

Passion for Innovation.
Compassion for Patients.™



FY2018 R&D Day

DAIICHI SANKYO CO., LTD

George Nakayama
Chairman and CEO

December 12, 2018

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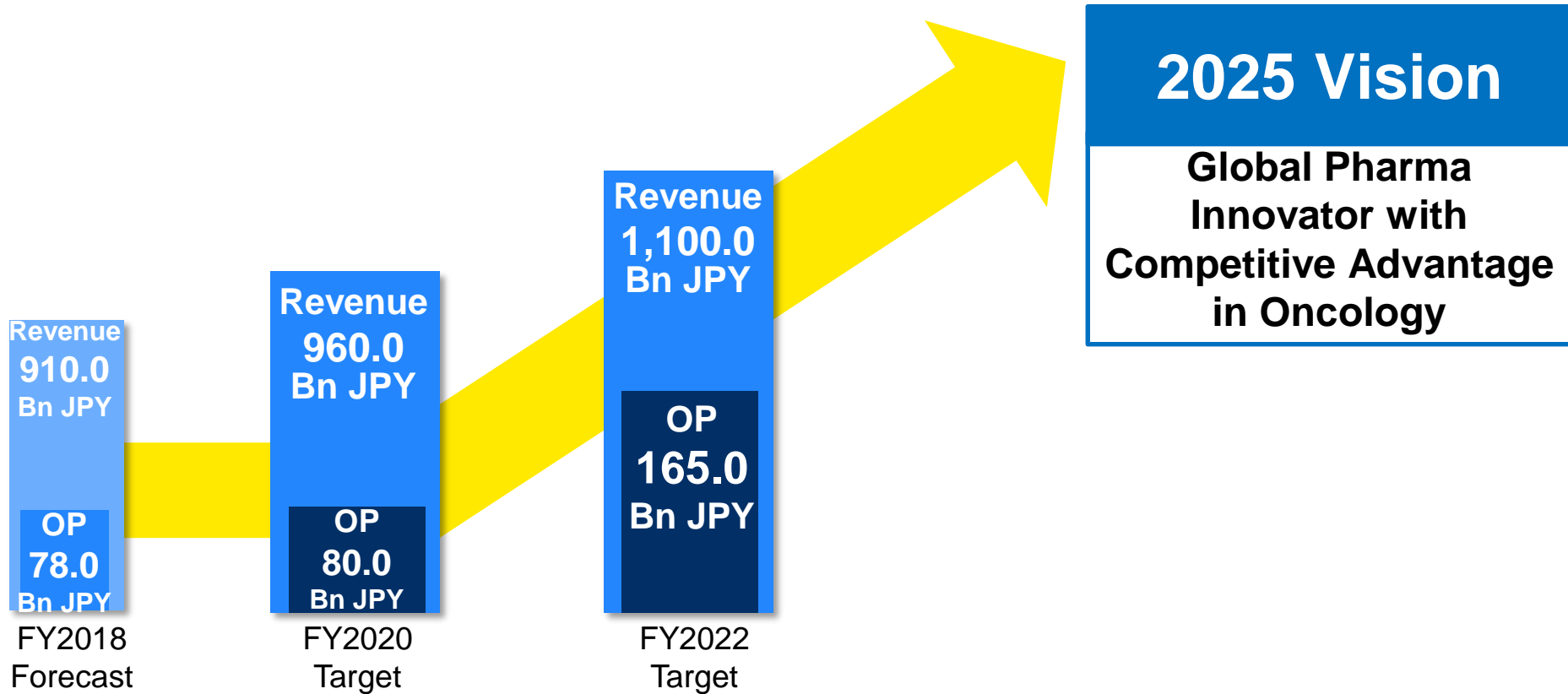
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Toward 2025 Vision & 5-Year Business Plan



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

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

CE 2025 Vision

ADC Franchise

3

AML Franchise

3

Breakthrough Science

1

Deliver 7 NMEs in 8 years

SM 2025 Vision

Maximize near-term revenue

2 NMEs in 2018-20

Grow future franchises

3 NMEs 2021-25

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



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

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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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

7 in **8**
NMEs years

Lead in Smart-Treatment
with BIC & FIC ADC

3

Establish a Competitive
Hematology Franchise

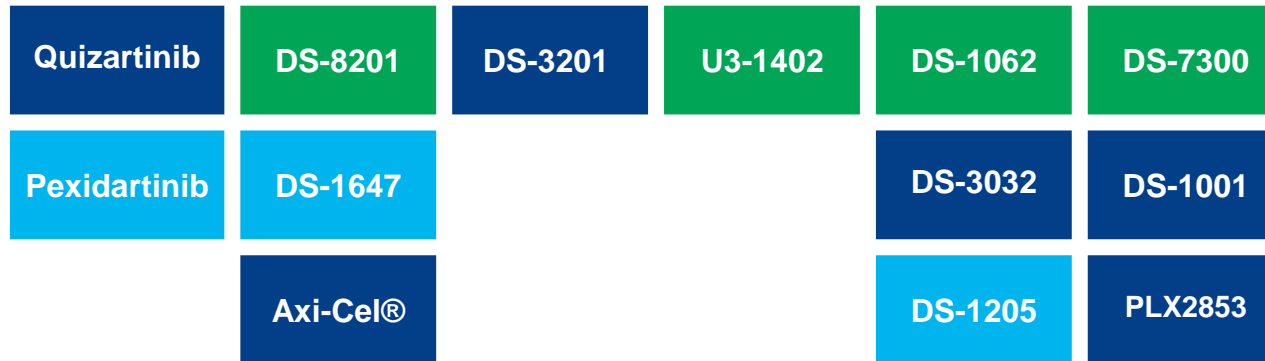
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Lead with Breakthrough
Science

1

FY2018

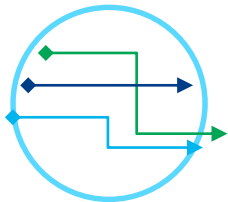
2025





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



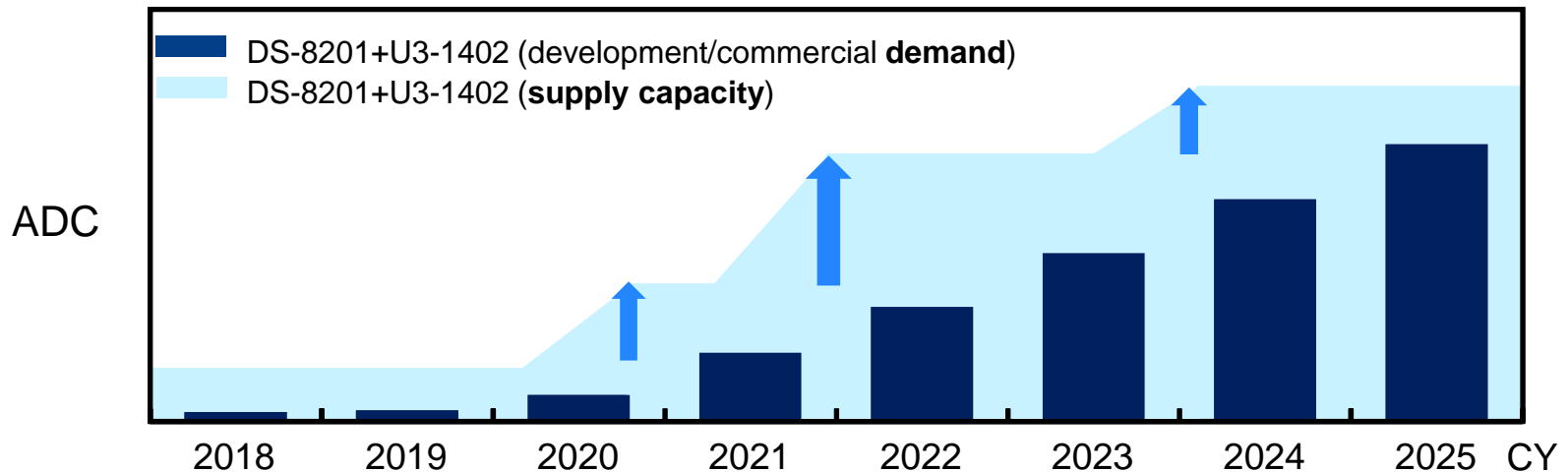
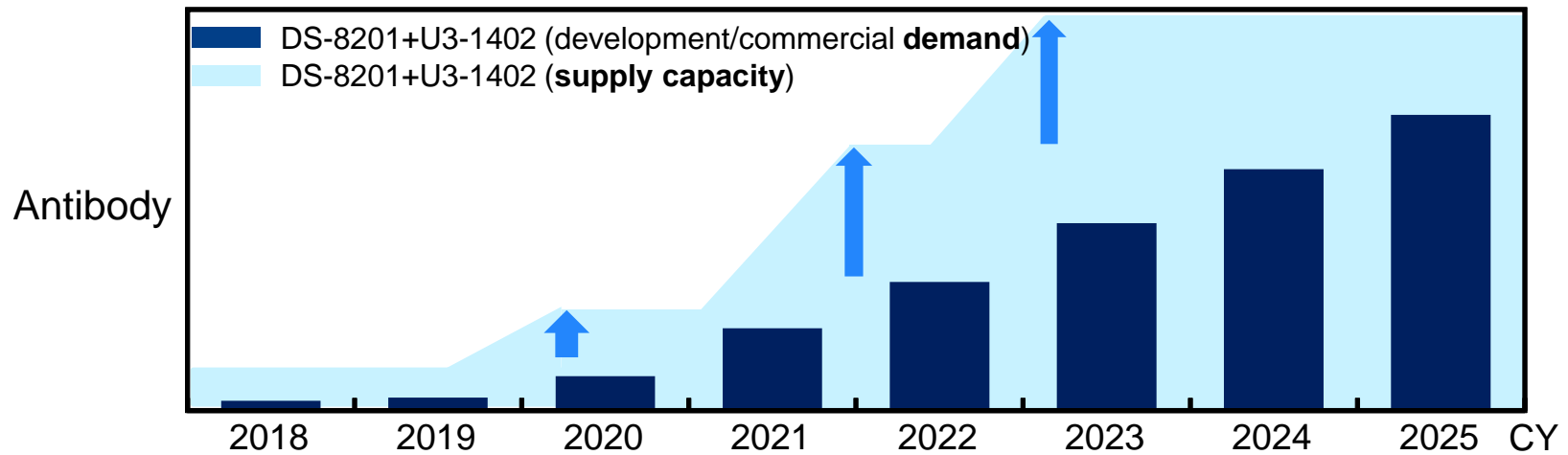
Manufacturing of development and commercial supplies

- ◆ Massive acceleration and scaling up is underway

ADC Manufacturing

Meeting Massive Increase in Demand

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 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



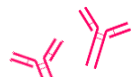
New global operating model in place

- ◆ **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)

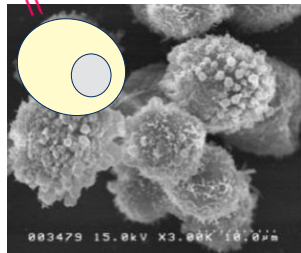


- ◆ Healthy flow of **new drug candidates**, in ADC beyond DXd, in Hematology and in Breakthrough Science
- ◆ Establishing clinical analysis function in RD Novare to strengthen **translational science capability**
- ◆ Establishing a **state-of-the-art Bio-IT Omics platform**
- ◆ **CMC process and scale**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





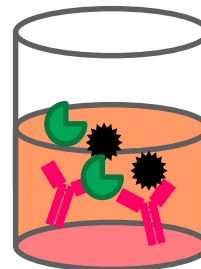
cell substrate



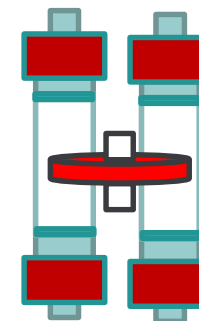
DS expression system
Cell cloning technology for high-producing cell isolation



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

ADC Franchise

 Clinical stage

	Project (Target)	Potential Indications	Discovery	Pre-Clinical	Ph 1	Pivotal
1	DS-8201 (HER2)	Breast, Gastric, CRC, NSCLC				
2	U3-1402 (HER3)	Breast, NSCLC				
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

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DS-8201 Flagship Asset

FDA Breakthrough Therapy Designation (BTD)



