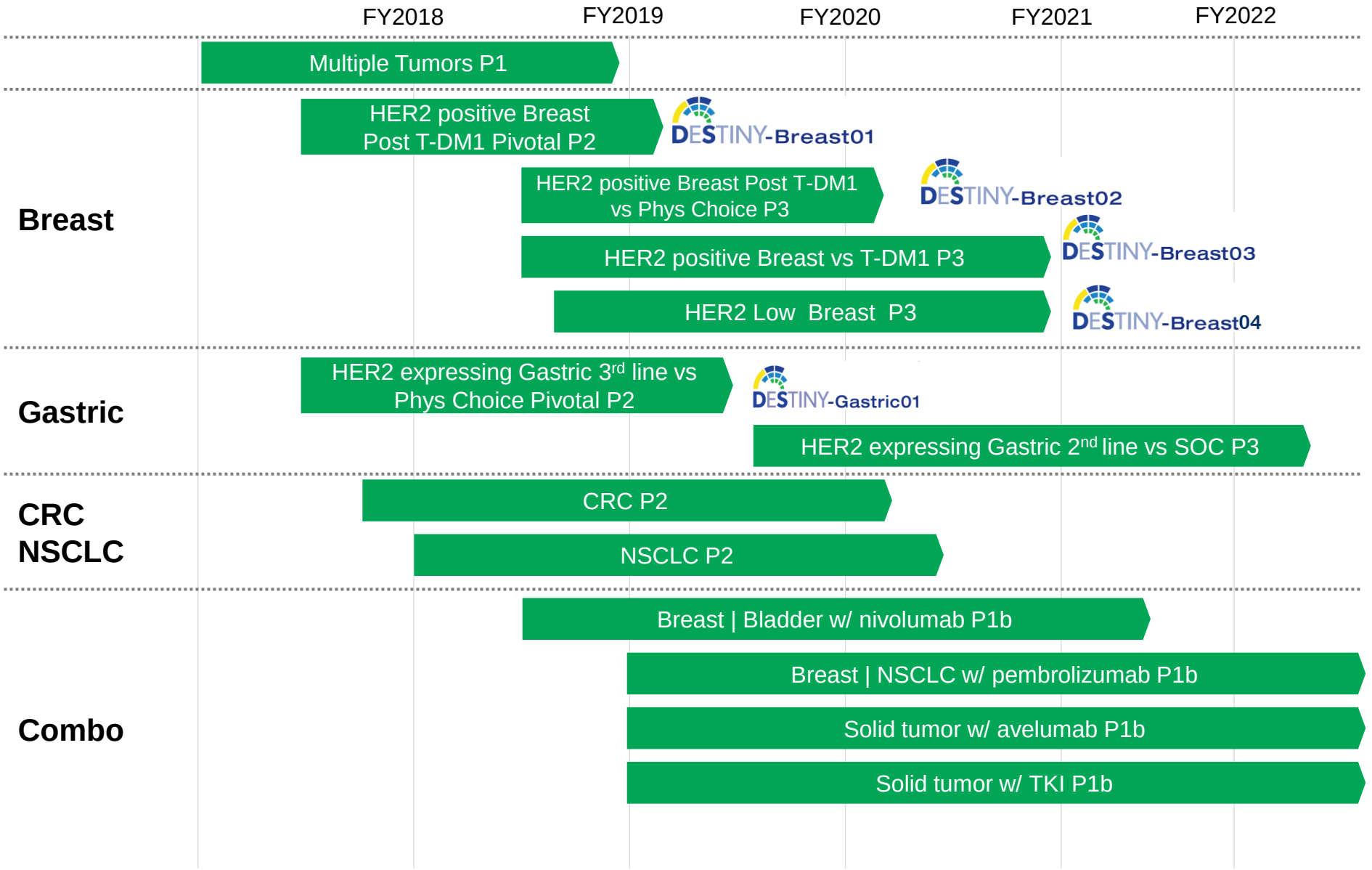
- Earlier lines, Lung, colorectal, combinations (TKI, CDK4/6i, hormonal therapy, PARPi, IO)

Focus

- **HER2 positive Breast Cancer: Duration of Response in Ph 1 Study J101**
- **HER2 Low Breast Cancer**
- **Tracking to plan** for 2020 submissions - **Contemplating BLA in 1H FY2019**
  Will not be confirmed before end 4Q FY2018
- **Expand program**
- **Continue drastic scaling up of production**

DS-8201 | Clinical Program

As of Dec 2018



DS-8201 | Clinical Program

As of Dec 2018

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Current/future trials for further data-gated development

New plans

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

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 1	Grade 2	Grade 3	Grade 4	Grade 5	Total
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

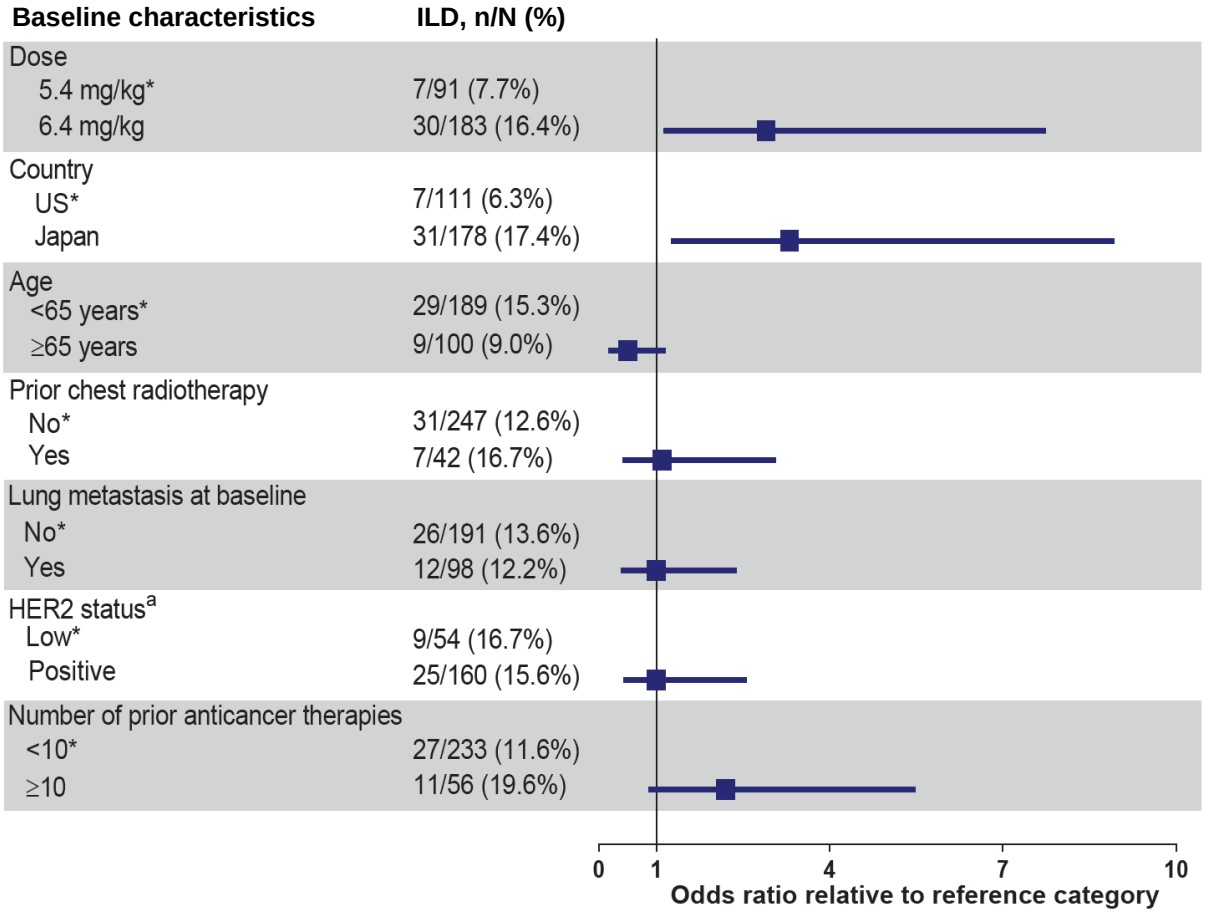
- Median duration of treatment 108 days
- 29.5% subjects on treatment for ≥180 days
  - Median time to onset of ILD 149 days

- **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

DS-8201 | HER2 Positive Breast Cancer: *New Data*

Duration of Response > 20 months

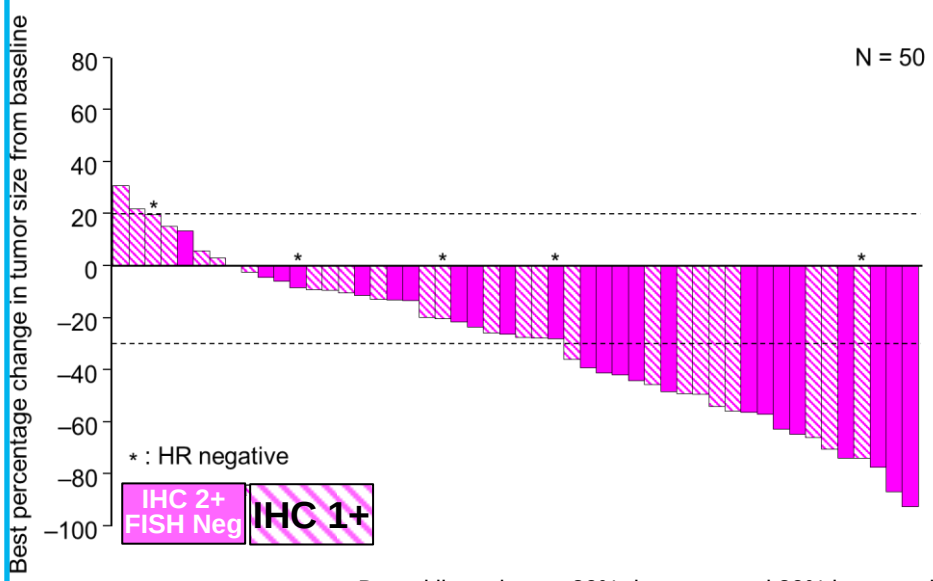
Efficacy Outcomes in Subjects with HER2 Positive Breast Cancer in the Ongoing Ph 1 Trial (Aug 10, 2018 data cutoff)[1]

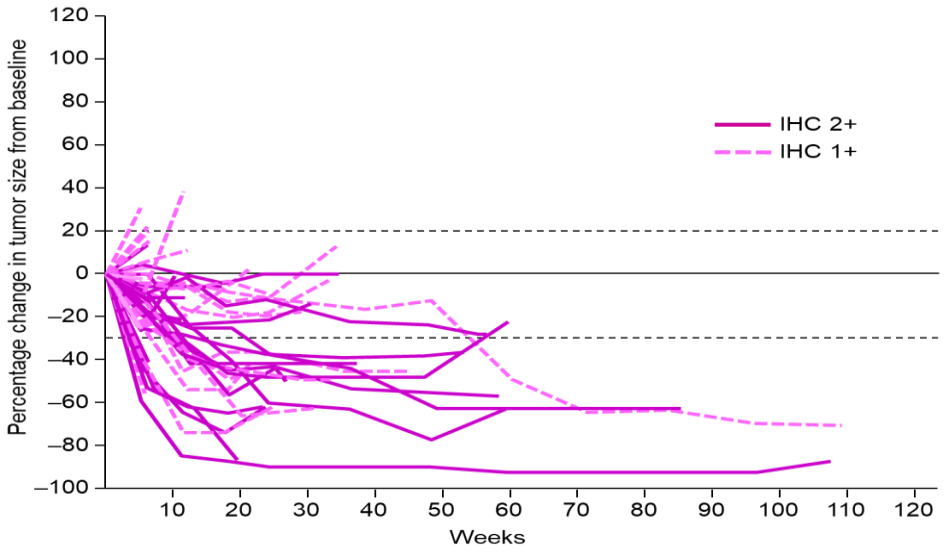
	HER2 Positive (IHC 3+ or IHC 2+/ISH+) Breast Cancer
Confirmed Overall Response Rate (66/111)[a]	59.5% (95% CI 49.7, 68.7)
Median duration of response	**20.7 months** (range 0.0+, 21.8+)

[a]Subjects who received 5.4 or 6.4 mg/kg with ≥2 postbaseline scans, or who had progressive disease or discontinued treatment for any reason before second postbaseline scan.
DCR, disease control rate; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; ORR, objective response rate.