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

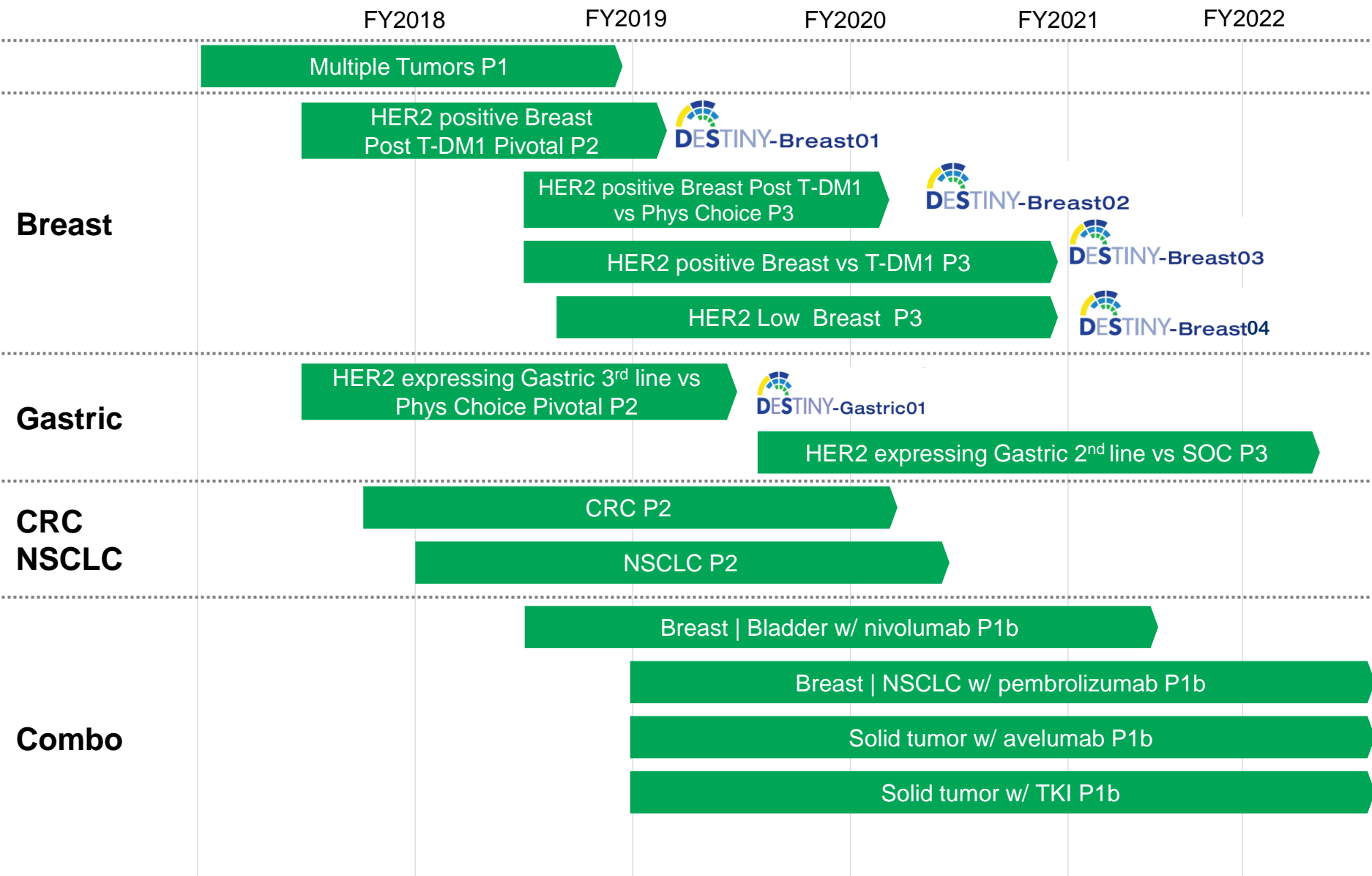
Planned further development

- 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**



Current/future trials for further data-gated development

Directions (Ph 1-3)

New plans

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

- ◆ More than 380 medications known to induce respiratory disease, mostly ILD¹
- ◆ 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

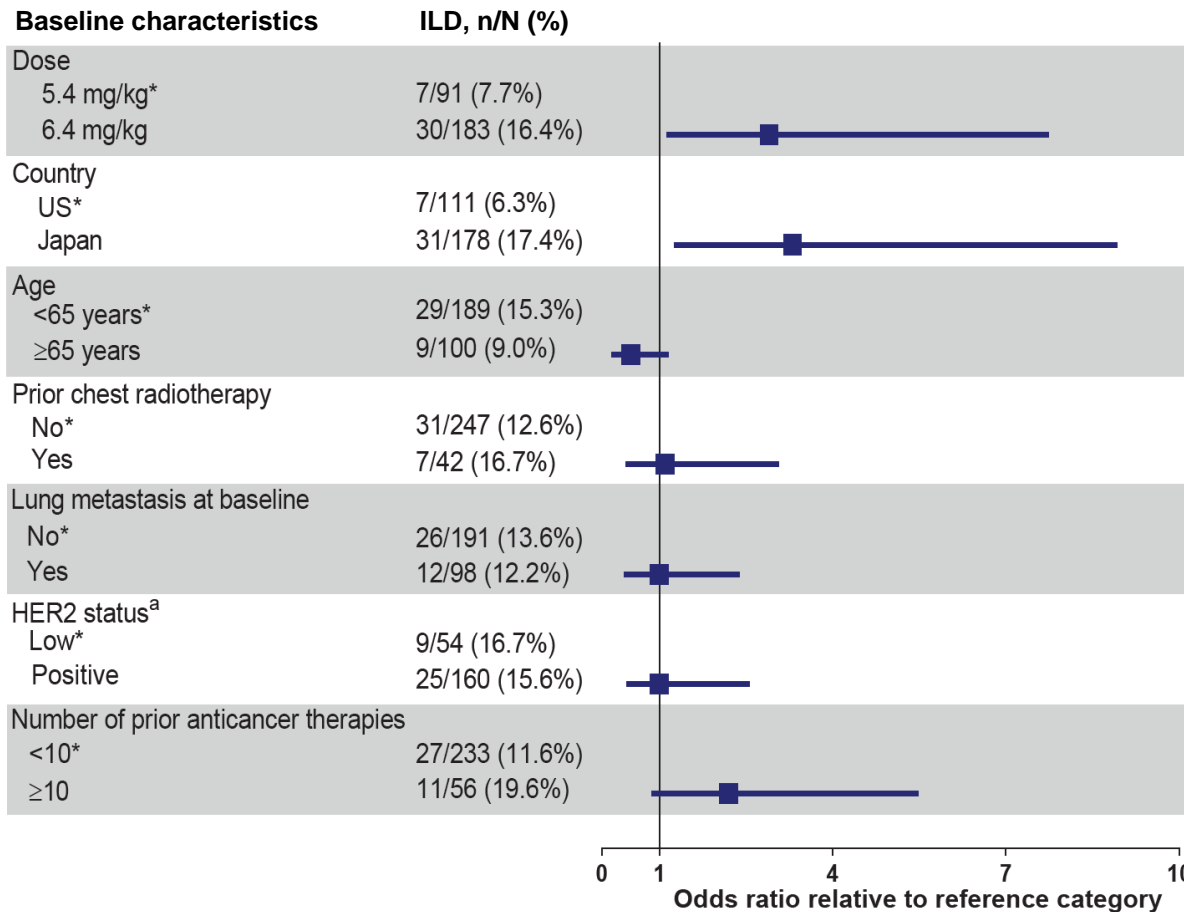
Investigator-Reported and Adjudicated Cases of ILD

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

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.

^aHER2 status was only available for breast and gastric cancer.

- ◆ 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

ILD experience in breast cancer at 5.4 mg/kg

Population	Adjudication status	ILD Severity Grade					Total
		1	2	3	4	5	
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

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

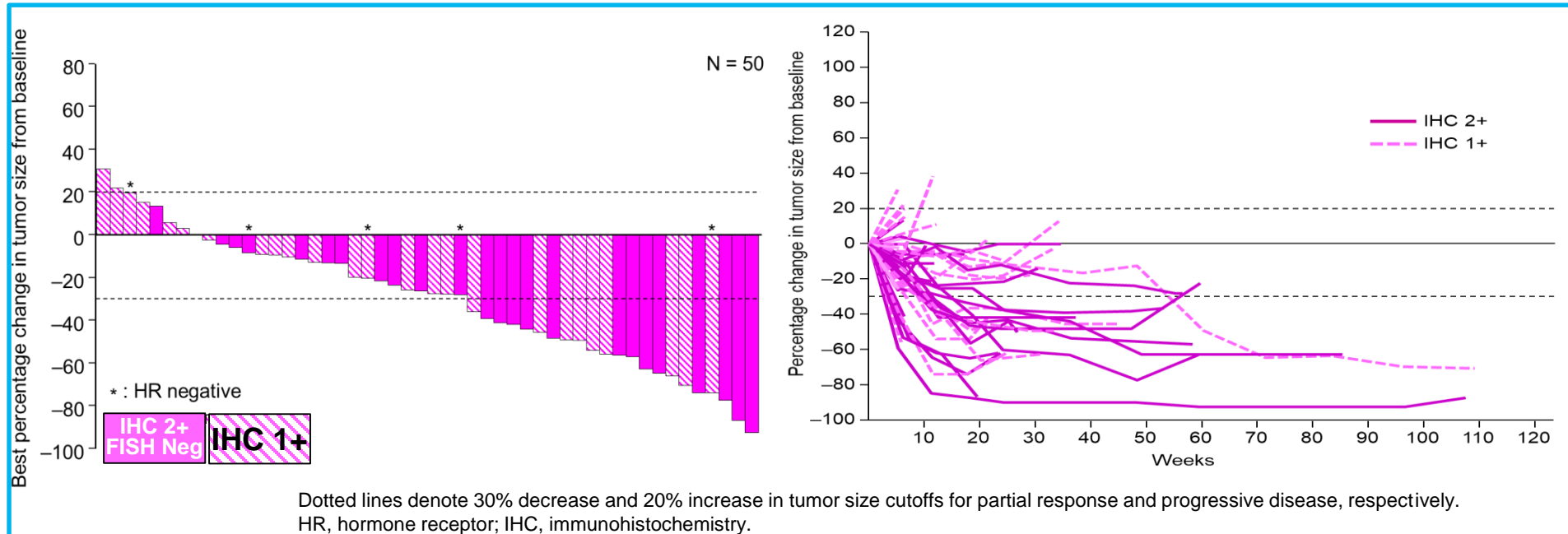
59.5% (95% CI 49.7, 68.7)

Median duration of response

20.7 months (range 0.0+, 21.8+)

^aSubjects 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.

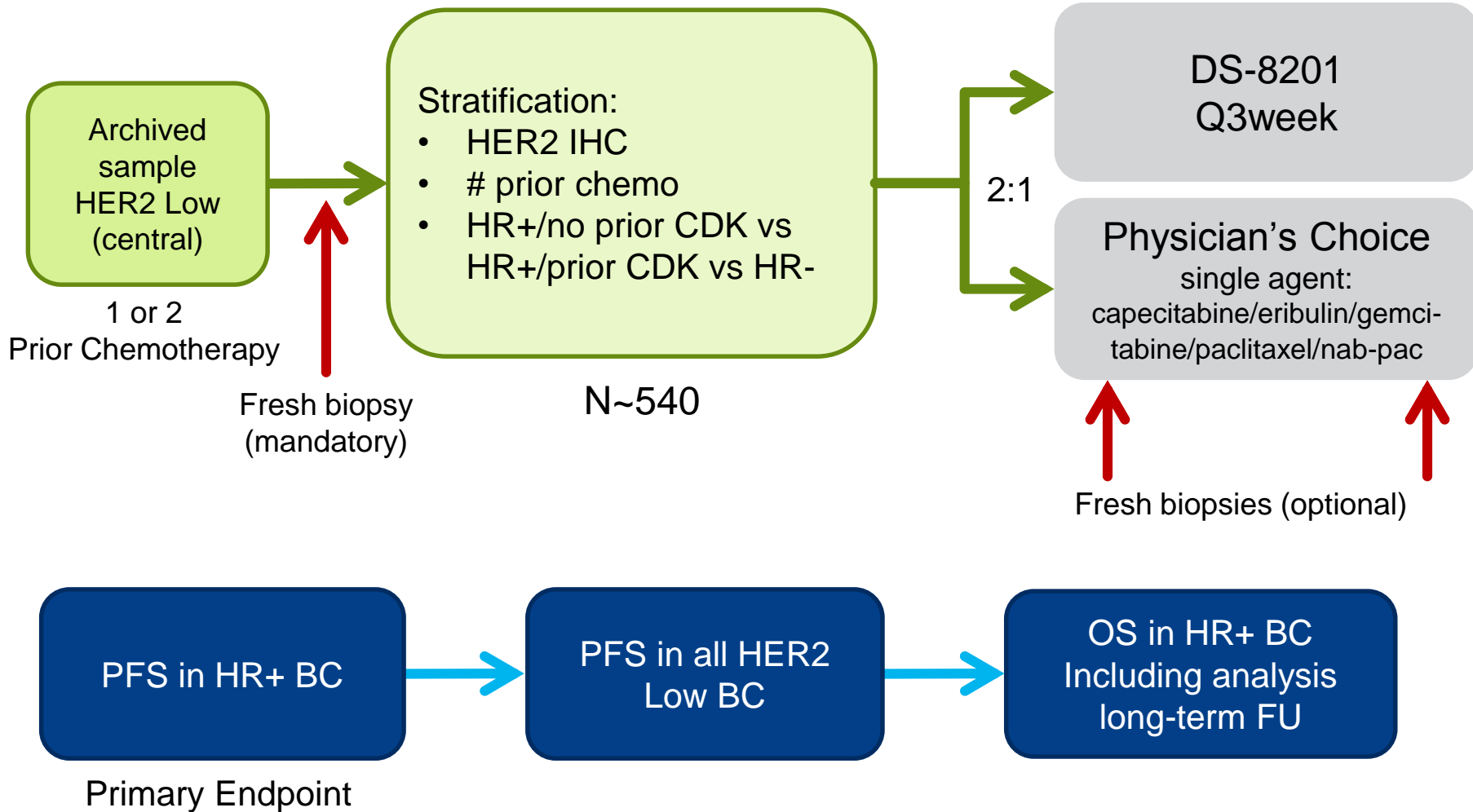
DCR, disease control rate; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; ISH, in situ hybridization; ORR, objective response rate.

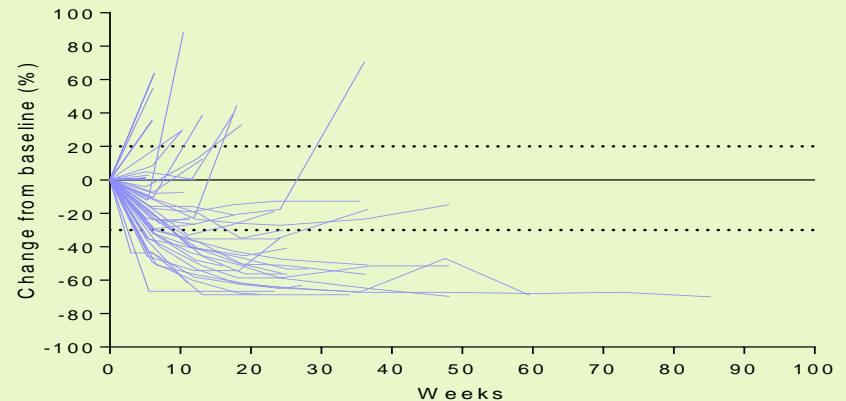
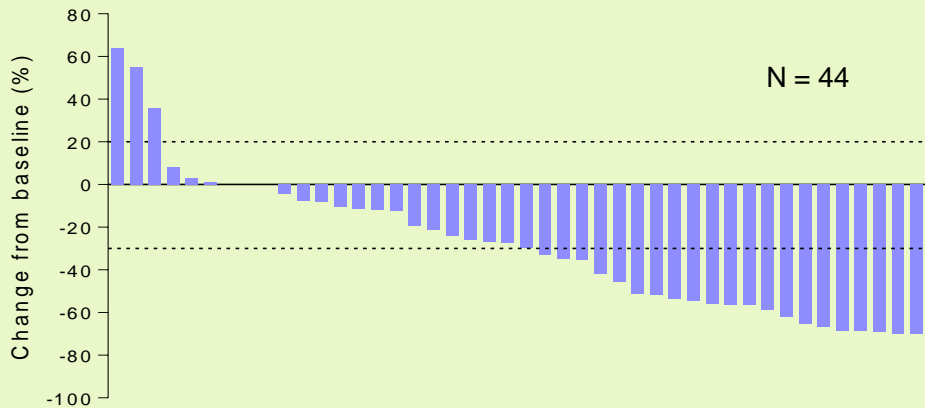


	Confirmed ORR, n/N (%)	Confirmed DCR, n/N (%)	Duration of Response, median (range), mo	PFS, median (95% CI), mo
All (N = 51)	19/43 (44.2)	34/43 (79.1)	9.4 (1.5+, 23.6+)	7.6 (4.9, 13.7)
Subgroups				
IHC 1+ (n = 27)	7/21 (33.3)	14/21 (66.7)	7.9 (2.1+, 11.3)	5.7 (1.4, 7.9)
IHC 2+ (n = 24)	12/22 (54.5)	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)

DS-8201 | HER2 Low Breast Cancer P3 Study Design

CT.gov: NCT03734029/JapicCTI-184223

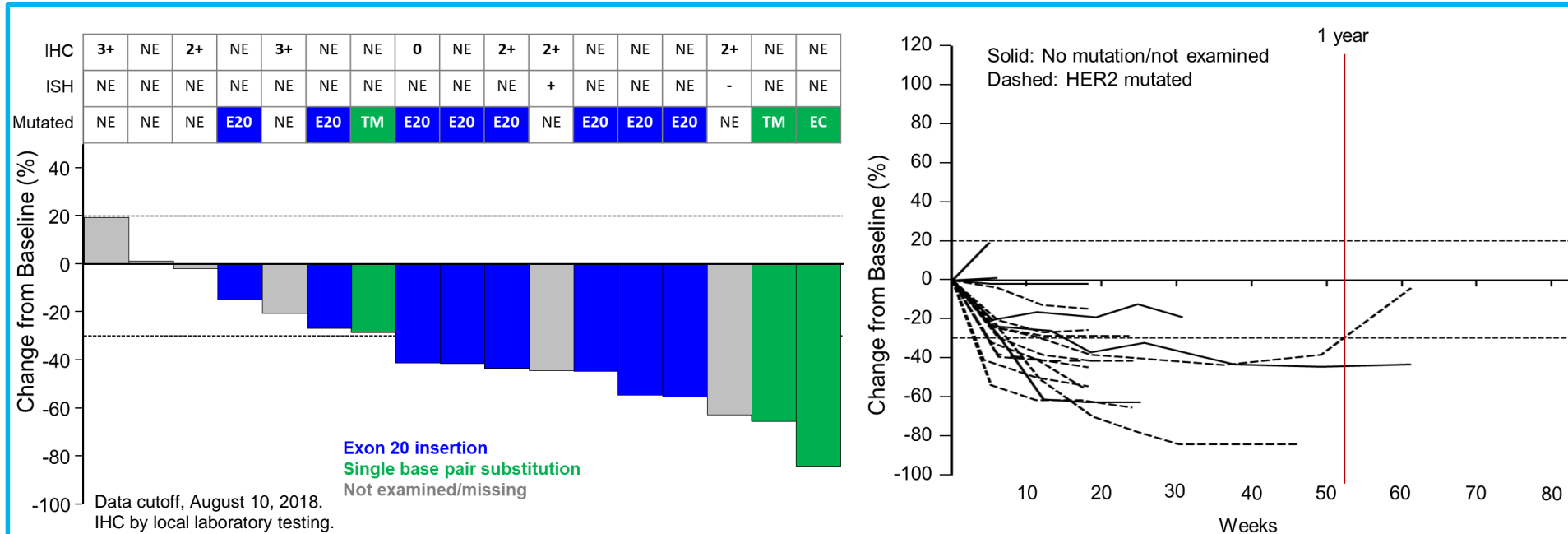




Includes subjects who had ≥ 1 postbaseline scan. Dotted lines denote 20% increase and 30% reduction in tumor size, respectively.

*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.

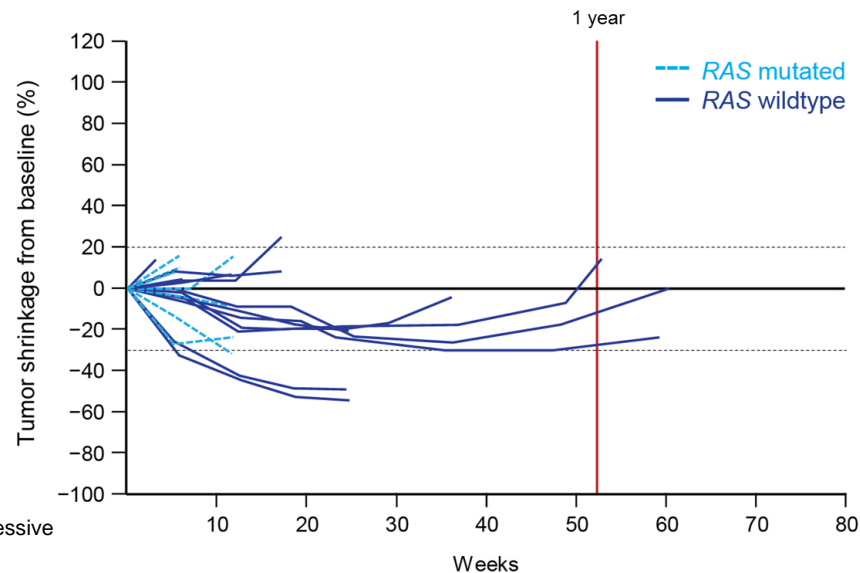
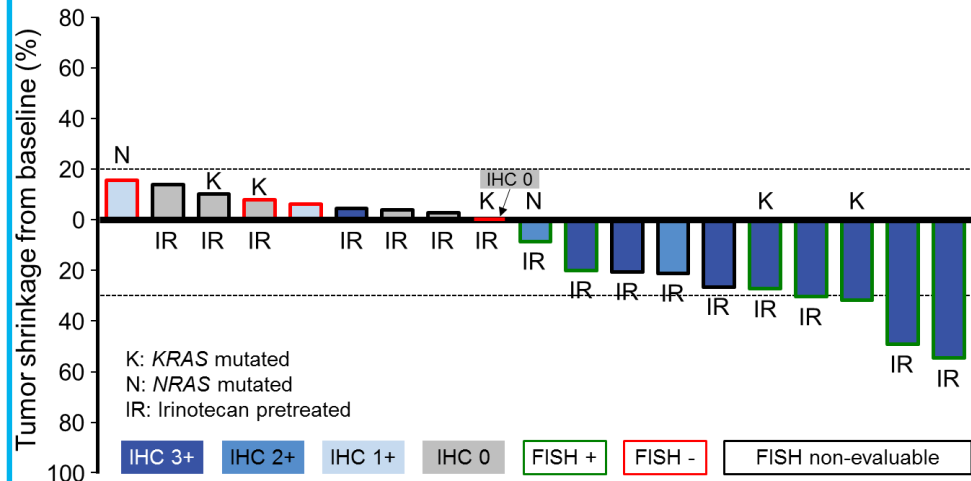
	Confirmed ORR (n/N) (95% CI)	DCR % (n/N)	DOR, Median (95% CI), months	PFS	
				Median, (95% CI)	Min, max
HER2 Positive Gastric Cancer N = 44	43.2% (19/44) (28.3, 59.0)	79.5% (35/44)	7.0 (NA)	5.6 months (3.0, 8.3)	1.2, 19.6+



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.