[1] Daiichi Sankyo Data on File

DS-8201 | HER2 Low Breast Cancer





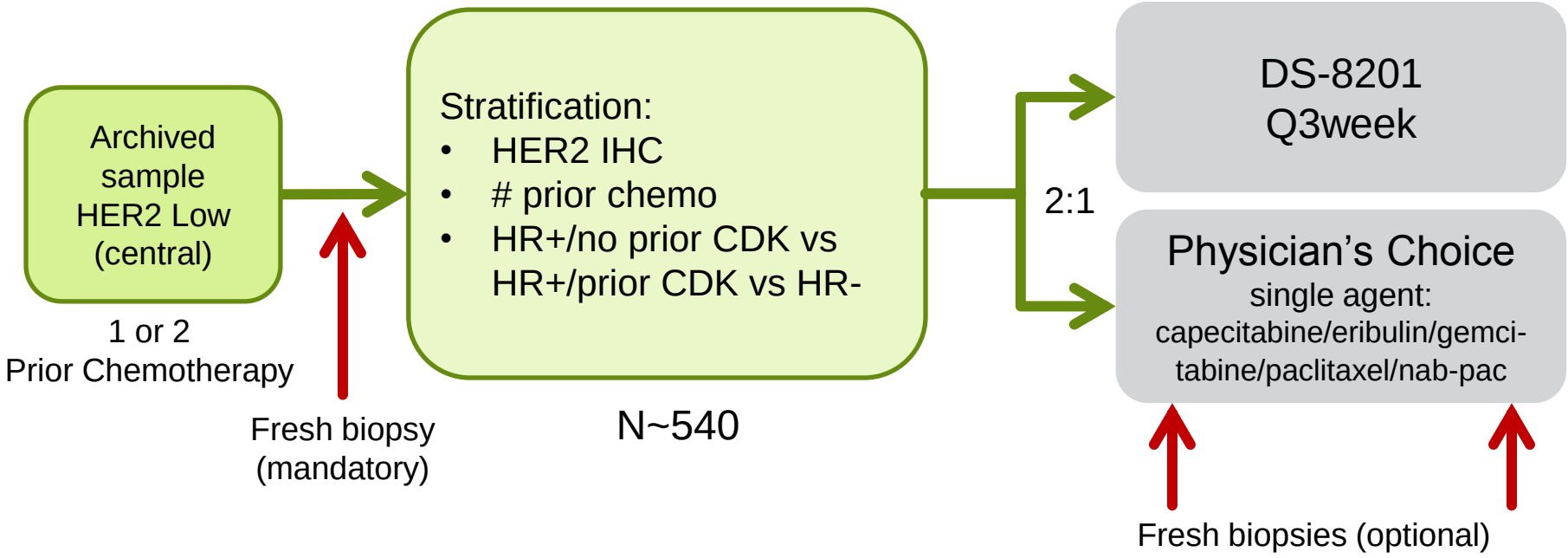
Dotted lines denote 30% decrease and 20% increase in tumor size cutoffs for partial response and progressive disease, respectively.
HR, hormone receptor; IHC, immunohistochemistry.

	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)

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

DS-8201 | HER2 Low Breast Cancer P3 Study Design

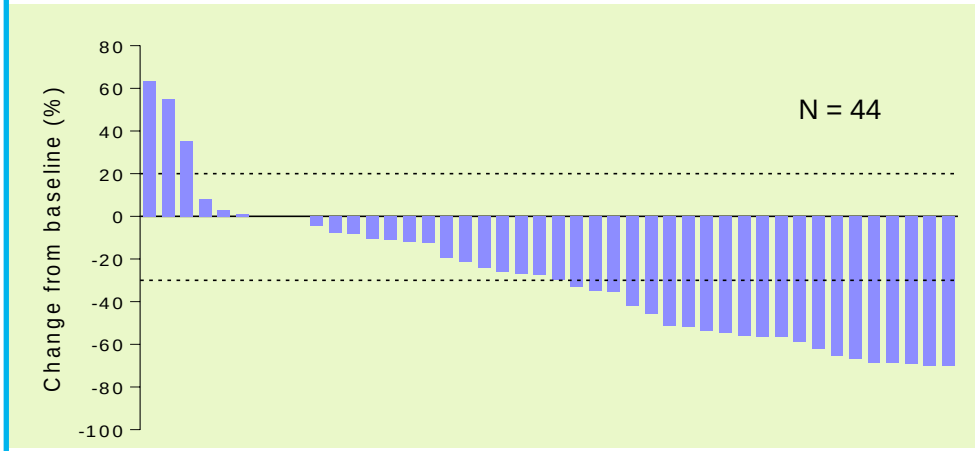
CT.gov: NCT03734029/JapicCTI-184223

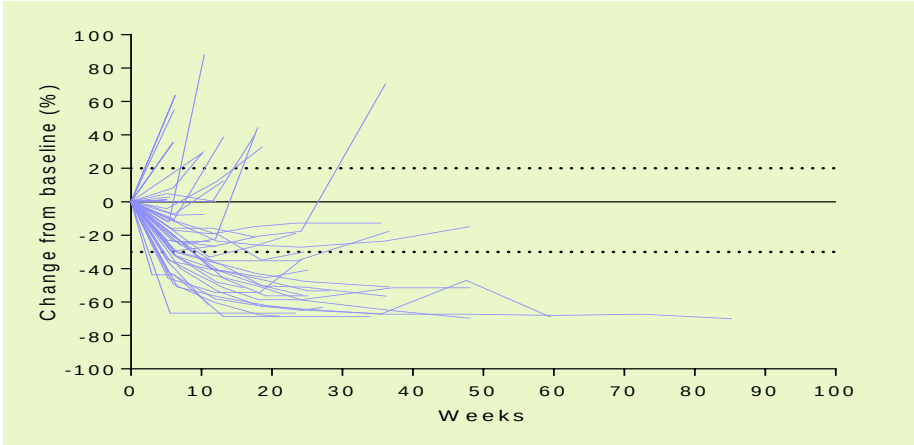


PFS in HR+ BC → PFS in all HER2 Low BC → OS in HR+ BC Including analysis long-term FU

Primary Endpoint

DS-8201 | HER2 Positive Gastric Cancer





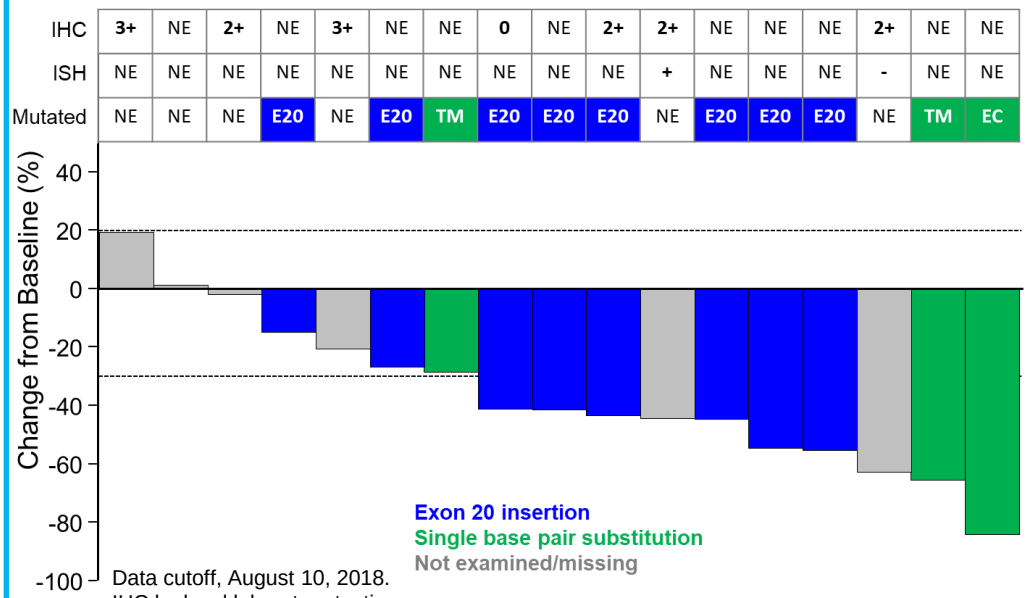
Includes subjects who had ≥1 postbaseline scan. Dotted lines denote 20% increase and 30% reduction in tumor size, respectively.
*Confirmed response includes subjects who had ≥2 postbaseline scans, progressive disease, or discontinued treatment for any reason prior to second postbaseline scan.
Data cutoff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

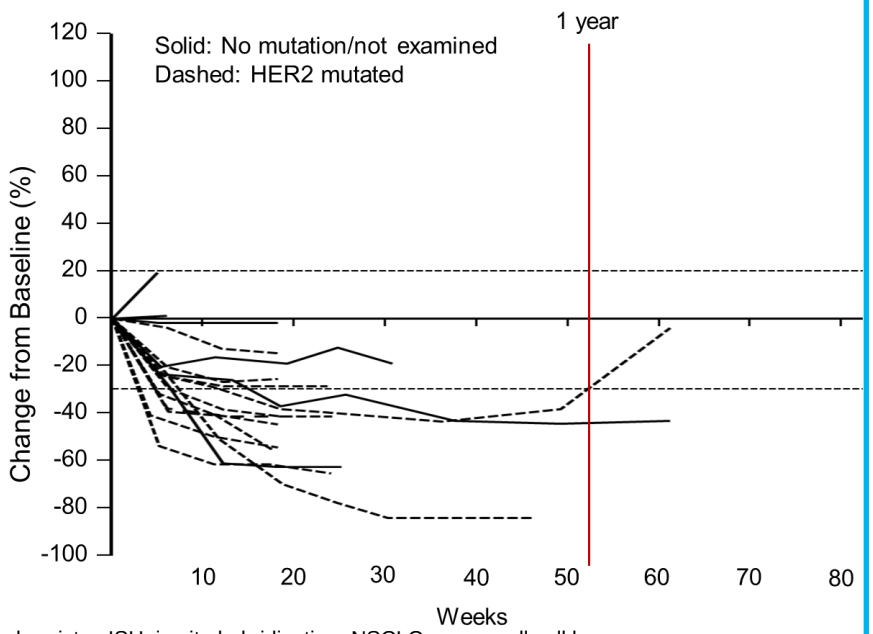
	Confirmed ORR (n/N) (95% CI)	DCR % (n/N)	DOR, Median (95% CI), months	PFS	
				Median, (95% CI)	Min, max
HER2 Positive Gastric Cancer N = 44	43.2% (19/44) (28.3, 59.0)	79.5% (35/44)	7.0 (NA)	5.6 months (3.0, 8.3)	1.2, 19.6+

ASCO JUN 2018

Iwata et al. ASCO 2018. Abstract # 2501

DS-8201 | NSCLC HER2 Mutated or Expressing





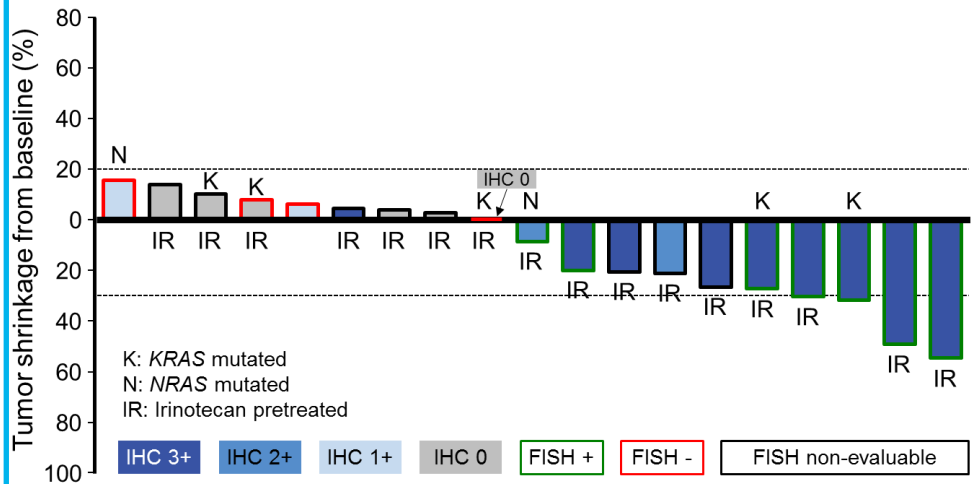
Data cutoff, August 10, 2018.
IHC by local laboratory testing.
E20, exon 20 insertion; EC, single base pair substitution at extracellular domain; IHC, immunohistochemistry; ISH, in situ hybridization; NSCLC, non-small cell lung cancer; NE, not examined or missing; TM, single base pair substitution in transmembrane domain.

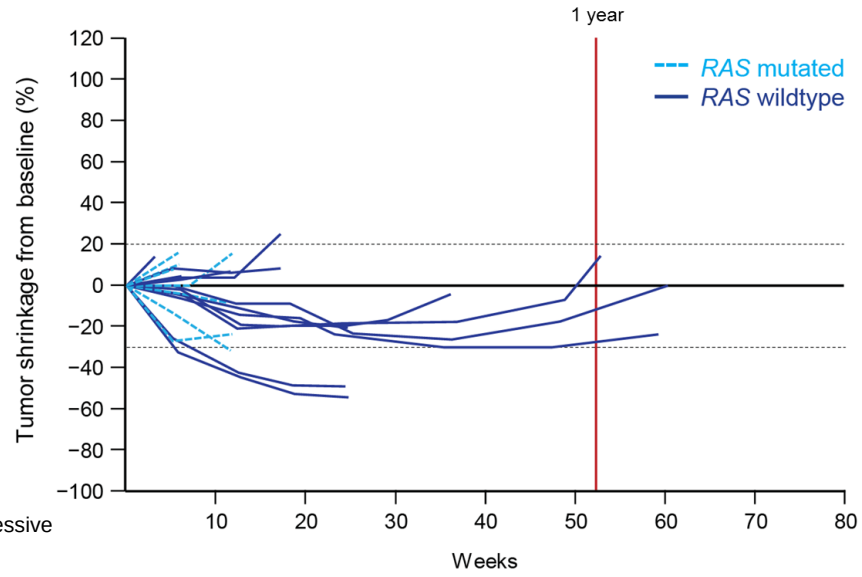
	Comfirmed ORR, % (n/N)	Comfirmed DCR, % (n/N)	DOR, median (range), months	PFS, median (range), months
HER2-expressing or HER2-mutated NSCLC N = 18	58.8% (10/17)	88.2% (15/17)	9.9 (0.0+, 11.5)	14.1 (0.9, 14.1)
HER2-mutated NSCLC N = 11	**72.7% (8/11)**	100% (11/11)	**11.5 (0.03+, 11.5)**	14.1 (4.0+, 14.1)

WCLC SEP 2018 Tsurutani et al, WCLC, 2018; Abstract #13325

DS-8201 | CRC by HER2 Status IHC/FISH

ORR 27.3% (3/11) in HER2 (IHC 2+, 3+)





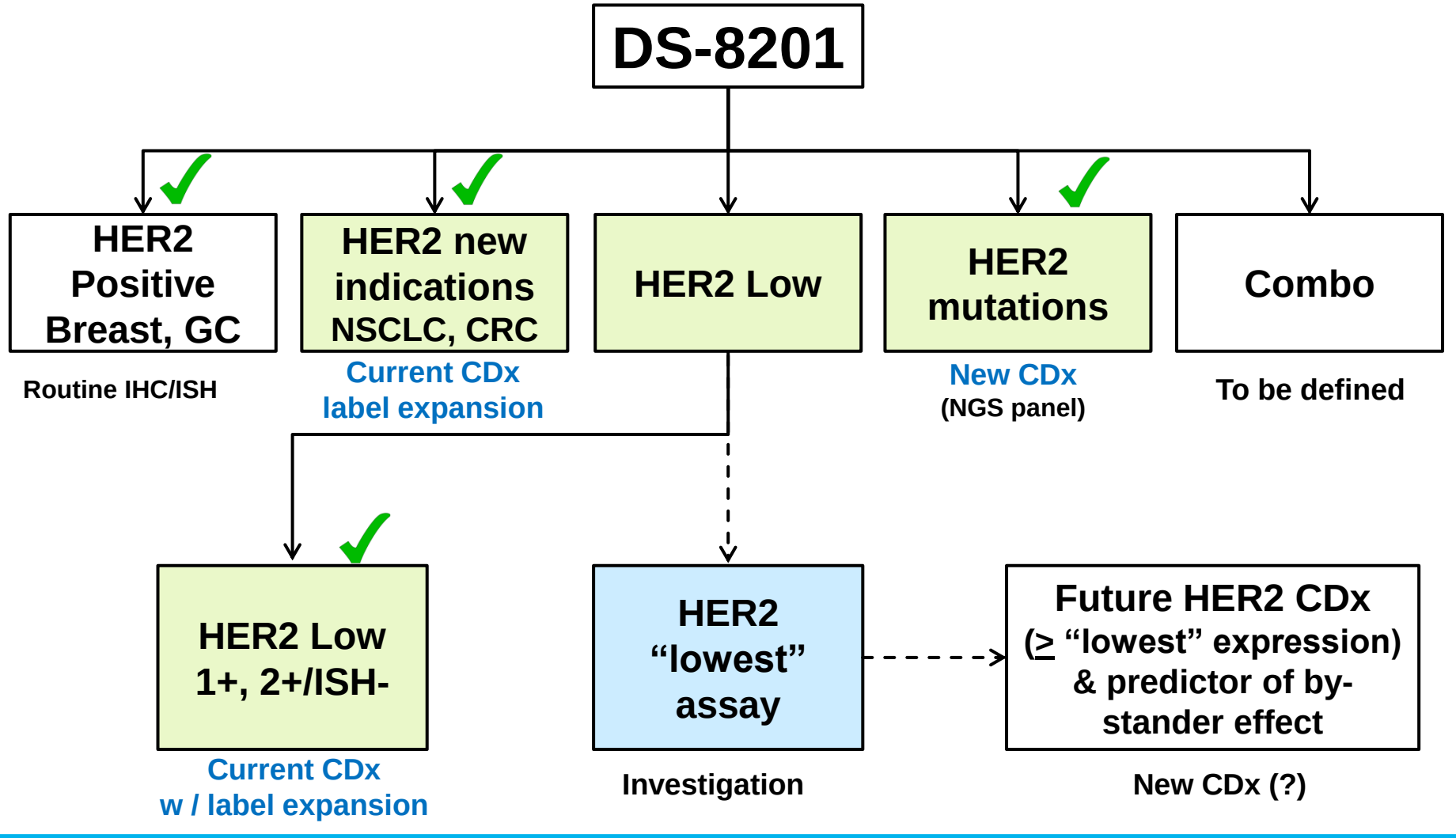
HER2 status based on centrally assessed retrospective analysis of archival samples.
Dotted lines denote 30% decrease and 20% increase in tumor size cutoffs for partial response and progressive disease, respectively.
FISH, fluorescence in situ hybridization; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; IR, irinotecan pretreated; K, *KRAS* mutation; N, *NRAS* mutation.

	Confirmed ORR, % (n/N)	Confirmed DCR, % (n/N)	DOR, median (range), months	PFS, median (range), months	OS, median (range), months
CRC N=19*	15.8% (3/19)	84.2% (16/19)	NR (0.0+, 5.5+)	3.9 (2.1,8.3)	NR (1.0+, 17.9+)

* Evaluable patients (one IHC 0 patient was not evaluable out of 20 enrolled)

Yoshino et al, ESMO 2018; Poster #563P

DS-8201 | Patient Selection & CDx Strategy



Biology of HER2 receptor varies: IHC is not fully portable
Developing new CDx Assays lead to select the right patients for DS-8201

CDx : Companion Diagnostic, NGS: next generation sequencing

DS-8201 is Leading the Second Generation HER2 ADC Race with the Most Ongoing Trials

HER2 ADCs

Pivotal stage

Project (Payload)	Potential Indication	Pre-Clinical	Ph1	Pivotal
DS-8201 Topoisomerase I inhibitor	**Breast, Gastric, CRC, NSCLC**			P3, P2, P1
SYD985 DNA alkylator (Duocarmycin)	**Breast, Gastric**			P3, P1
BAT8001 Maytansine derivative	**Breast, Gastric**			P3
RC-48 (MMAE) Tubulin Inhibitor	**Breast, Gastric, Bladder**			P2
XMT-1522 Tubulin inhibitor	**Breast, Gastric, NSCLC**			P1
ARX-788 Tubulin inhibitor	**Breast, Gastric**			P1
PF-06804103 (MMAE) Tubulin inhibitor	**Breast, NSCLC, Gastric, GEJ**			P1
DHES-0815A PBD-MA	**Breast**			P1
ALT-P7 Tubulin inhibitor	**Breast**			P1
A166 Unknown	**Solid Tumor**			P1/2

CRC: colorectal cancer, NSCLC: non-small cell lung cancer, GEJ: gastroesophageal junction

Sources: clinicaltrials.gov, BioThera Press release

DS-8201 | What Have We Learned?

- FY2019 first BLA remains an upside possibility
- Vast majority of breast cancers are in scope
- Earlier lines and critical combos (CDK4/6i, hormonal therapy, pertuzumab) are key to unlock the full potential of the drug in BC
- ILD at 5.4 mg/kg in Breast cancer appears as a well characterized risk
- Duration of Response in HER2 positive Breast cancer Ph 1 is > 20 months
- Biology of HER2 receptor varies: IHC is not fully portable

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3 U3-1402

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- Fast to market strategy and program scope

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- Others

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U3-1402 (HER3 ADC)

First Time in Human Safety Profile to Date (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

U3-1402 | Efficacy Data in Ph 1, Breast Cancer Study

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Efficacy Assessed by Investigators

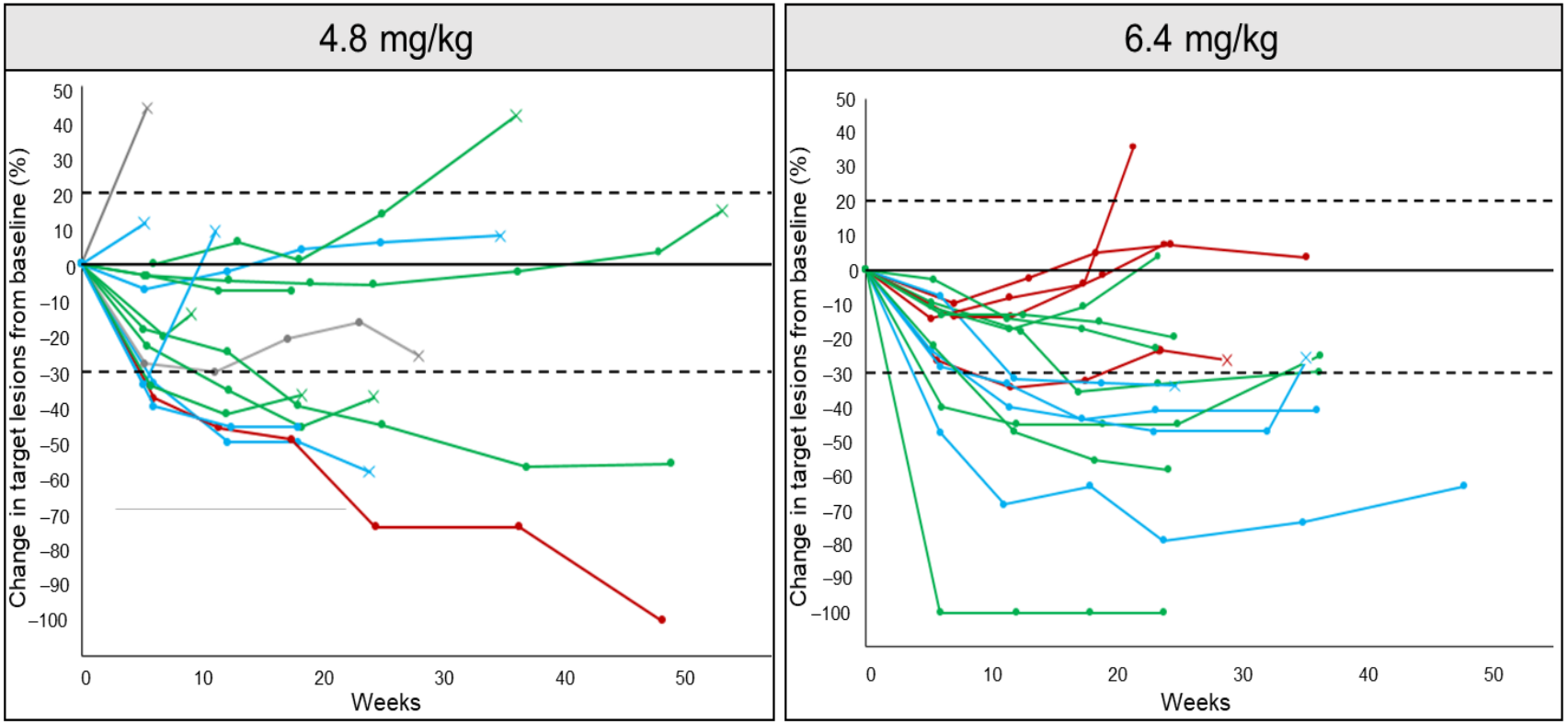
Efficacy Measures	Dose Escalation and Dose Finding		
	4.8 mg/kg (N = 15)	6.4 mg/kg (N = 15)	All dose levels (N = 42)
Overall Response Rate n/N (%)	6/15 (**40.0%**)	9/15 (**60.0%**)	18/42 (**42.9%**)
Duration of Response median (range), months	Not Reached (2.8, 9.8+)	Not Reached (2.9+, 9.8+)	Not Reached (2.8, 13.8+)
Time to Response median (95% CI), months	2.1 (1.3, 4.1)	2.7 (1.4, 2.8)	2.6 (1.4, 2.8)
Disease Control Rate n/N (%)	13/15 (**86.7%**)	15/15 (**100.0%**)	38/42 (**90.5%**)
PFS median (range), months	8.0 (1.2, 12.3+)	Not Reached (5.0, 11.1+)	8.3 (1.2, 16.8+)

Efficacy evaluable set for confirmed response based on RECIST version 1.1 includes subjects who had ≥2 postbaseline scans, progressive disease at the first scan, or discontinued treatment for any reason.
Data cutoff: November 6, 2018

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

U3-1402 | Efficacy by Dose Level in Ph 1 BC Study

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.