	Confirmed ORR, % (n/N)	Confirmed 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)

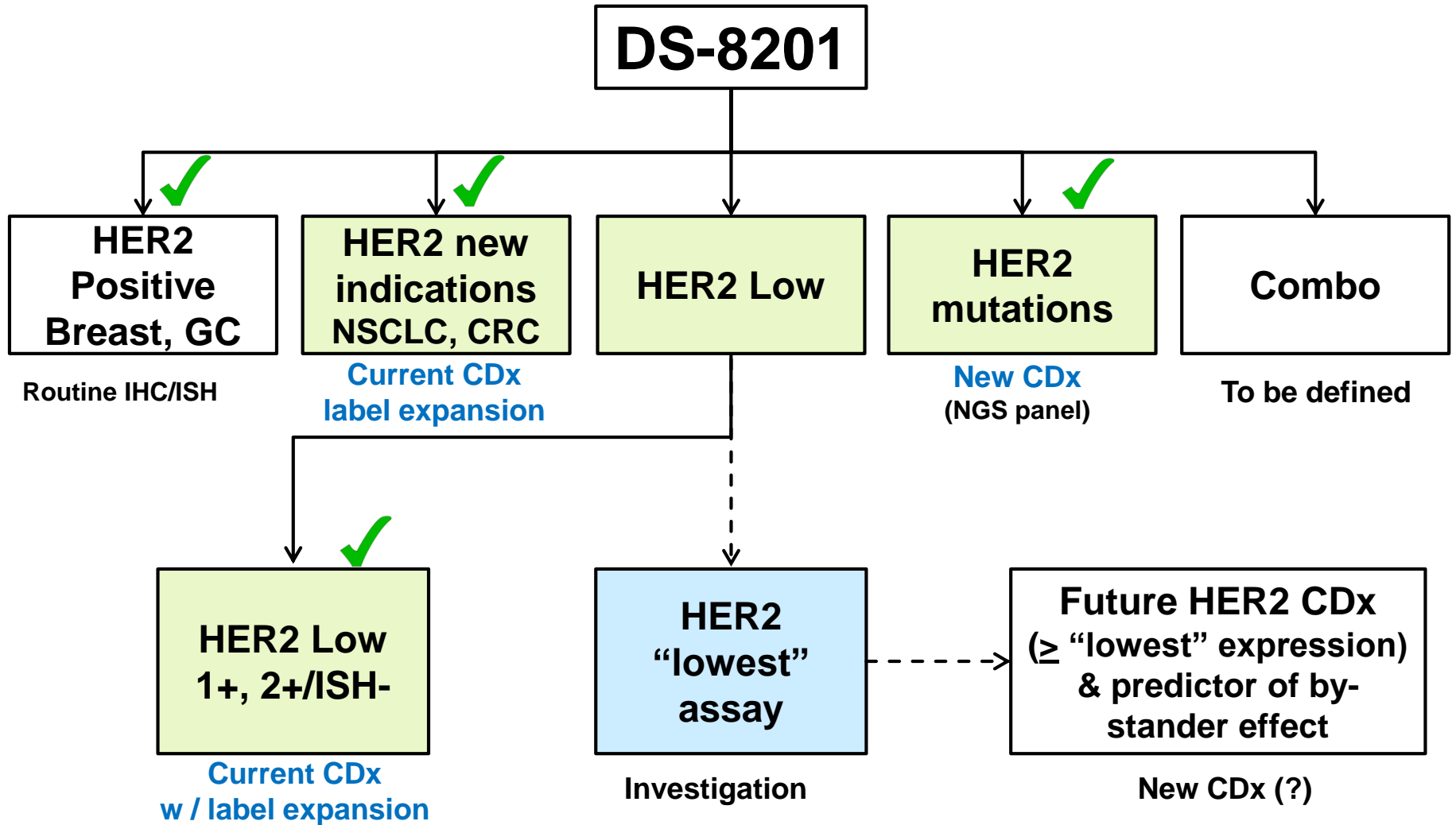
ORR 27.3% (3/11) in HER2 (IHC 2+, 3+)



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)



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

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		

- ◆ 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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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

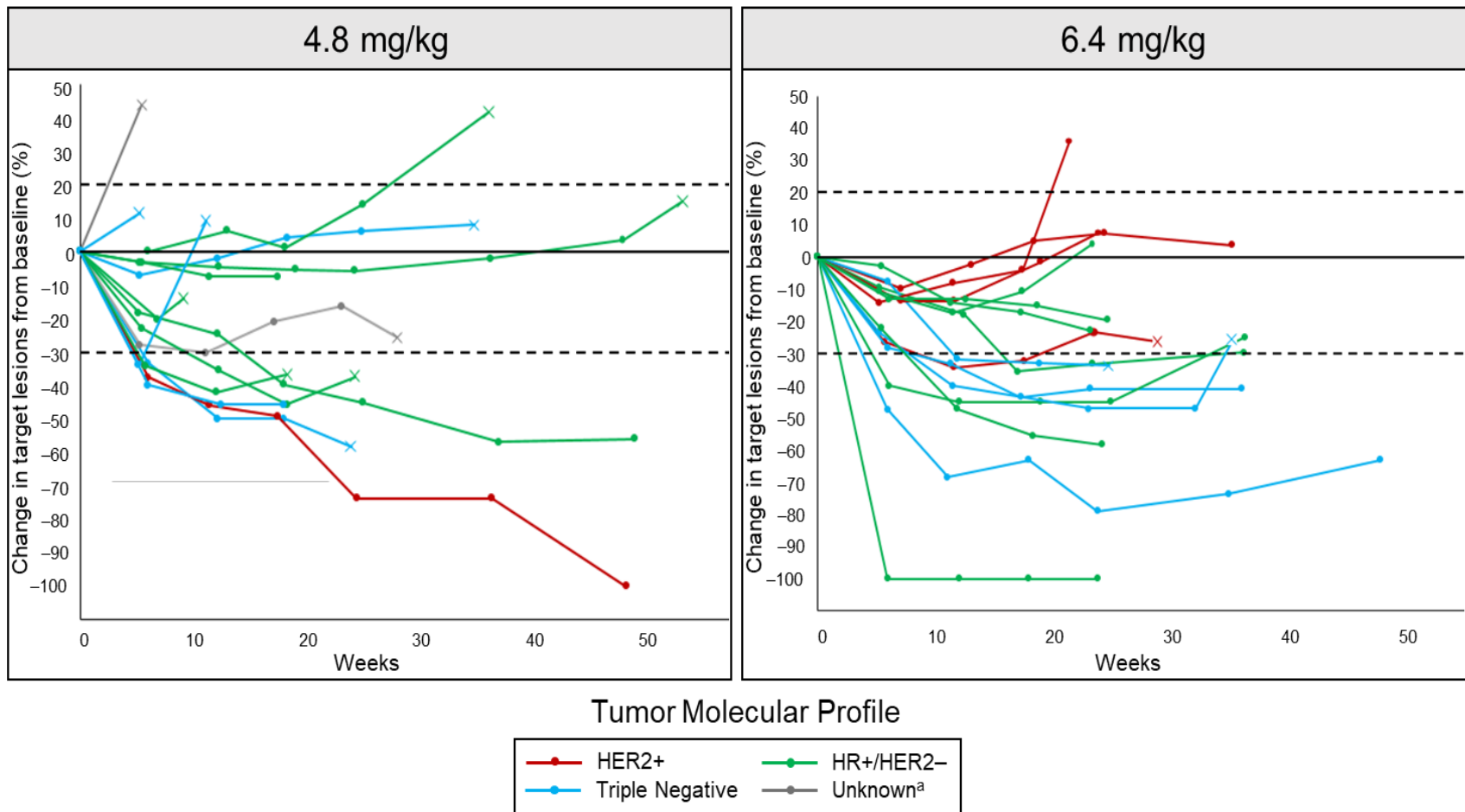
Efficacy Assessed by Investigators

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

Percentage Change in Target Lesions from Baseline



Data cutoff date of November 6, 2018. X indicates patients who discontinued treatment.

^aUnknown 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.

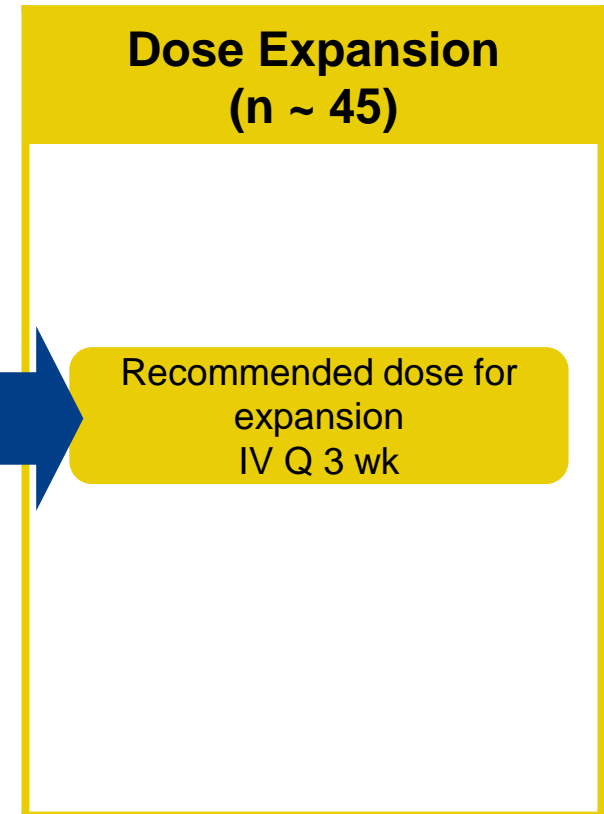
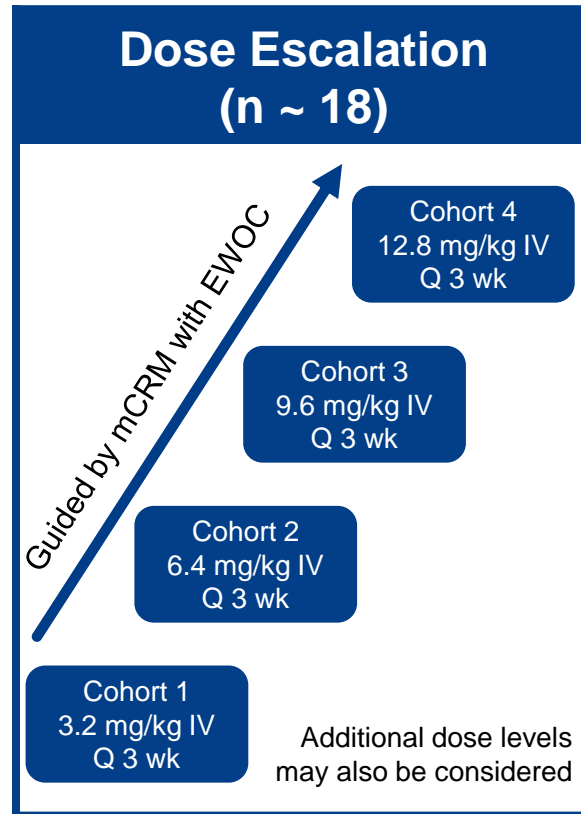
Dotted lines denote 30% decrease and 20% increase in tumor size threshold for partial response and progressive disease, respectively.

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.

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

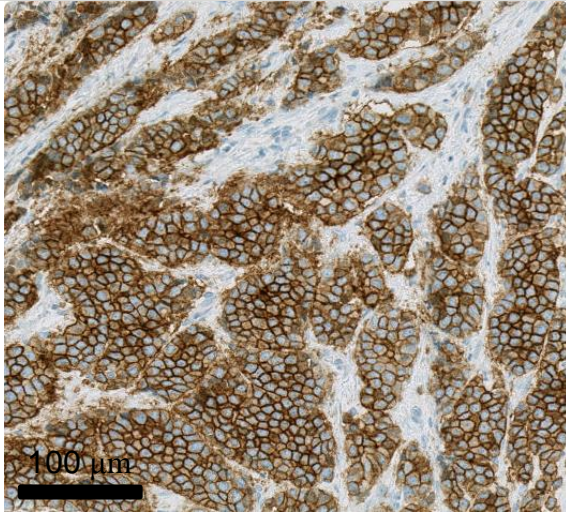
- ◆ Metastatic or unresectable **EGFR-mutant NSCLC** with
 - T790M mutation-negative tumor after progression with erlotinib, gefitinib, or afatinib
 - or**
 - Progression on osimertinib
- ◆ Clinically inactive CNS metastases allowed
- ◆ ECOG PS 0 or 1



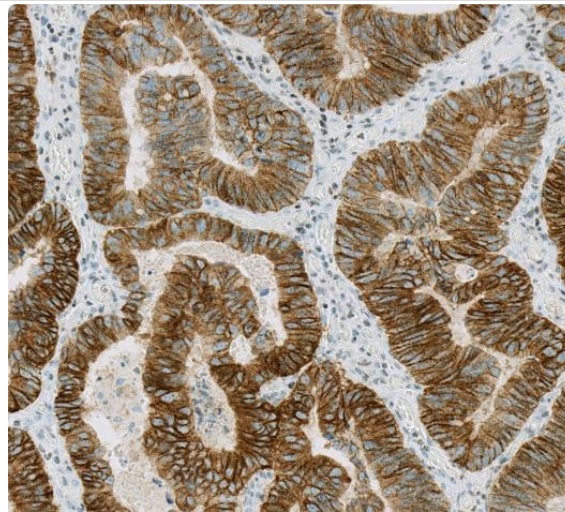
No selection based on HER3 expression. HER3 (IHC) is examined retrospectively.