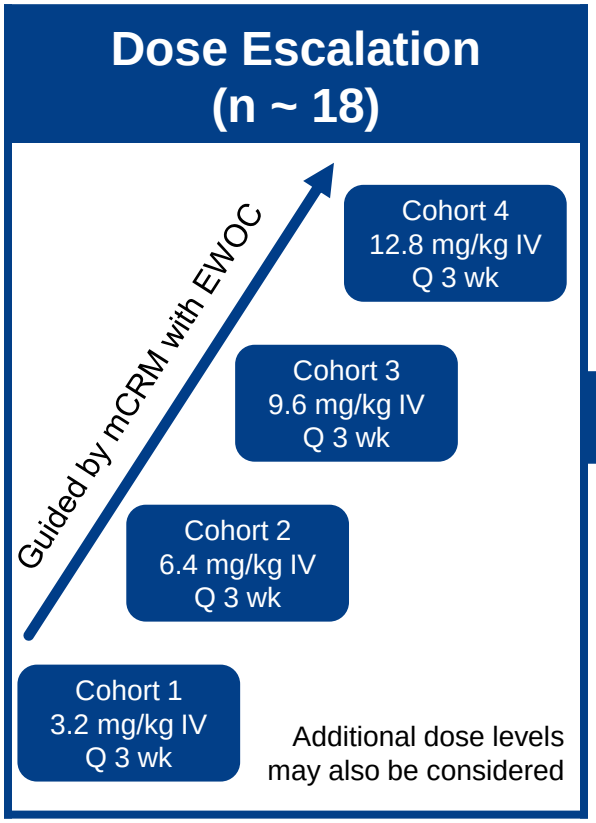
Masuda et al, SABCS, 2018; Poster # PD1-03 , Abstract #1024

U3-1402 | NSCLC Ph 1 Study

Ph 1, Multicenter, Open-label, Dose Escalation and Dose Expansion Study in NSCLC

- Metastatic or unresectable **EGFR-mutant NSCLC** with
  - T790M mutation-negative tumor after progression with erlotinib, gefitinib, or afatinib

  or
  - Progression on osimertinib
- Clinically inactive CNS metastases allowed
- ECOG PS 0 or 1

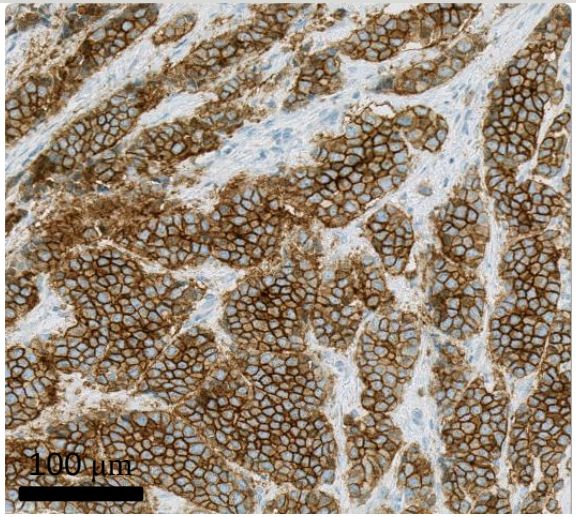


No selection based on HER3 expression. HER3 (IHC) is examined retrospectively.

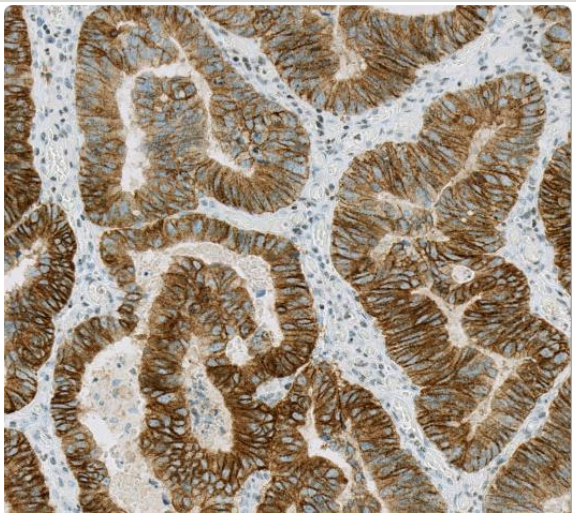
Dose escalation data to be presented at ASCO 2019

ECOG PS: Eastern Cooperative Oncology Group Performance Status, mCRM = modified Continual Reassessment Method; EWOC: Escalation with Overdose Control, Q3 wk: once in 3 weeks

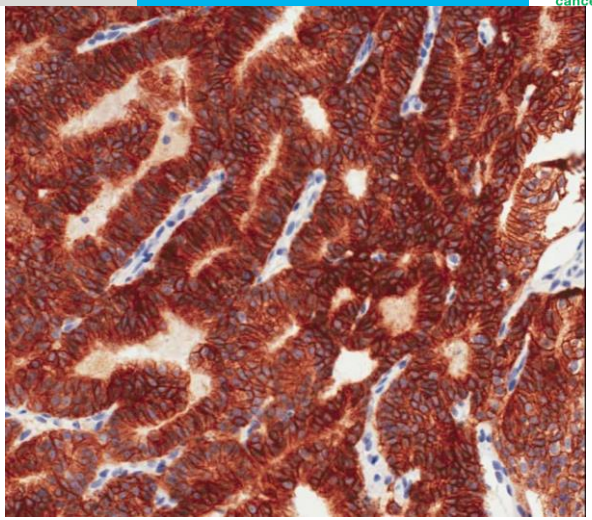
U3-1402 | HER3 Expression in Cancer (IHC)



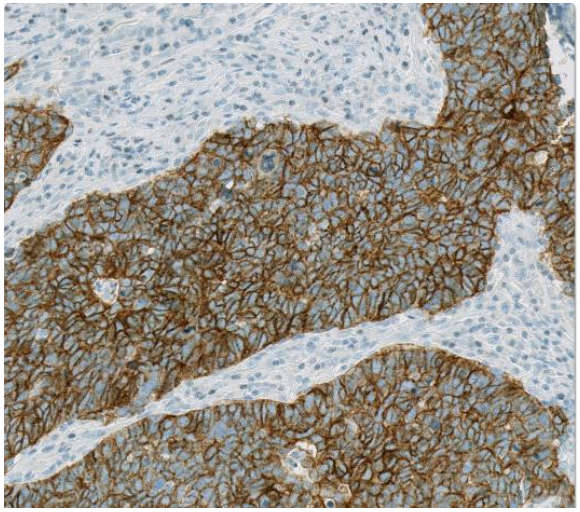
Breast cancer



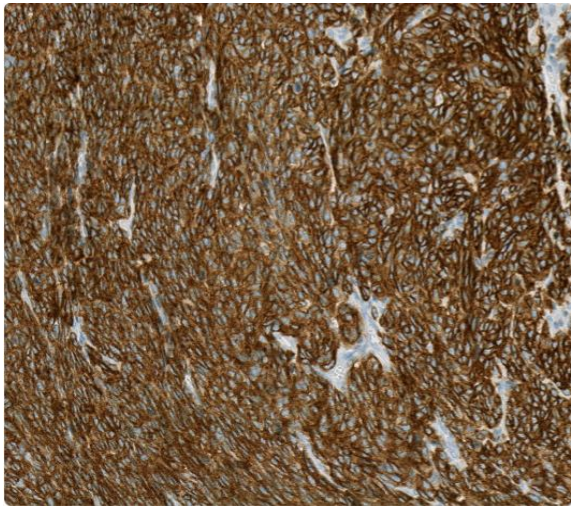
Colorectal cancer



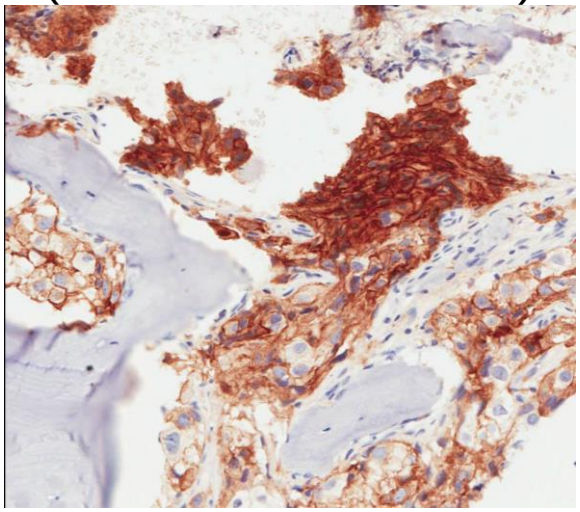
Prostate cancer
(soft tissue metastasis)



NSCLC



Malignant melanoma



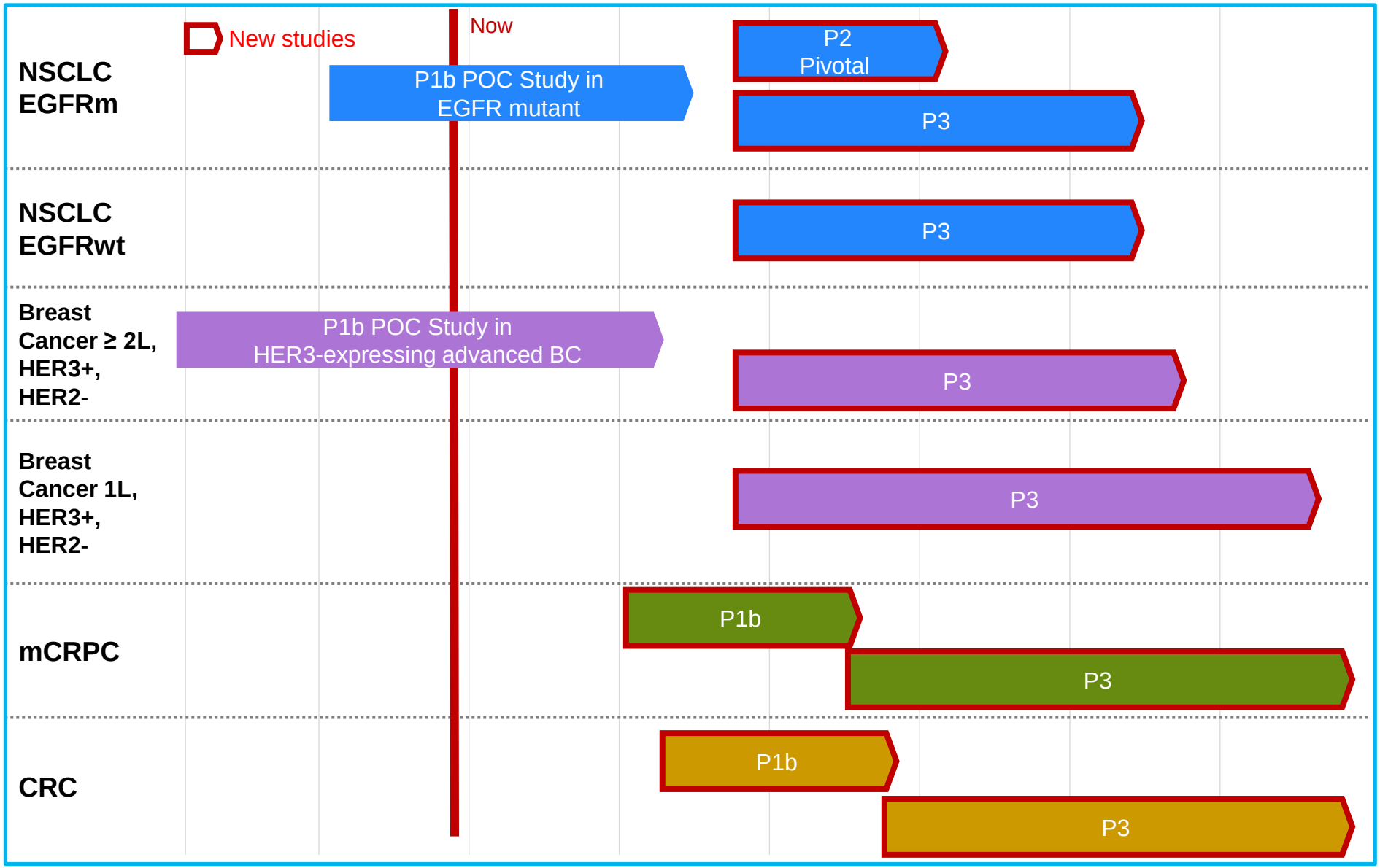
Prostate cancer
(Bone marrow metastasis)