Dose escalation data to be presented at ASCO 2019

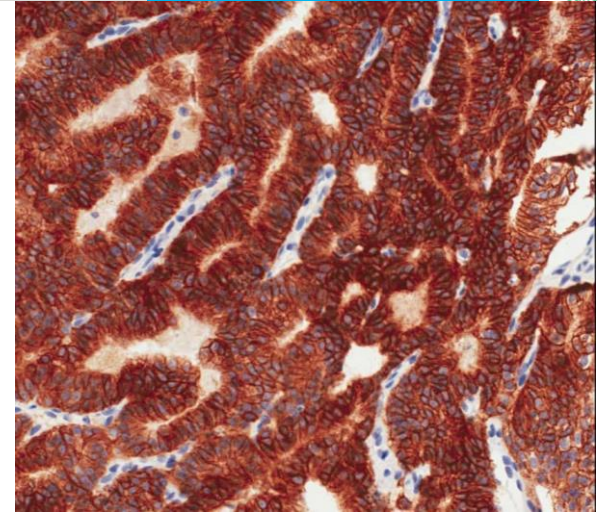
U3-1402 | HER3 Expression in Cancer (IHC)



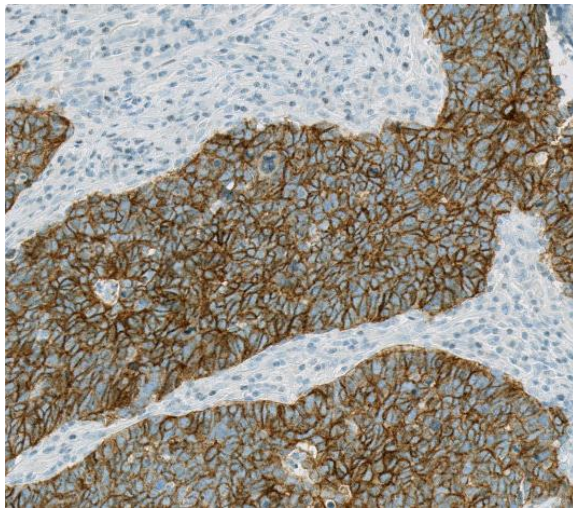
Breast cancer



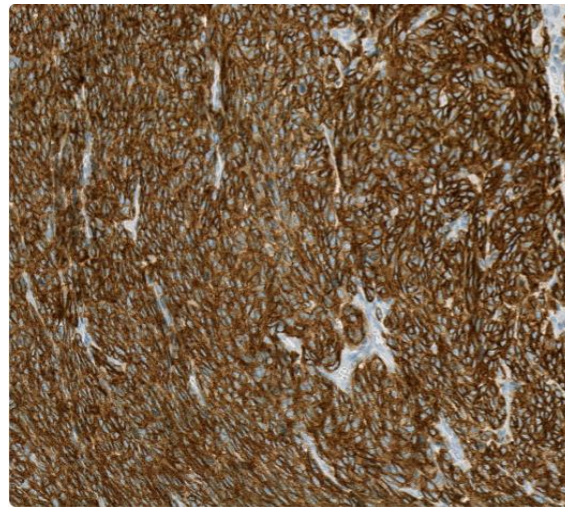
Colorectal cancer



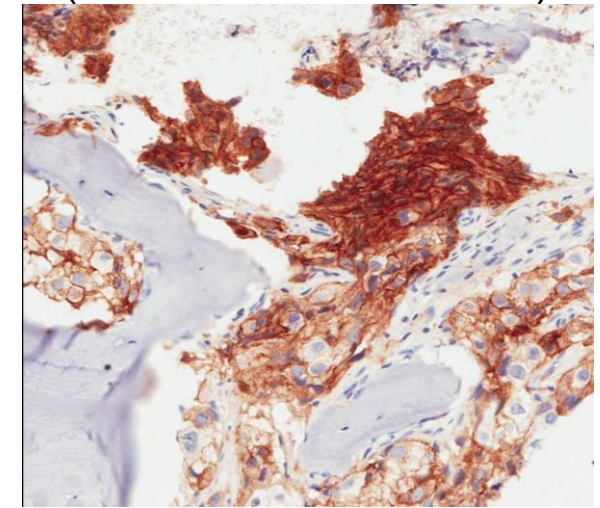
Prostate cancer
(soft tissue metastasis)



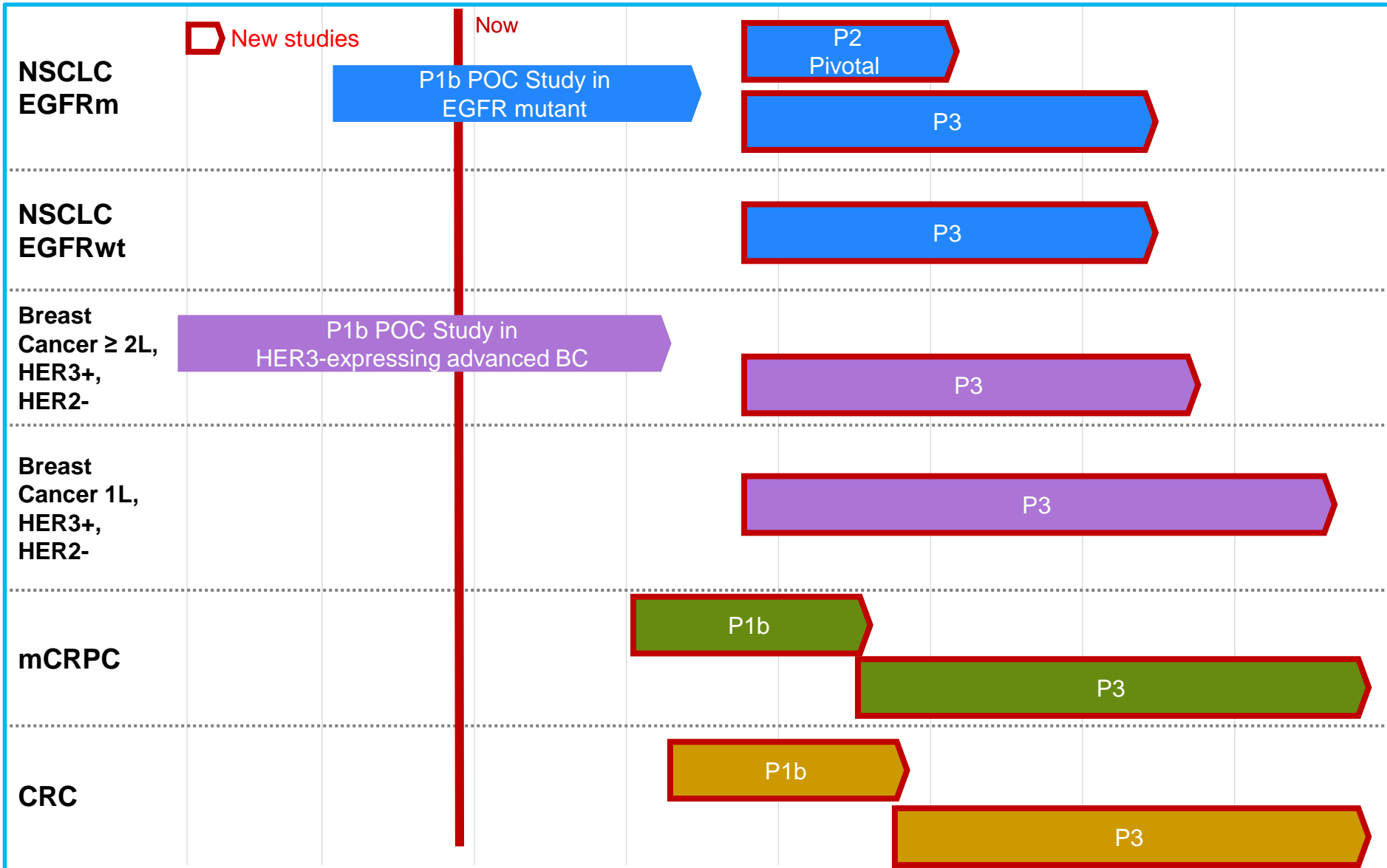
NSCLC



Malignant melanoma



Prostate cancer
(Bone marrow metastasis)



HER2 and HER3 ADCs' Overlap

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

Historical State: HR and HER2 as oncogenic drivers

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

All Patients
n=288,550

HR-/HER2+ 6.8% n=19,730	HR+/HER2+ 13.5% n=38,835
HR-/HER2- 12.5% n=36,125	HR+/HER2- 67.2% n=193,860

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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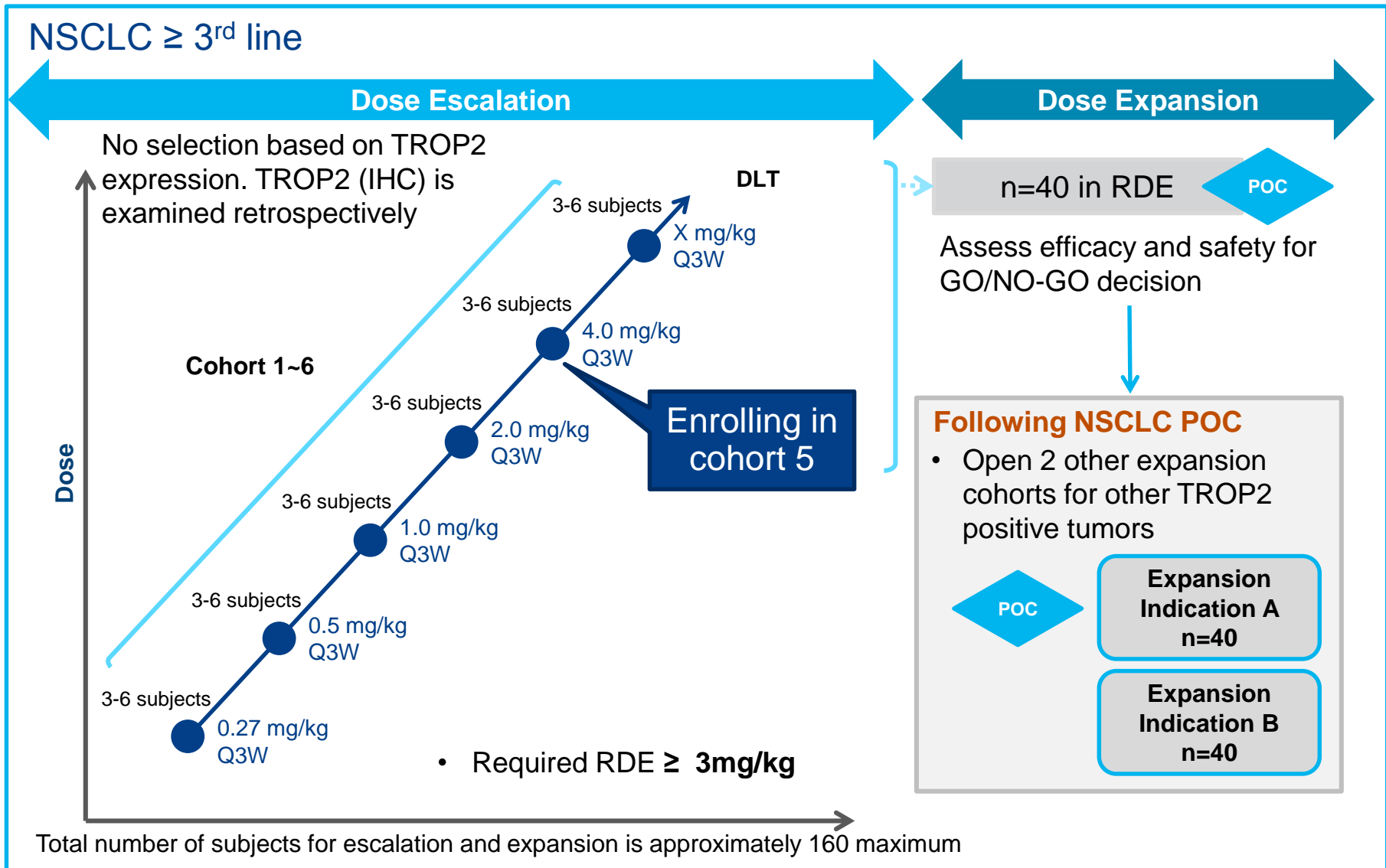
6 Pexidartinib

- Submission status
- ENLIVEN

7 Recap

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





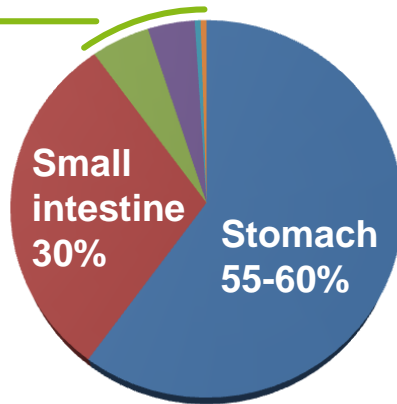
Dose escalation data to be presented at ASCO 2019

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

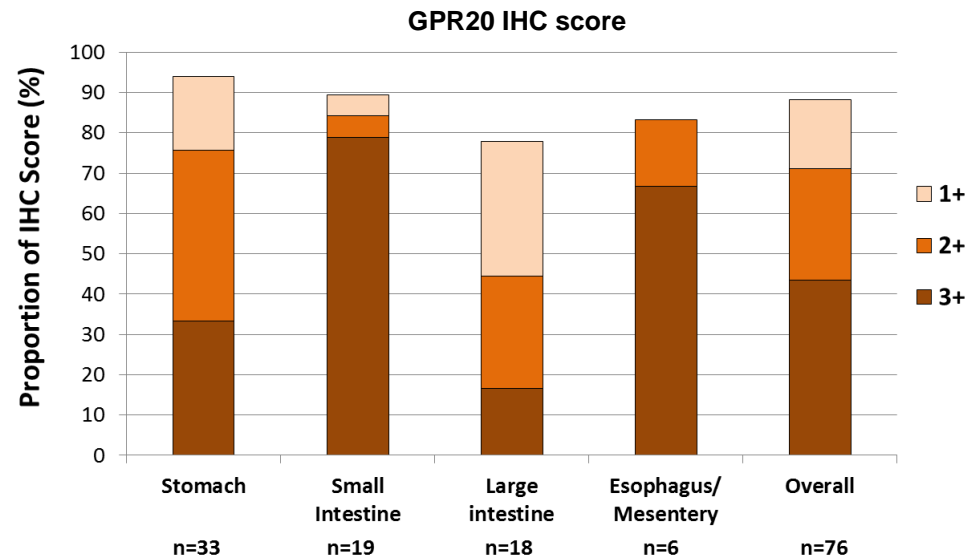
Condition		
Target	High expression	B7-H3 is overexpressed frequently in various tumors (more than HER2 in breast cancer)
	Tumor selectivity	B7-H3 is overexpressed in tumors with low expression in normal tissues
mAb	Internalization	Anti-B7-H3 ADC antibody internalization rate 19-27%/3hr, comparable to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

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

duodenum (5%)
colorectum (<5%)
esophagus (<1%)
appendix (<1%)



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

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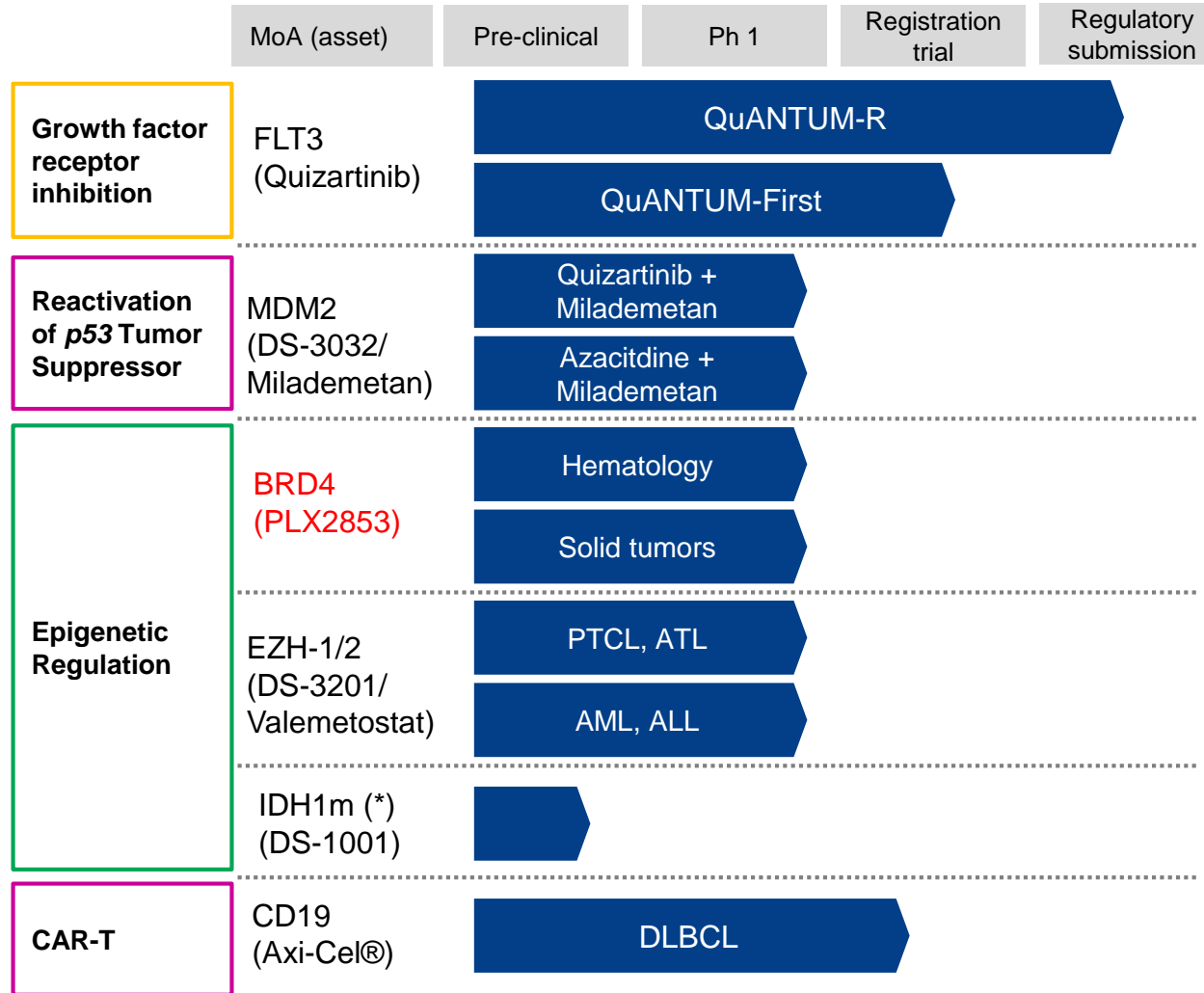
7 Recap

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AML/Hematology Franchise

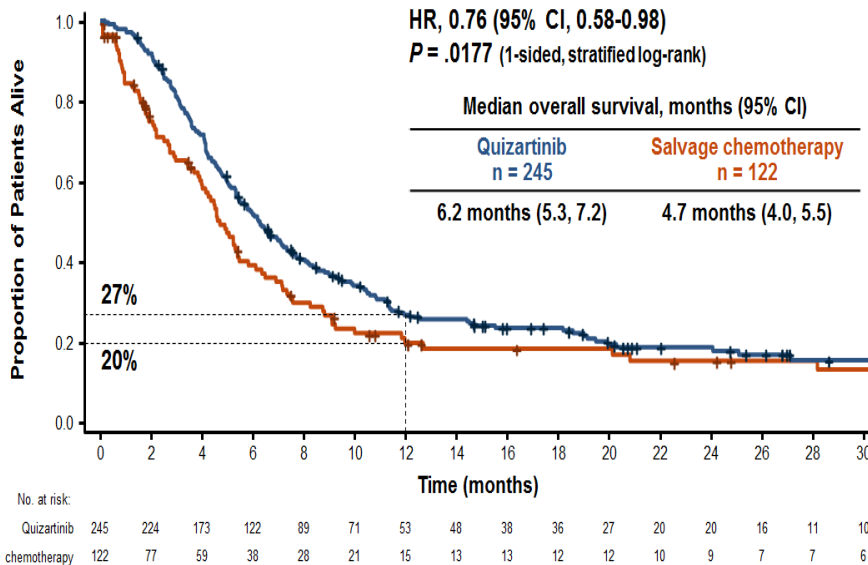


- ◆ Quicker development of combinations
- ◆ Address emergence of resistance

(*): 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

Quizartinib | Refractory / Relapsed FLT3-ITD AML



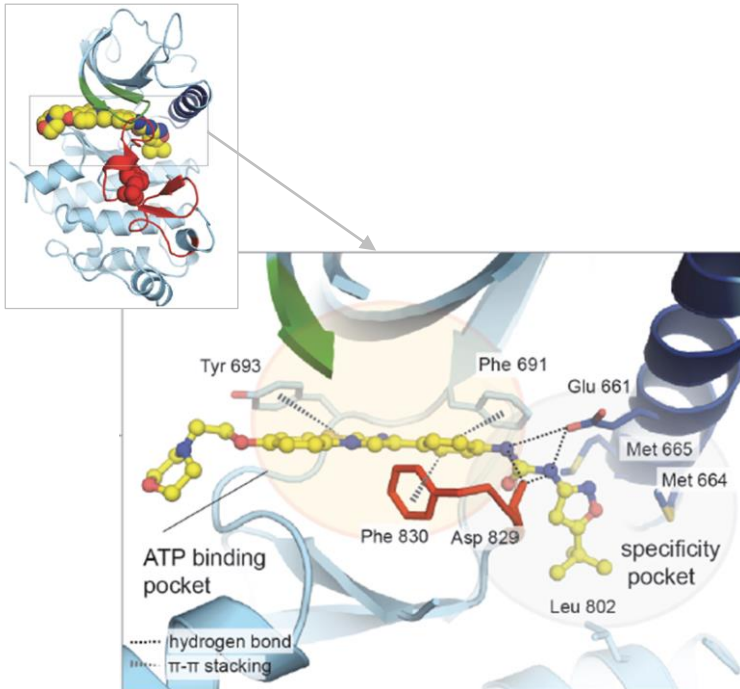
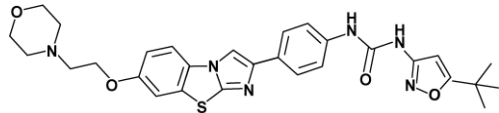
• Median follow-up: 23.5 months

- ◆ 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

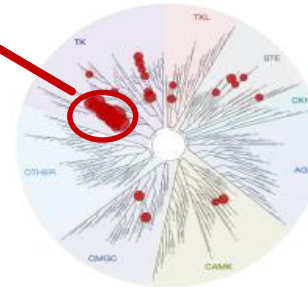
Highly Potent and Selective Type II Kinase Inhibitor

Type II kinase inhibitor: binds outside the ATP binding pocket



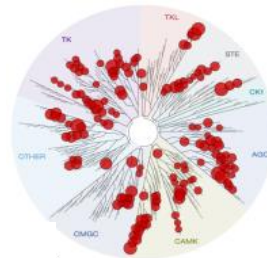
Quizartinib¹

FLT3
C-KIT

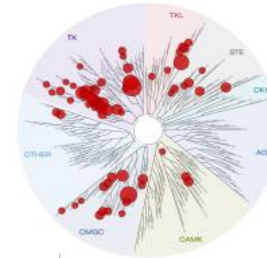


$K_d < 1 \text{ nM}$
 $1 \text{ nM} \leq K_d < 10 \text{ nM}$
 $10 \text{ nM} \leq K_d < 100 \text{ nM}$
 $100 \text{ nM} \leq K_d < 1000 \text{ nM}$