Breast cancer, NSCLC and Colorectal cancer data is in-house IHC

Prostate cancer data is courtesy Prof Johann de Bono Royal Marsden London, UK

U3-1402 | Directional Development Plan

As of Dec 2018



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

HER2 and HER3 ADCs' Overlap

New and Enhanced Biomarkers will Drive Precision Treatment of Metastatic Breast Cancer

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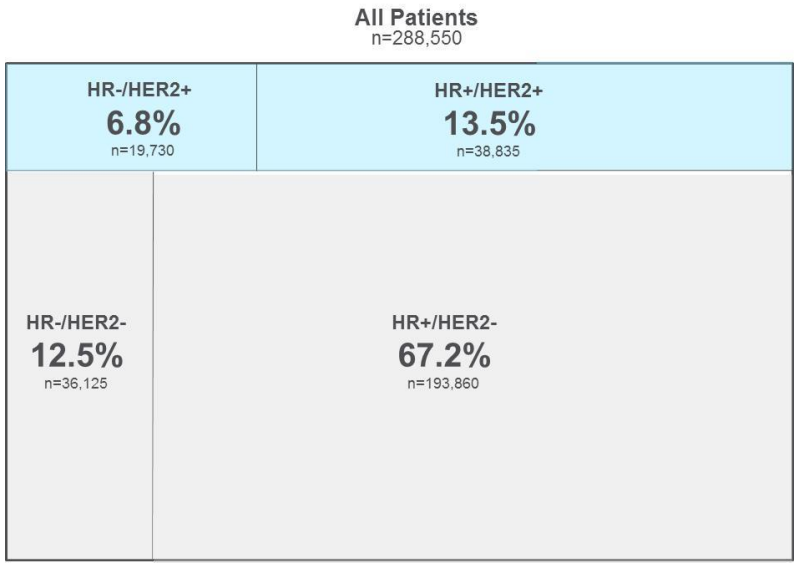
Historical State: HR and HER2 as oncogenic drivers

Decision matrix driven by HR status and conventional HER2 (tissue derived IHC/ISH)



Emerging Addition of New Standard of Practice

Enhanced understanding of disease biology leading to more advanced patient segmentation to predict the role of ADCs & other agents

- Liquid Biopsy
- Advanced HER2 measurement (eg mRNA / predicting DXd by-stander effect, etc.)
- PI3K mutations
- BRCA mutations
- PDL1 Status
- Role of HER3
- Role of TROP2

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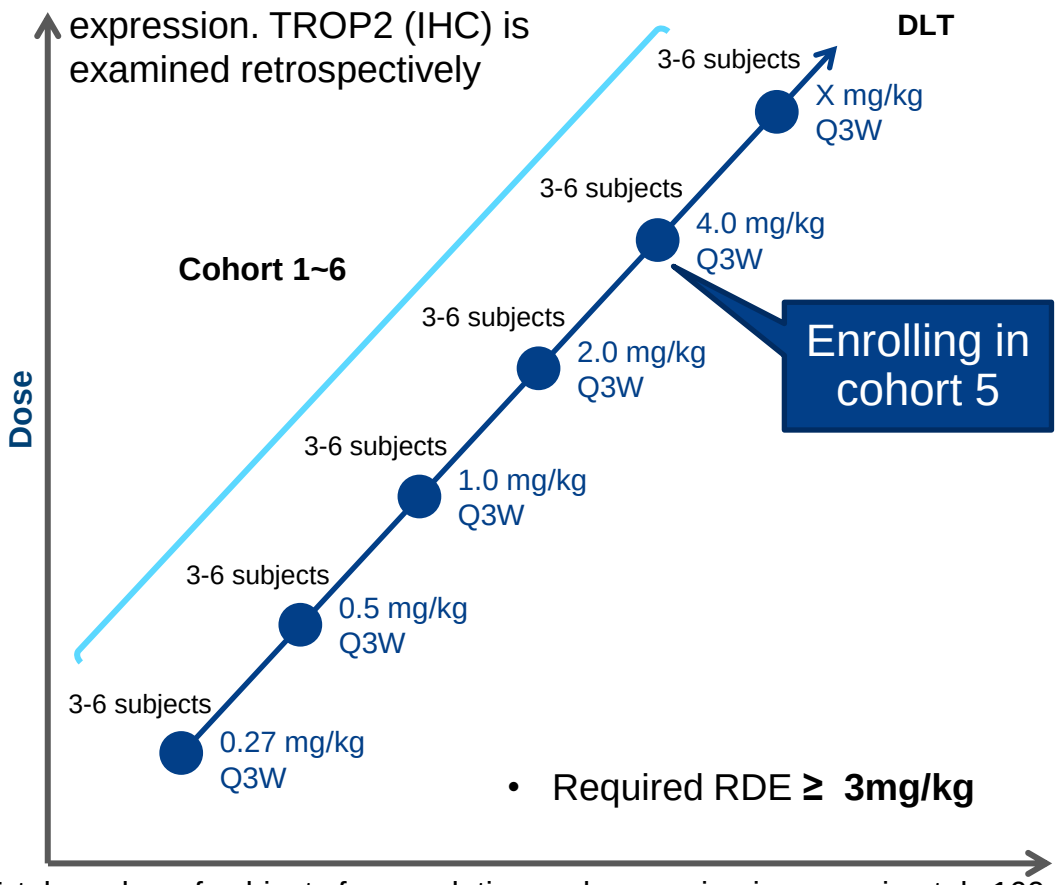
DS-1062 TROP2 ADC | Ph 1 Study : Lean Plan to POC

NSCLC ≥ 3rd line

Dose Escalation

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



- Required RDE ≥ **3mg/kg**

Total number of subjects for escalation and expansion is approximately 160 maximum

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

Dose escalation data to be presented at ASCO 2019

POC: Proof of Concept, RDE: Recommended Dose for Expansion, Q3W: once in 3 weeks

B7-H3 | An Attractive Target for ADC Therapy

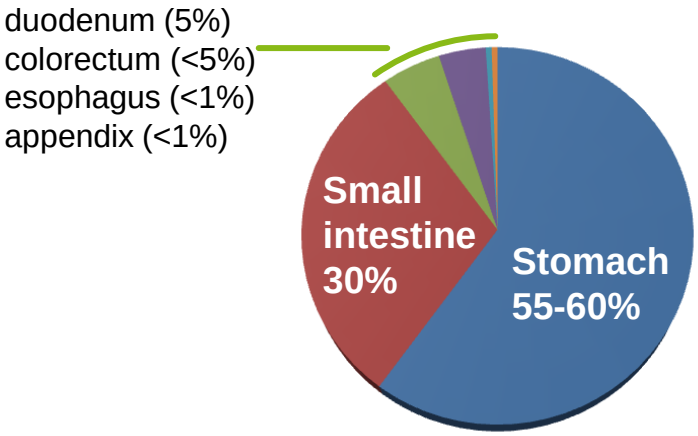
FTIH study for DS-7300 planned through Sarah Cannon Research Institute with Japan collaboration – FY2019

Condition		
Target	High expression	B7-H3 is overexpressed frequently in various tumors (more than HER2 in breast cancer)
	Tumor selectivity	B7-H3 is overexpressed in tumors with low expression in normal tissues
mAb	Internalization	Anti-B7-H3 ADC antibody internalization rate 19-27%/3hr, comparable to trastuzumab

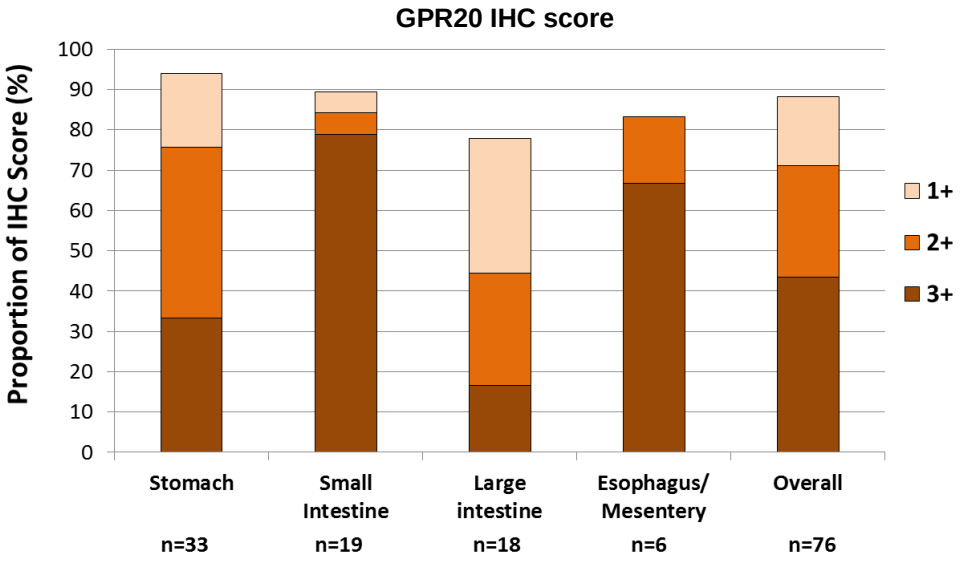
FTIH: First Time in Human

DS-6157 | First-in Class GPR20 ADC

- **Concept:** treatment of GPR20 positive GIST, regardless of TKI-resistance mutation
- **Fast-to-market:** Imatinib-resistant GIST (2nd line, salvage line)



IHC in GIST (US Biomax GIST801 tissue microarray)



- 88% of primary GIST is GPR20 positive (score >1+)
- GPR20 is highly expressed in more aggressive small intestinal GIST
- GPR20 expression was also observed in PDGFRA D842V GIST and wild type GIST

GPR20: G protein-coupled receptor 20; PDGFA: Platelet-derived growth factor receptor alpha; GIST: Gastrointestinal stromal tumor; TKI: Tyrosine kinase inhibitor

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AML/Hematology | Steady Progress

As of Dec 2018

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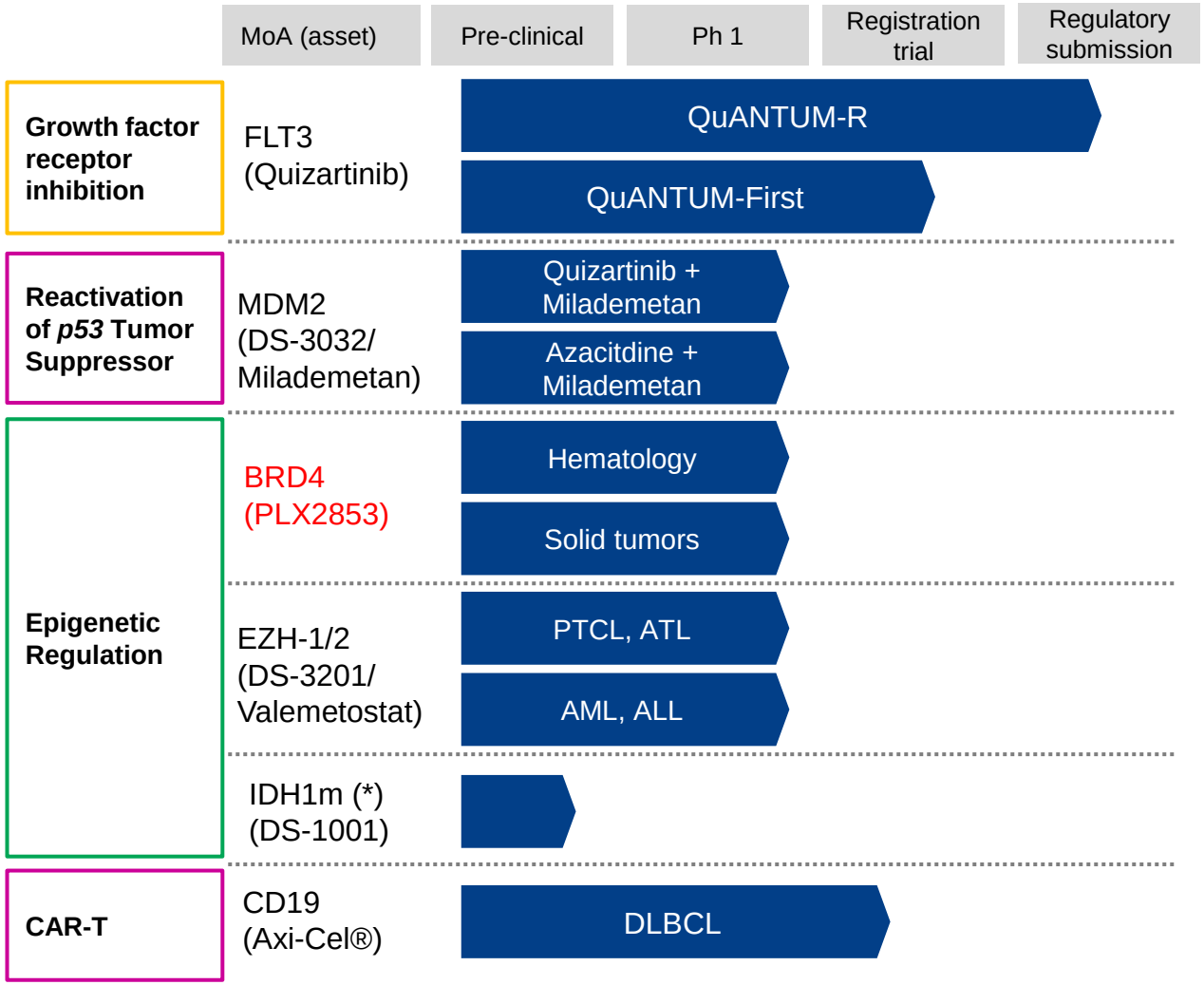
AML/Hematology Franchise



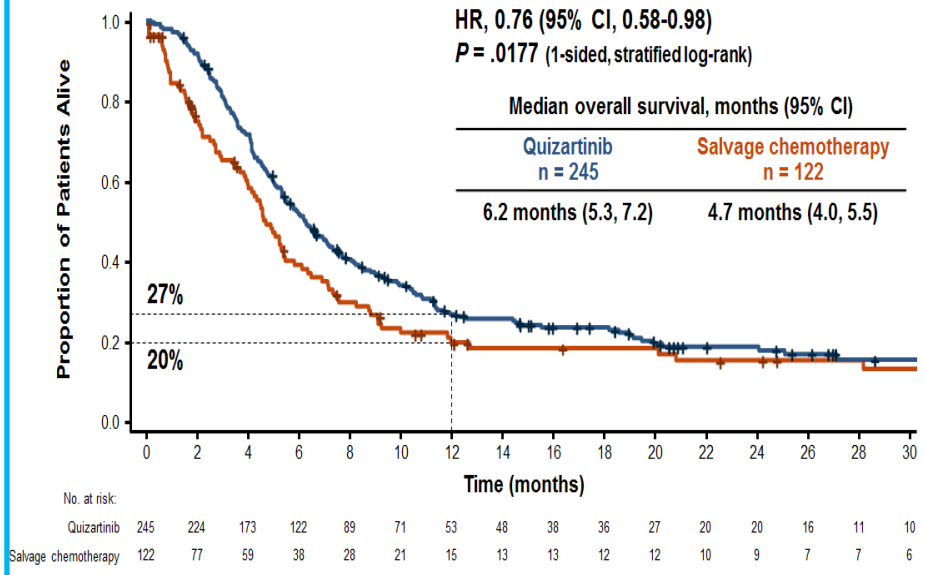
- Quicker development of combinations
- Address emergence of resistance

(*): Ph1 in glioma. Preclinical development in AML.
ALL: acute lymphoblastic leukemia, AML: acute myeloid leukemia, ATL/L: adult T-cell leukemia/lymphoma, DLBCL: diffuse large B-cell lymphoma, PTCL: peripheral T-cell lymphoma

Red: New

Quizartinib | Refractory / Relapsed FLT3-ITD AML

QuANTUM-R STUDY



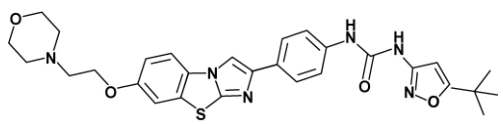
- Median follow-up: 23.5 months

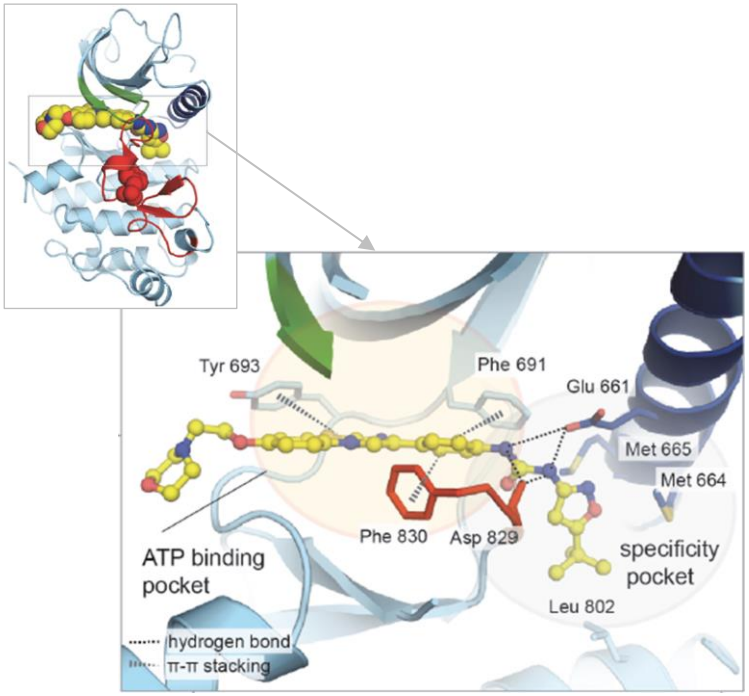
- Positive Ph 3 with 24% reduction in the risk of death; early separation of survival curves
- Global simultaneous submission in US, EU and JP (achieved in less than a month)
  - US: BTD and Orphan Drug designations; PDUFA date May 25, 2019
  - EU: Accelerated assessment and Orphan Drug designations
  - JP: Orphan Drug designation
- CDx submission on-track
- Preparing for global launch 1H FY2019

Quizartinib

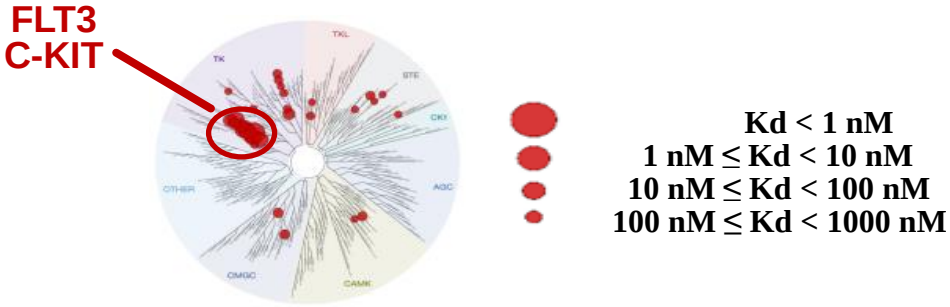
Highly Potent and Selective Type II Kinase Inhibitor

Type II kinase inhibitor: binds outside the ATP binding pocket

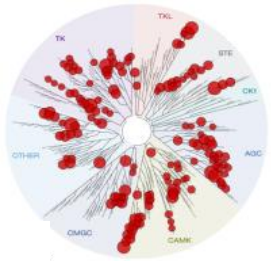




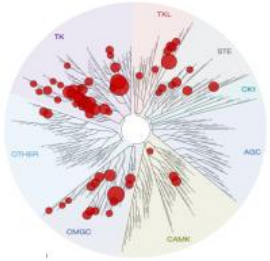
Quizartinib[1]



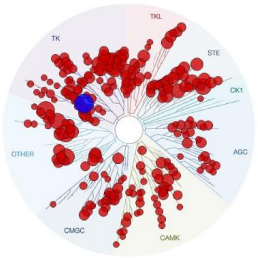
Midostaurin[1]



Sorafenib[1]



Gilteritinib[2]



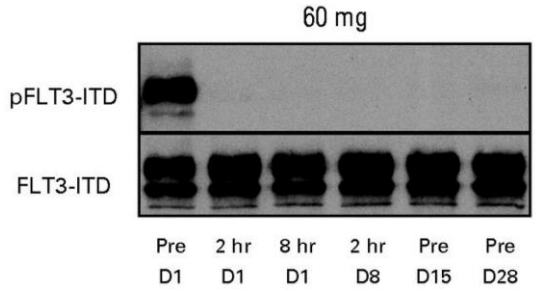
1 Davis MI, et al. 2011. *Nat Biotechnol*. 29:1046-1051, 2 Cortes JE, et al, ASH 2018; Oral, Abstract #563

Quizartinib | Clarification of the Mechanism of Action

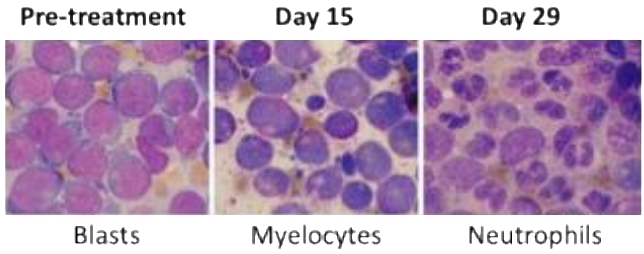
- Quizartinib is a potent and selective type II FLT3 inhibitor (and partial c-kit inhibitor)
- "CR with incomplete count recovery" is fast and most common response

Quizartinib

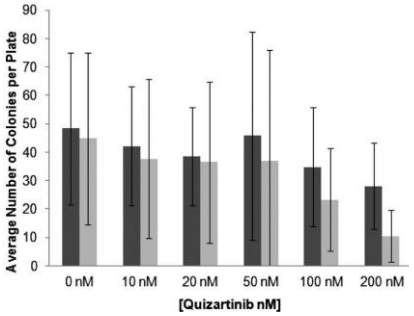
Sustained Inhibition of FLT3-ITD Autophosphorylation[1,2]

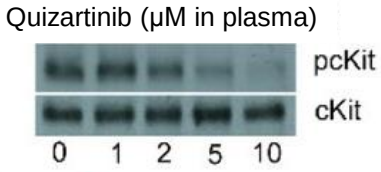


Rapid clearance of blasts from peripheral blood and terminal differentiation of bone marrow blasts[5]



Partial, selective inhibition of c-Kit[3,4]





Delayed hematologic recovery

Complete remission with incomplete count recovery

GM-CFU, colony forming unit, granulocyte, monocyte; BFU-E. Erythropoietin, erythroid burst-forming unit

*Other kinases with K_d within 10-fold that of *FLT3* were closely related RTKs, eg, KIT

[1]Zarrinkar P, et al. *Blood*. 2009;114(14):2984-2992; [2]Cortes JE, et al. *J Clin Oncol*. 2013;31(29):3681-3687; [3]Galanis A, et al. 2014. *Blood*. 123(1):94-100; [4]Galanis A & Levis M, 2015. *Haematologica*. 100(3):e77-9; [5]Sexauer et al. 2012 *Blood*. 120:4205-4214

Early leukemic blast clearance in blood and differentiation in bone marrow

QuANTUM-FIRST | Front-line AML

Evaluating Quizartinib as a Backbone Option in FLT3-ITD AML

Hypothesis: Synergistic anti-leukemic effect, when added to chemotherapy, to:

- Increase remission rate
- Delay relapse

QuANTUM-FIRST STUDY

Newly Diagnosed AML 18-75 years of age FLT-ITD(+) N=536

R

Test arm: Quizartinib add-on

Control arm: Placebo

	Induction	Consolidation	Continuation (12 cycles)
Test arm	Quizartinib + Cytarabine + Daunorubicin or Idarubicin	Quizartinib + Cytarabine +/- HSCT	Quizartinib + Surveillance
Control arm	Placebo + Cytarabine + Daunorubicin or Idarubicin	Placebo + Cytarabine +/- HSCT	Placebo + Surveillance

Primary endpoint: Event-free survival

Competitive advantage: ahead of competition; mostly enrolled

HSCT: hematopoietic stem cell transplantation

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TGCT is Rare, Non-malignant Disease with Large Pool of Prevalent Patients