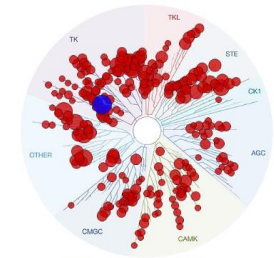
Midostaurin¹



Sorafenib¹

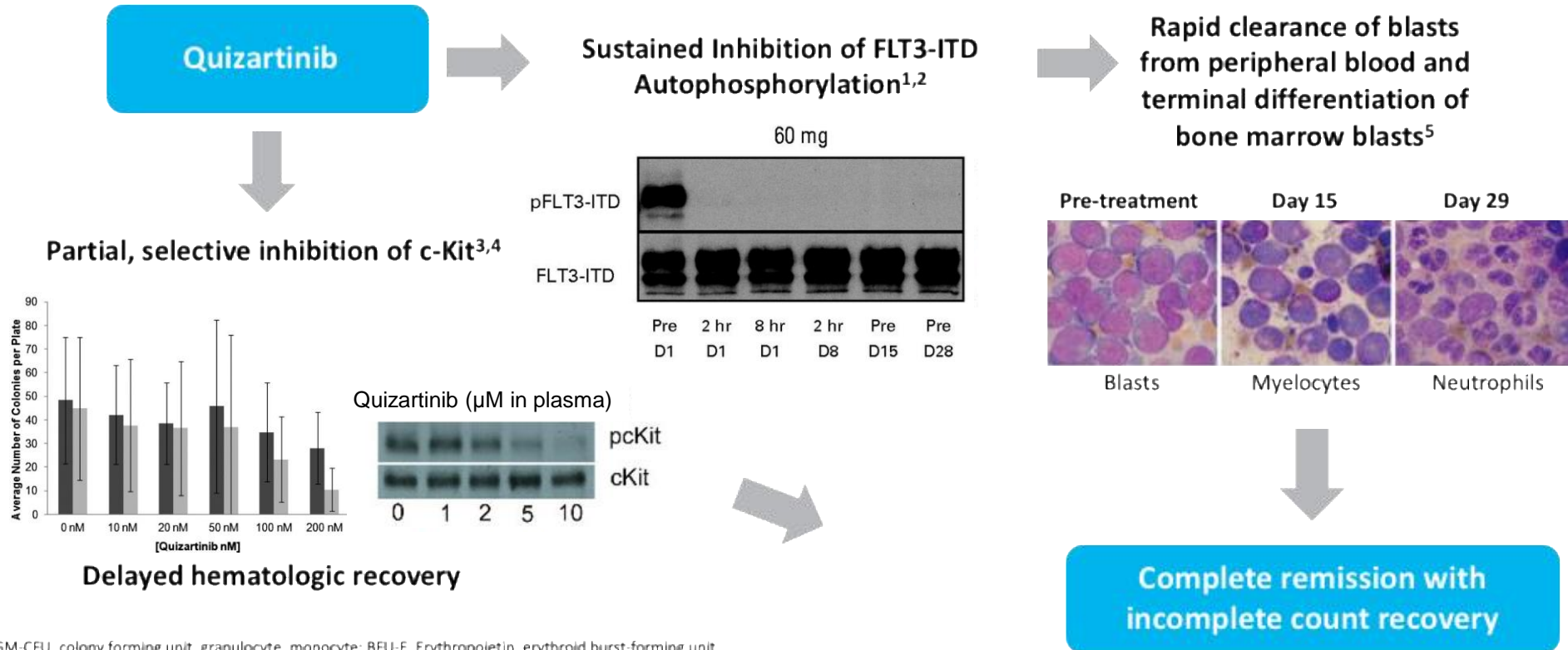


Gilteritinib²



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



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

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

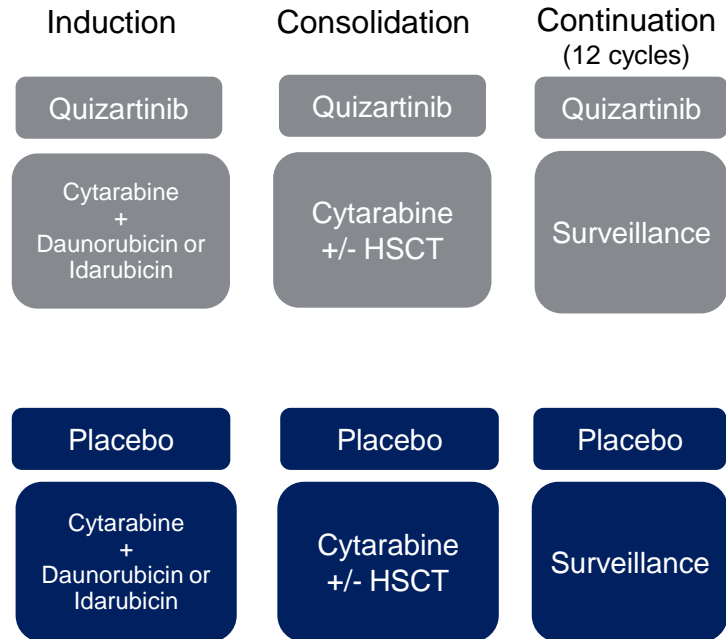


Newly Diagnosed AML
18-75 years of age
FLT-ITD(+)
N=536

Test arm:
Quizartinib add-on



Control arm:
Placebo



Primary endpoint: Event-free survival

Competitive advantage: ahead of competition; mostly enrolled

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

Incidence

Localized TGCT (extremities)

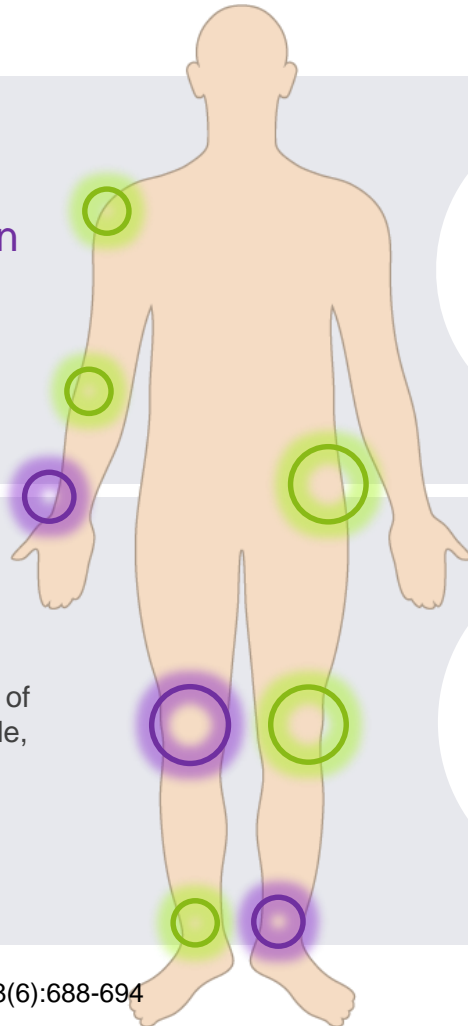
WW: 10.2 cases per million

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

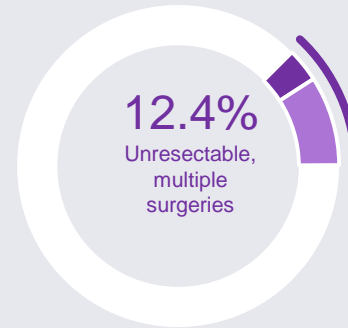
Diffuse TGCT

WW: 4.1 cases per million

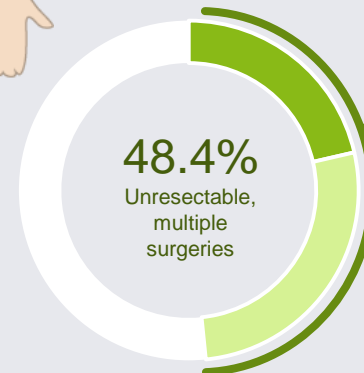
most commonly affects the knee (75% of cases), followed by the hip (15%), ankle, elbow, and shoulder



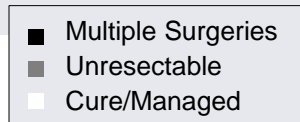
Prevalence* (in 2018)



Over 30 years
10,501 US
10,476 EU



Over 30 years
14,800 US
14,770 EU



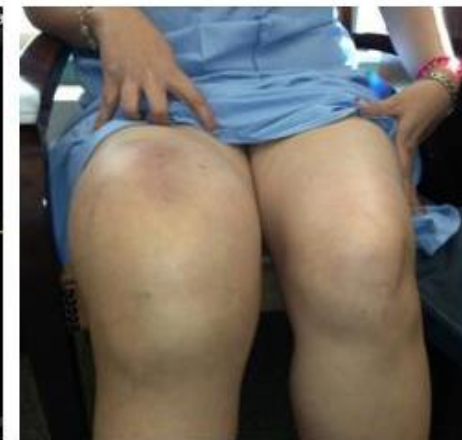
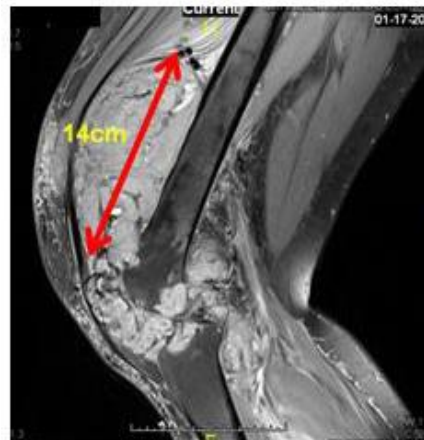
Source: Mastboom et al. *Acta Orthop.* 2017; 88(6):688-694

*Unresectable prevalent patient population

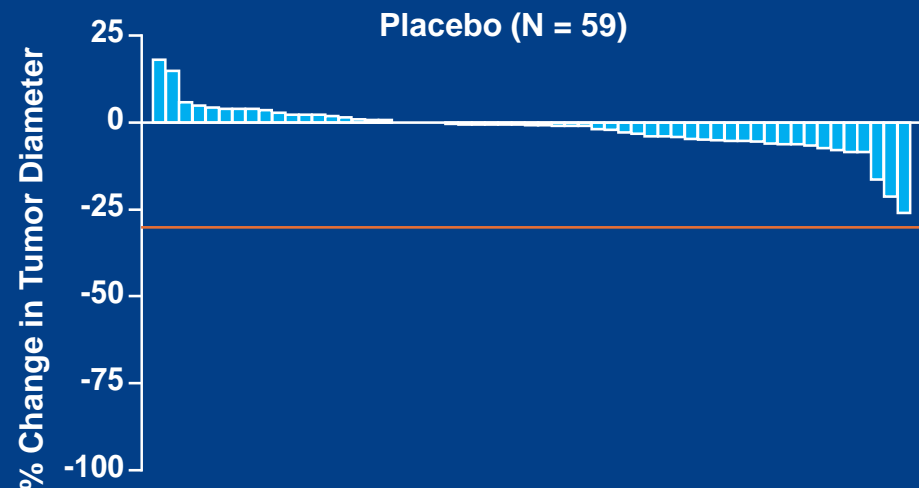
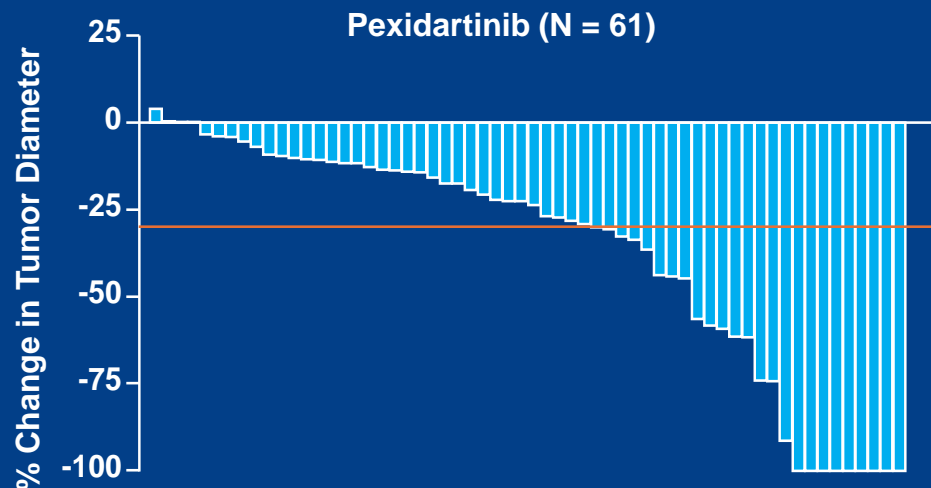
TGCT: tenosynovial giant cell tumor

“Pexidartinib” 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



- ◆ 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 $\geq 3 \times$ ULN	20 (33)	0	4 (13)
TBili $\geq 2 \times$ ULN	3 (5)	0	0
TBili $\geq 2 \times$ ULN and AST or ALT $\geq 3 \times$ ULN	3* (5)	0	0

All had ALP $\geq 2.5 \times$ ULN.