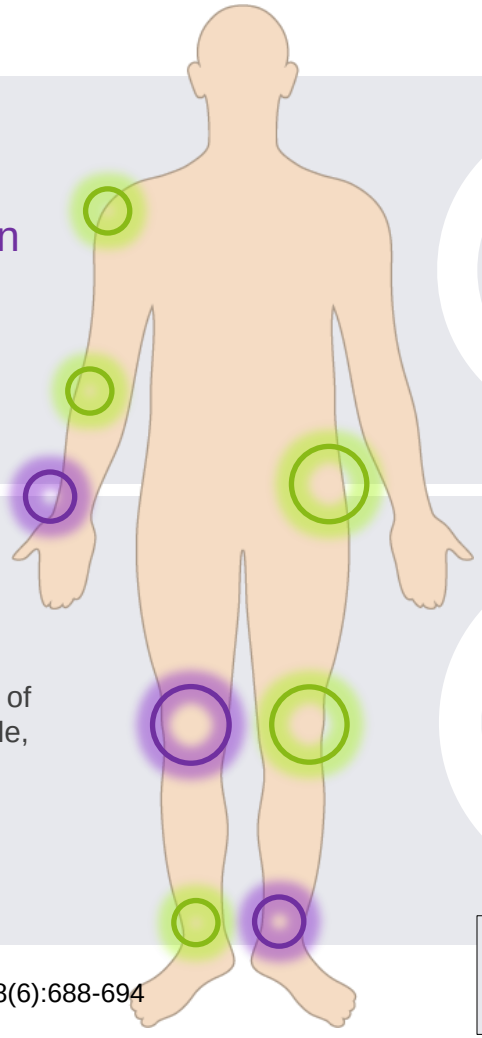
Incidence

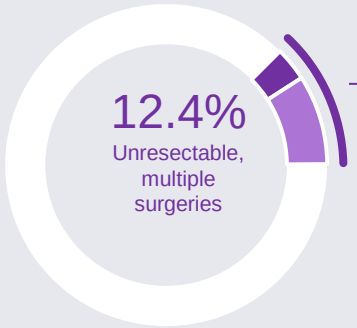
Prevalence*
(in 2018)

Localized TGCT (extremities)

WW: 10.2 cases per million

frequently affects the knee joint, other locations include the wrist and ankle



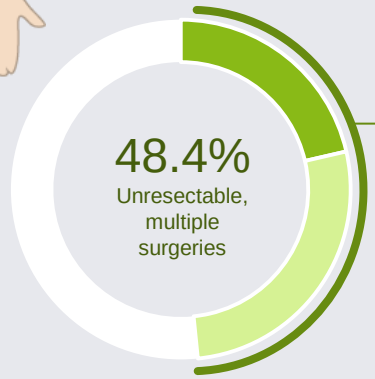


Over 30 years
10,501 US
10,476 EU

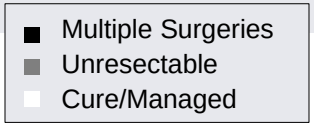
Diffuse TGCT

WW: 4.1 cases per million

most commonly affects the knee (75% of cases), followed by the hip (15%), ankle, elbow, and shoulder



Over 30 years
14,800 US
14,770 EU

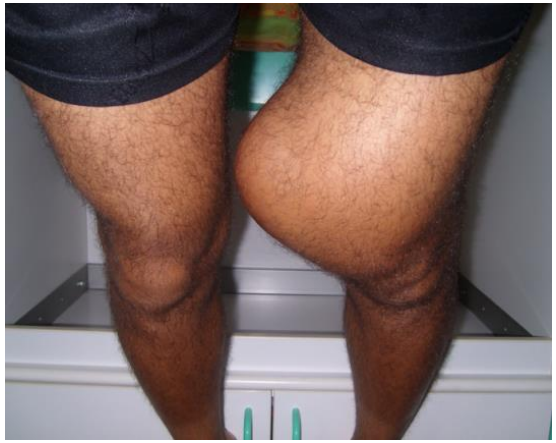
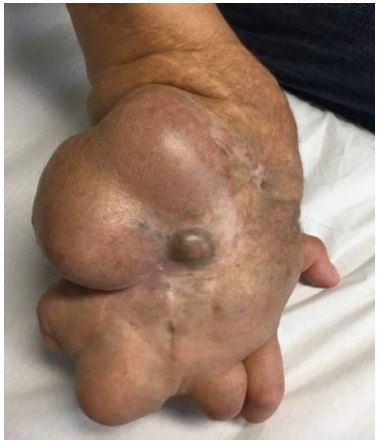
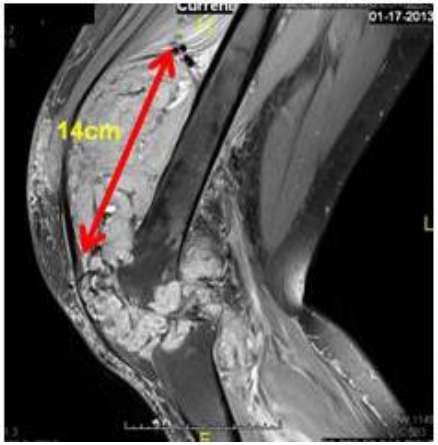


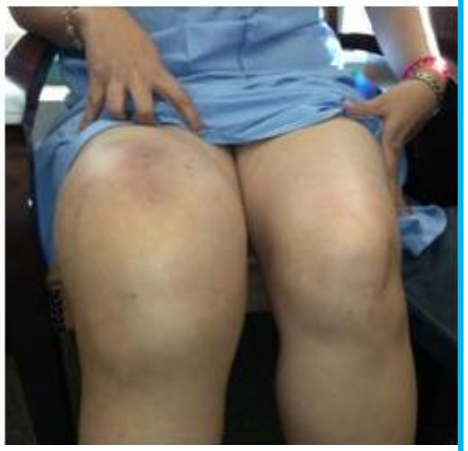
Source: Mastboom et al. *Acta Orthop*. 2017; 88(6):688-694
*Unresectable prevalent patient population
TGCT: tenosynovial giant cell tumor

Pexidartinib | Proposed Indication

"Pexidartinib" is indicated for treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT), which is associated with severe morbidity or functional limitations, and which is not amenable to improvement with surgery.

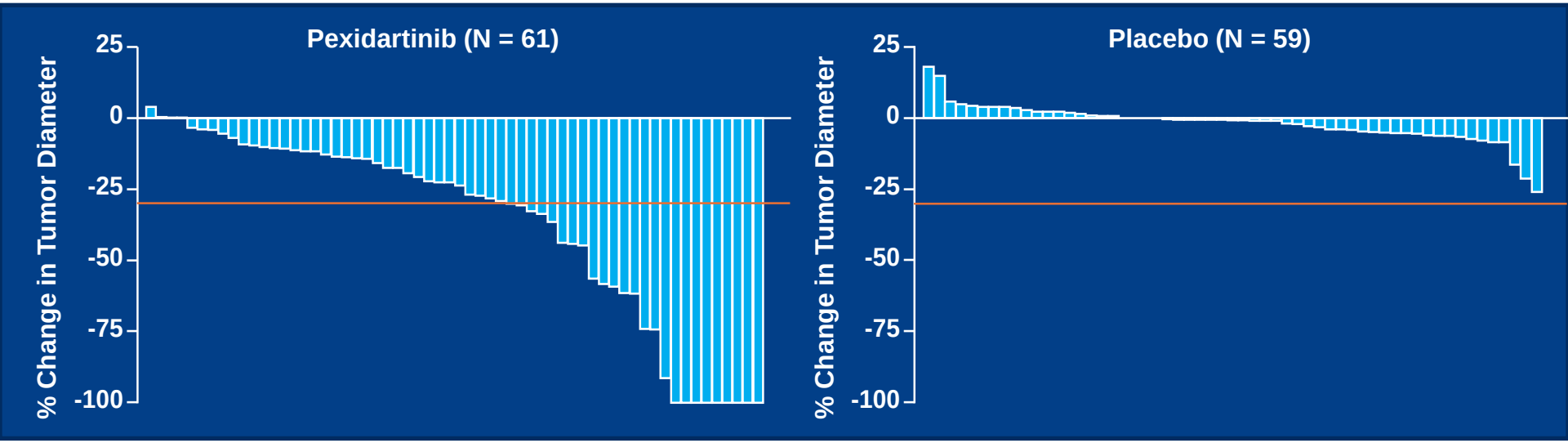
- **US NDA submission in 2H FY2018**



- TGCT: non-malignant tumor associated with pain, stiffness, and functional impairment
  - Analgesic use is common and may include opioids
- Large, diffuse disease is not amenable to surgical resection due to risk of morbidity or high risk of recurrence

Pexidartinib | ENLIVEN Study Efficacy & Safety



- TGCT: 4 non-fatal hepatic SAEs increased bilirubin, one lasting ~7 months
- Serious liver toxicity also observed in non-TGCT (N = 637), 1 case required liver transplant (breast cancer, in combination with paclitaxel) and 1 case associated with death (monotherapy in metastatic mucosal melanoma)
- Other AEs as previously reported

Liver Function, N (%)	Pexidartinib Part 1 N = 61	Placebo Part 1 N = 59	Pexidartinib Crossover 800 mg/d N = 30
AST or ALT ≥ 3 × ULN	20 (33)	0	4 (13)
TBili ≥ 2 × ULN	3 (5)	0	0
TBili ≥ 2 × ULN and AST or ALT ≥ 3 × ULN	3* (5)	0	0

All had ALP ≥ 2.5 × ULN.

Tap et al, ASCO, 2018; Abstract #11502

Today's Agenda

1 Cancer Enterprise 2025

- A Delivery Machine
- Scaling up the Enterprise
- Secure World-class Leadership in Science

2 DS-8201

- BLA FY2020 (upside 1H FY2019) on track
- Expanding program scope
- ILD well characterized
- Breast cancer: duration of response in Ph 1

3 U3-1402

- Breast cancer data at SABCS
- NSCLC EGFRm program progress
- Fast to market strategy and program scope

4 Next DXd ADCs

- DS-1062: Ph 1
- Others

5 Quizartinib

- Global US EU JP NDA submissions completed
- Biology and differentiation – the key role of QuANTUM First

6 Pexidartinib

- Submission status
- ENLIVEN

7 Recap

- DS is a science & technology company / future news flows

Cancer Enterprise | **Major Clinical Pipeline**

As of Dec 2018

Daiichi-Sankyo cancerenterprise

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

Cancer Enterprise | Upcoming Milestones

ADC Franchise

- Topline DS-8201 DESTINY-Breast01 results and update on potential1H FY2019 upside BLA submission
- Potential ASCO 2019 disclosures:
  - First disclosures for U3-1402 & DS-1062 in NSCLC
  - Updated U3-1402 breast cancer results

AML/Hematology Franchise

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

Breakthrough Science

- Pexidartinib US NDA submission in 2H FY2018

Cancer Enterprise | Deliver, Scale Up, Lead

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It's Our Obligation.