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Cancer Enterprise | Major Clinical Pipeline

As of Dec 2018



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 1 st / 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)
	Pexidartinib (CSF-1R)	TGCT				BTD (active submission)
Breakthrough	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



ADC Franchise

- ◆ Topline DS-8201 DESTINY-Breast01 results and update on potential 1H 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



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HER3 ADCs

 Clinical stage

	Project (Payload)	Potential Indication	Pre-Clinical	Ph 1	Pivotal
	U3-1402 Topoisomerase I inhibitor	Breast, NSCLC			
	MP-HER3-ADC Monomethyl Auristatin F	HER2+ BC post T-DM1			


TROP2 ADCs






 Clinical stage

	Project (Payload)	Potential Indication	Pre-Clinical	Ph 1	Pivotal
	DS-1062 Topoisomerase I inhibitor	NSCLC			
	IMMU-132 SN38 (Topoisomerase I inhibitor)	metastatic TNBC			


TNBC: triple-negative breast cancer




B7-H3 ADCs

 Clinical stage

	Project (Payload)	Potential Indication	Pre-Clinical	Ph 1	Pivotal
	DS-7300 Topoisomerase I inhibitor	Solid tumor			
	MGC018 Duocarmycin hydroxyBenzamide Azaidole	Advanced Solid Tumors			

GPR20 ADCs

 Clinical stage

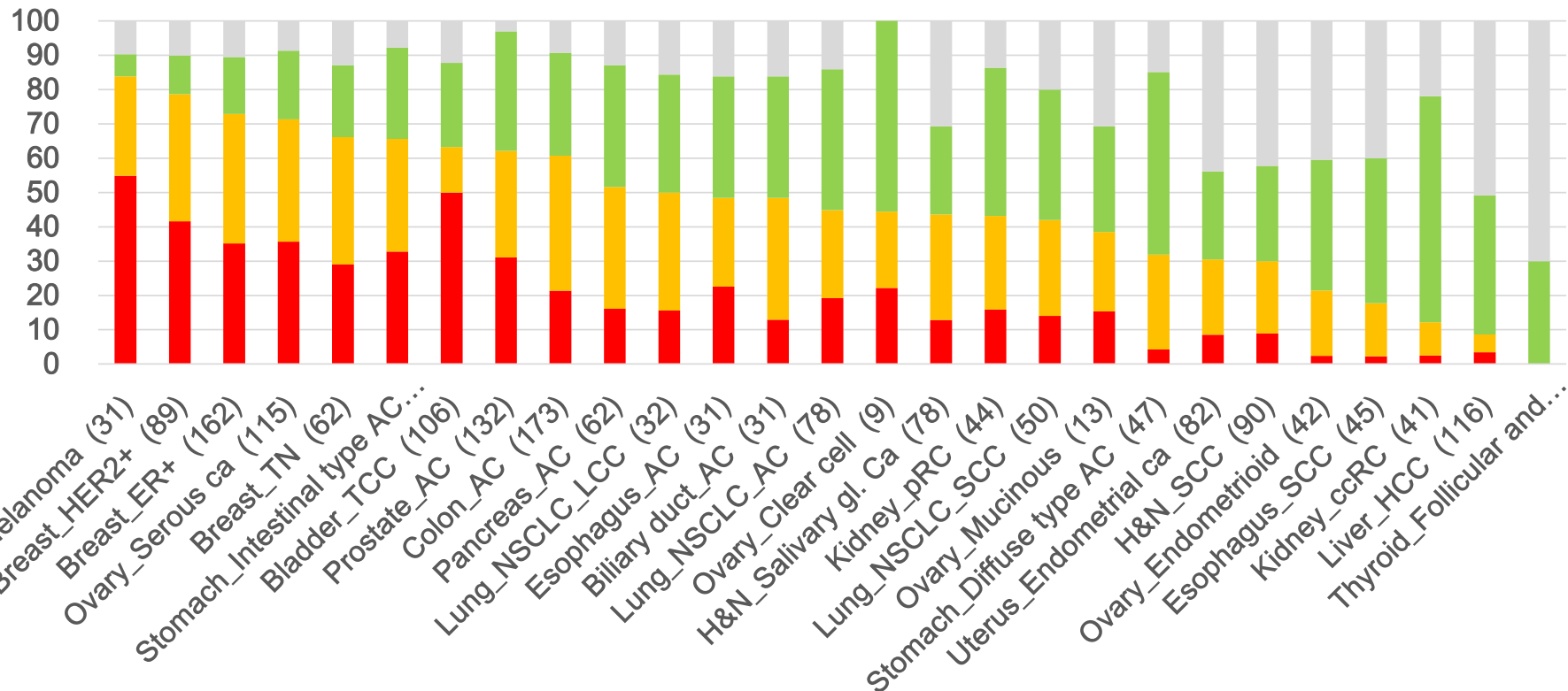
	Project (Payload)	Potential Indication	Pre-Clinical	Ph 1	Pivotal
	DS-6157 Topoisomerase I inhibitor	GIST			

GIST: Gastrointestinal stromal tumor

HER3 Protein Expression Across Cancers

HER3 Expression in Cancer

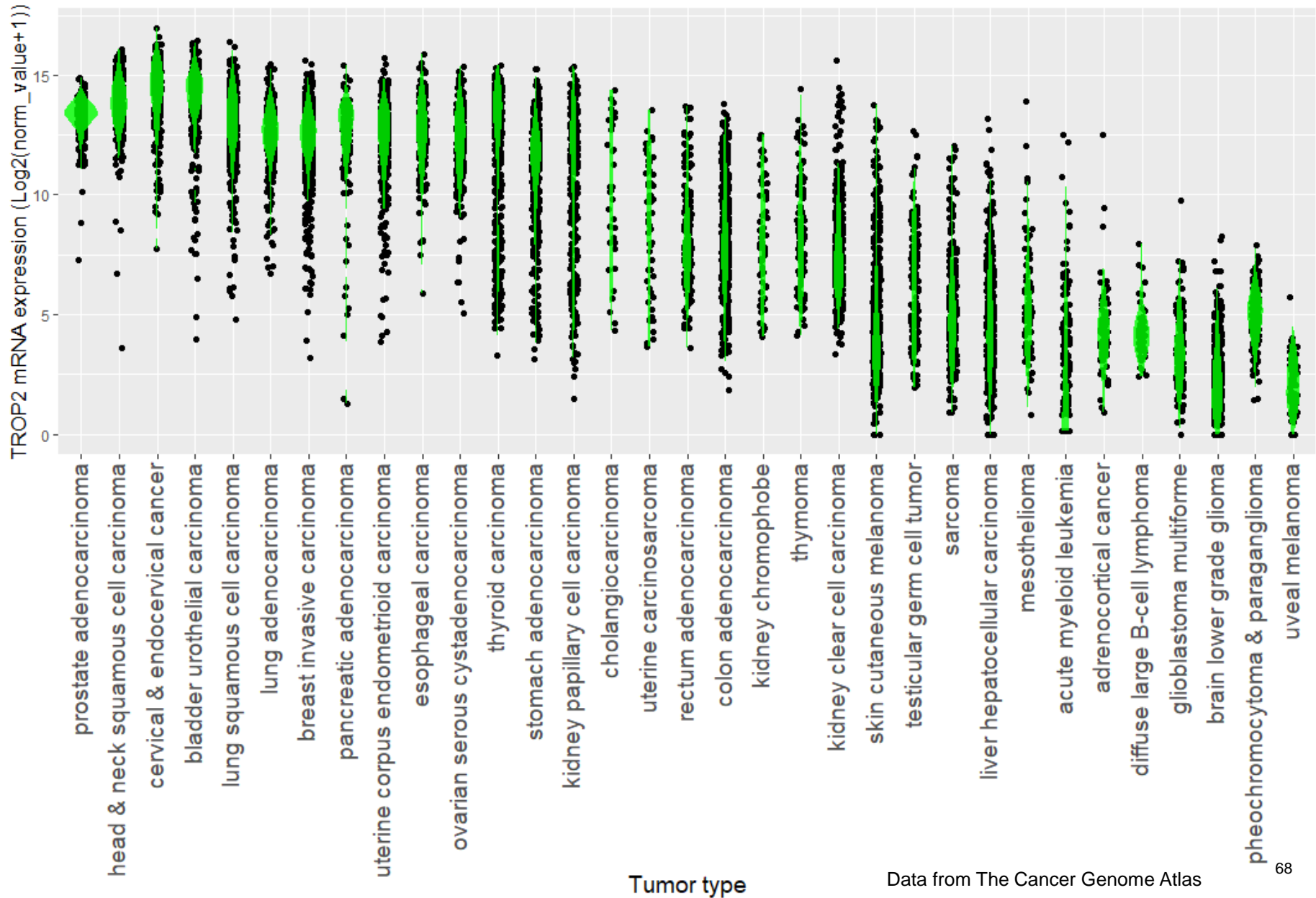
3+ 2+ 1+ 0



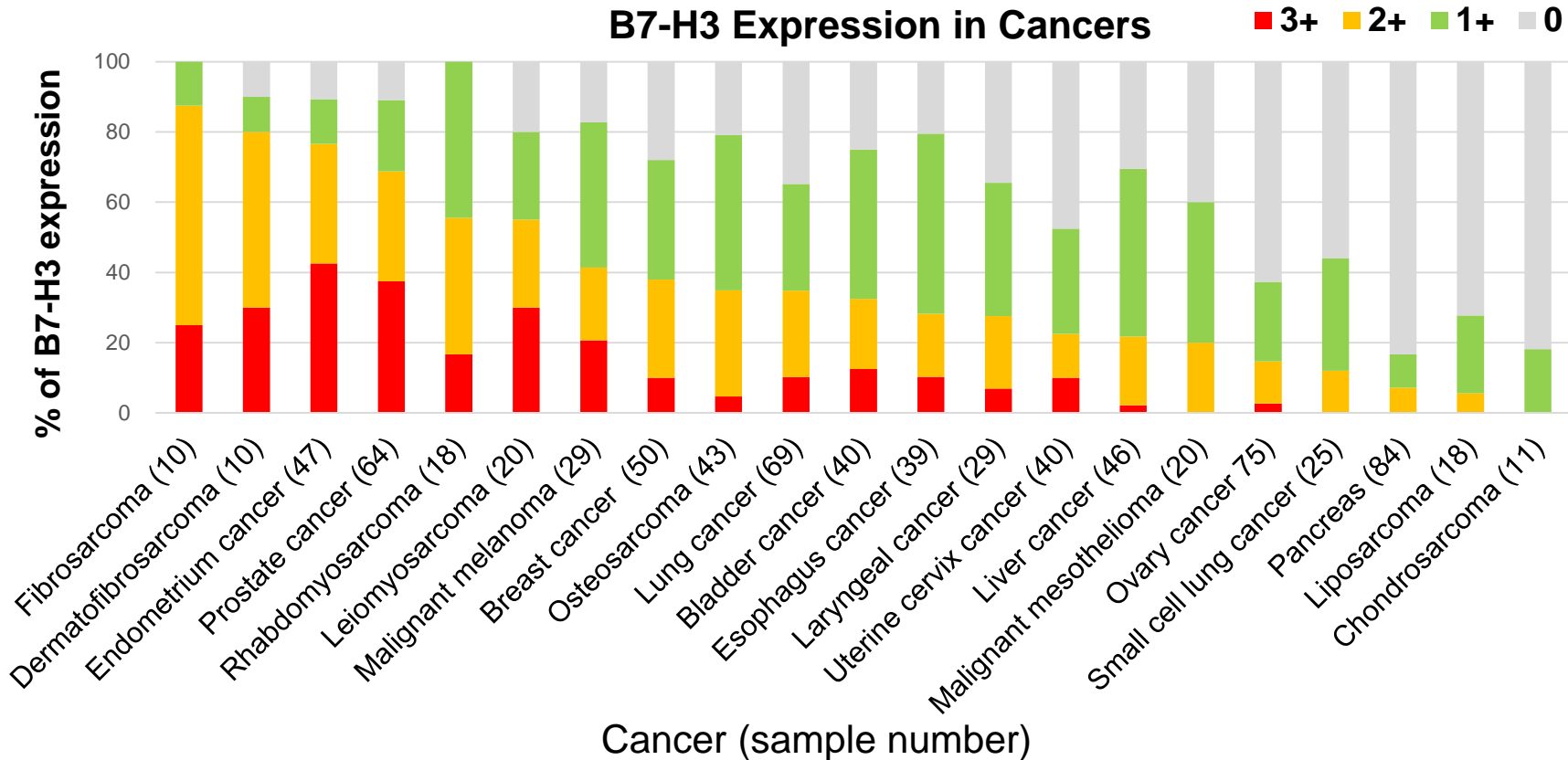
Data from internal analysis using in-house IHC assay of cancer tissue samples (TMA samples). Majority of tissue from primary tumor. Internal pathologist scored following internal HER3 scoring criteria.

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

TROP2 Expression in Various Cancers



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