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HER3 ADCs

HER3 ADCs

Clinical stage

	Project (Payload)	Potential Indication	Pre-Clinical	Ph 1	Pivotal
Daiichi-Sankyo cancerenterprise	**U3-1402** Topoisomerase I inhibitor	**Breast, NSCLC**	➡		
MediaPharma s.r.l. Antibodies are the answer	**MP-HER3-ADC** Monomethyl Auristatin F	**HER2+ BC post T-DM1**	➡		

TROP2 ADCs

TROP2 ADCs

Clinical stage

	Project (Payload)	Potential Indication	Pre-Clinical / Ph 1 / Pivotal
Daiichi-Sankyo cancerenterprise	**DS-1062** Topoisomerase I inhibitor	**NSCLC**	
Immunomedics	**IMMU-132** SN38 (Topoisomerase I inhibitor)	**metastatic TNBC**	**P3**

TNBC: triple-negative breast cancer

B7-H3 ADCs

B7-H3 ADCs

Clinical stage

	Project (Payload)	Potential Indication	Pre-Clinical	Ph 1	Pivotal
Daiichi-Sankyo cancerenterprise	**DS-7300** Topoisomerase I inhibitor	**Solid tumor**			
MacroGenics	**MGC018** Duocarmycin hydroxyBenzamide Azaidole	**Advanced Solid Tumors**	**P1/2**		

GPR20 ADCs

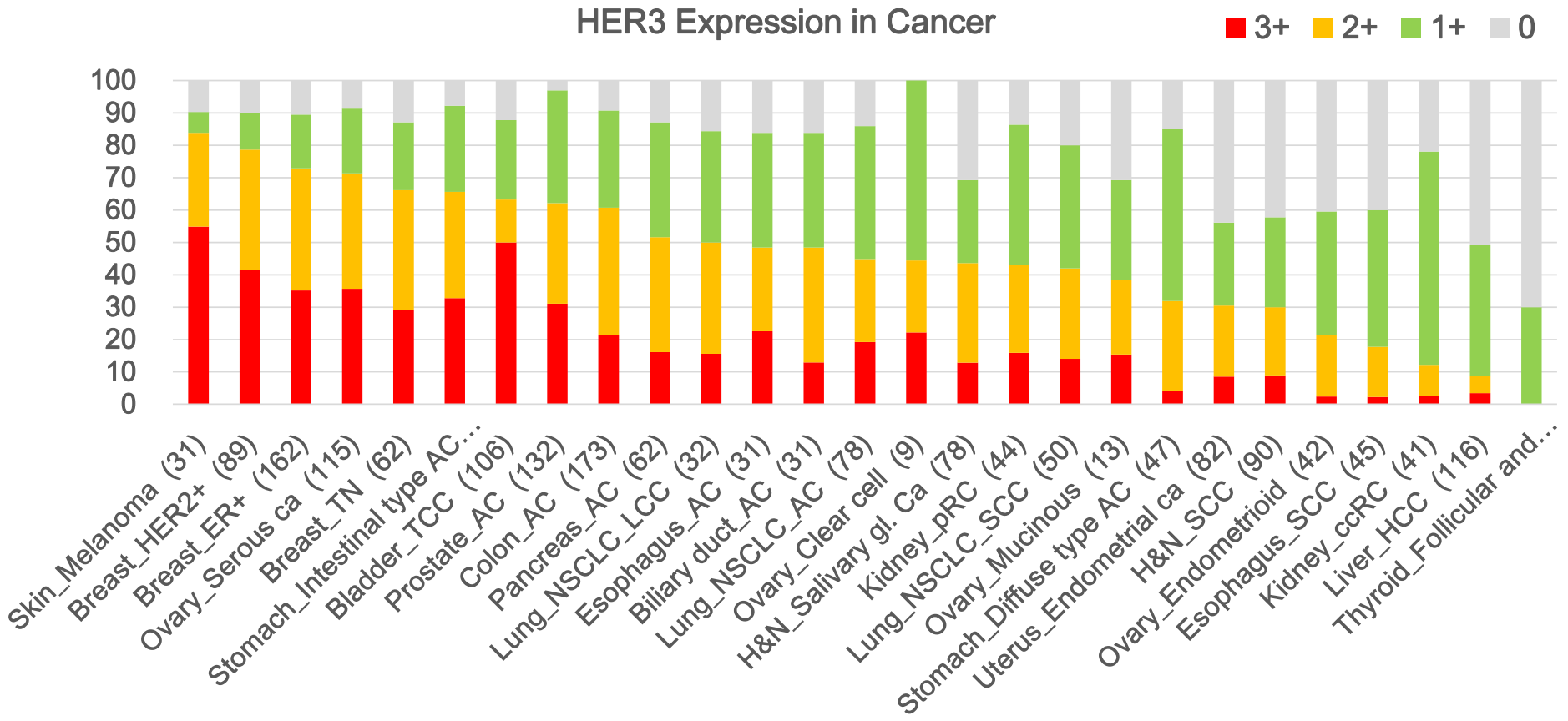
GPR20 ADCs

Clinical stage

	Project (Payload)	Potential Indication	Pre-Clinical	Ph 1	Pivotal
Daiichi-Sankyo cancerenterprise	**DS-6157** Topoisomerase I inhibitor	**GIST**			

GIST: Gastrointestinal stromal tumor

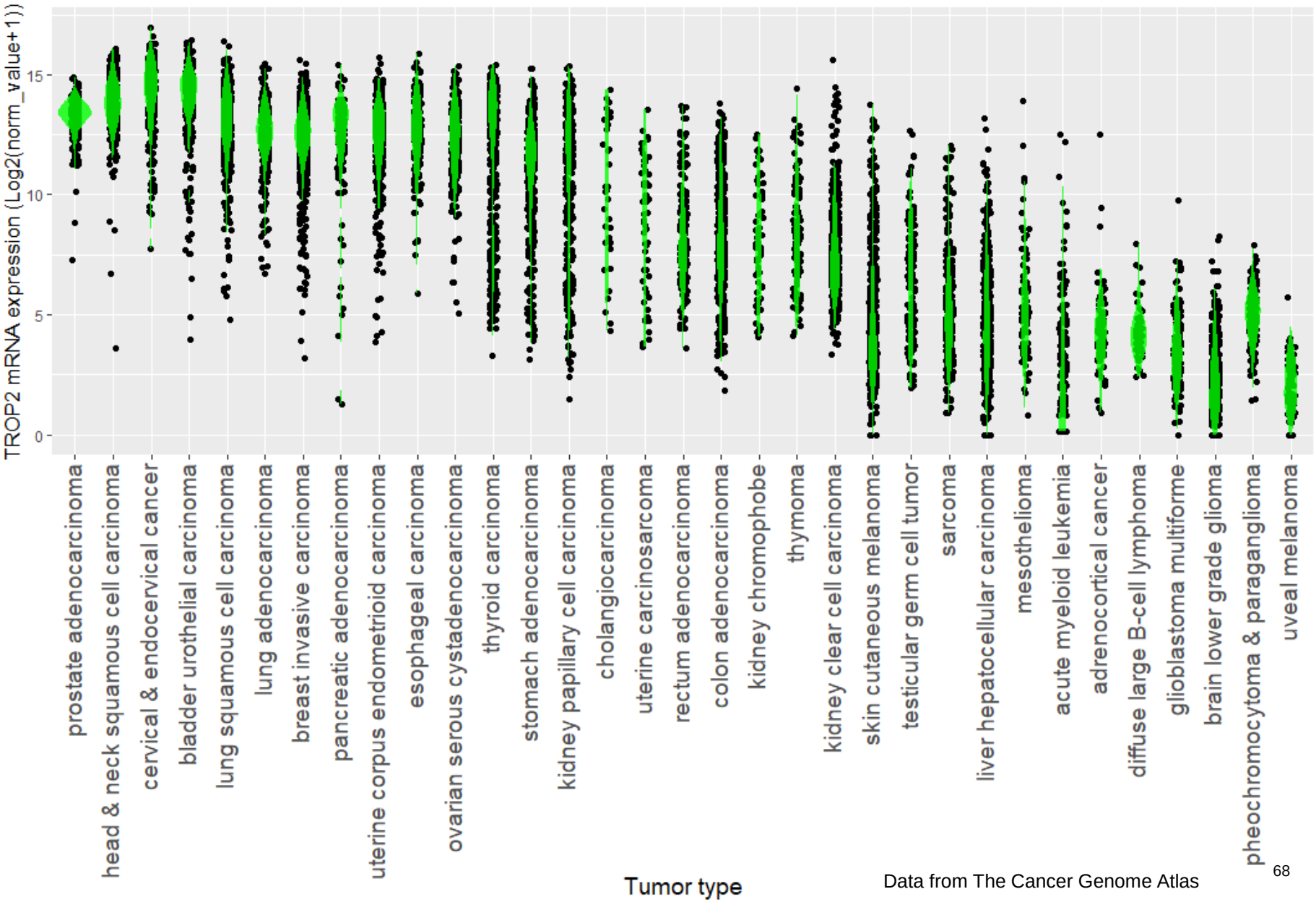
HER3 Protein Expression Across Cancers



Data from internal analysis using in-house IHC assay of cancer tissue samples (TMA samples). Majority of tissue from primary tumor. Internal pathologist scored following internal HER3 scoring criteria.

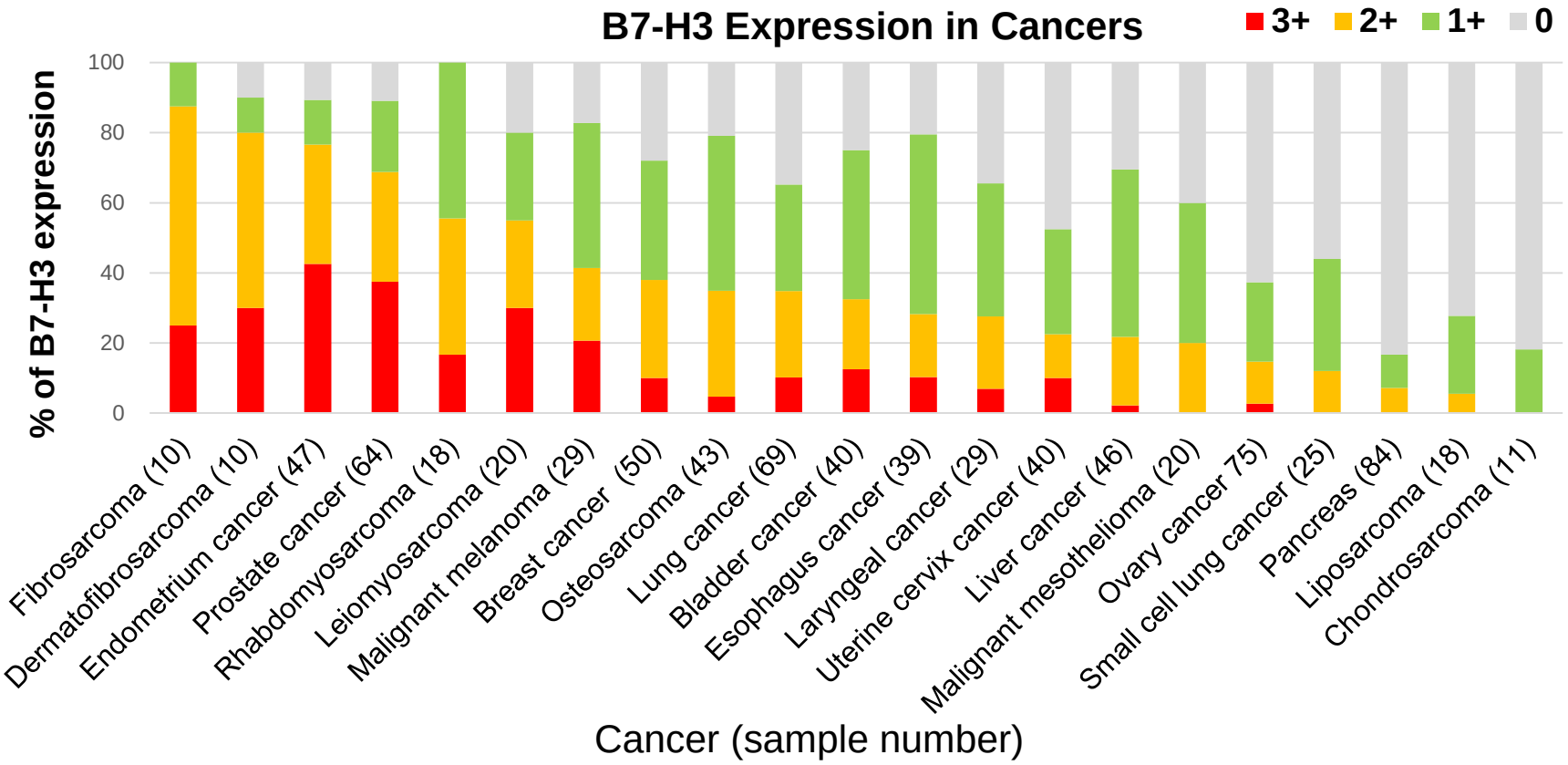
HER3-expression observed in many tumor types:
Breast, Lung, Prostate, Colorectal
Ovarian, Bladder, Melanoma, etc.

TROP2 Expression in Various Cancers



Data from The Cancer Genome Atlas

B7-H3 Protein Expression in Various Cancers



Data from internal analysis using in-house IHC assay of cancer tissue samples (purchased TMA samples). Majority of tissue from primary tumor. Internal pathologist scored following internal B7-H3 scoring criteria.

B7-H3-expression observed in several tumor types:
Sarcoma, Endometrium, Melanoma, Prostate, Breast, Lung cancer, etc.

Abbreviations

Abbreviation	
BTD	Breakthrough therapy designation
CR	Complete response
DCR	Disease control rate
DLT	Dose limiting toxicity
DOR	Duration of response
EGFR	Epidermal growth factor receptor
MTD	Maximum tolerated dose
NSCLC	Non-small-cell lung cancer
ORR	Overall response rate Objective response rate
OS	Overall survival
PD	Progress disease
PFS	Progression-free survival
PR	Partial response
RDE	Recommended dose for expansion
TTR	Time to response