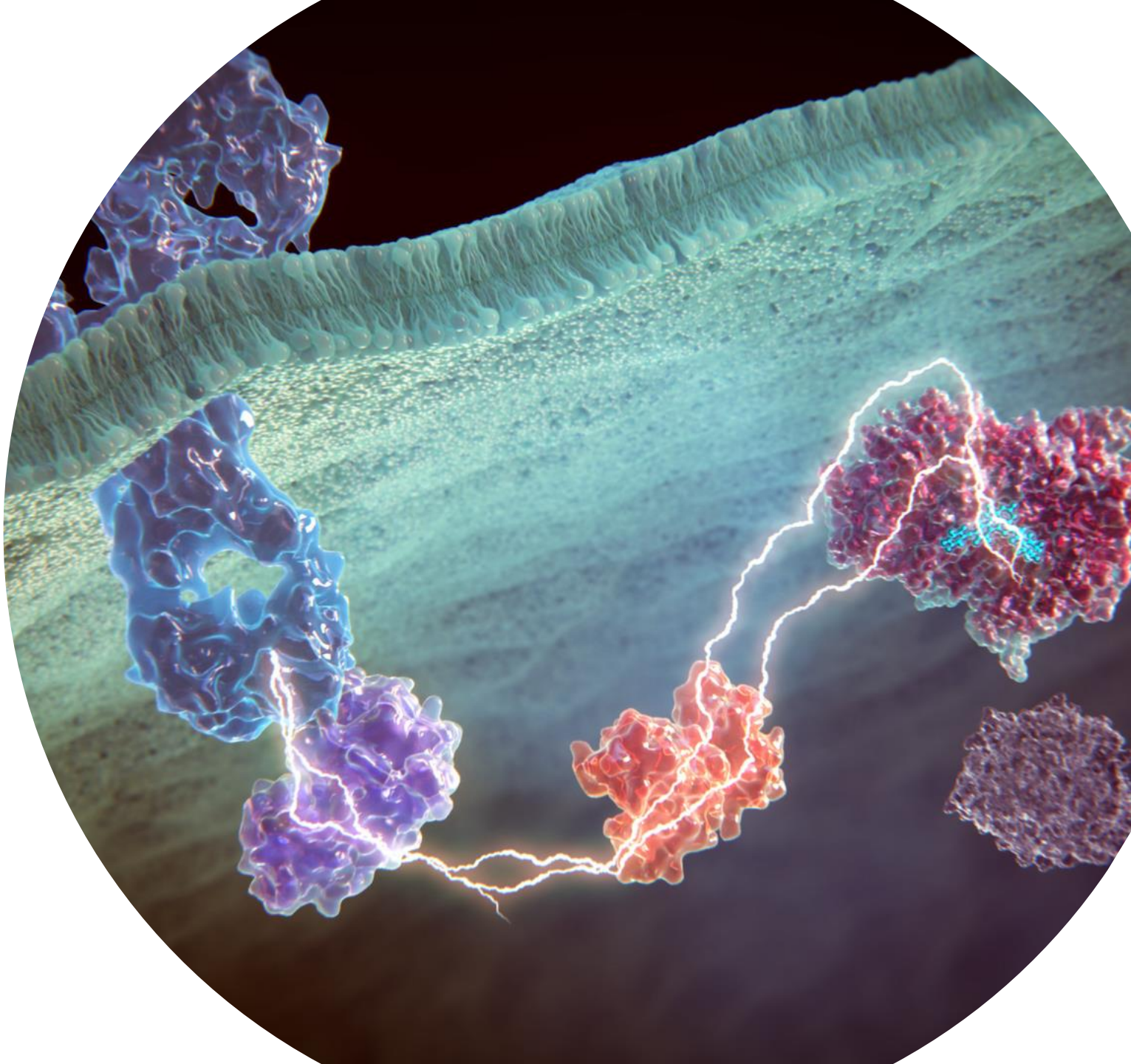
AstraZeneca

Meet AZN management: American Society of Clinical Oncology (ASCO) Cancers Symposium 2022

For investors and analysts



6 June 2022

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AstraZeneca

1. AstraZeneca @ ASCO 2022

Pascal Soriot
Chief Executive Officer

Speakers

Dr Aleix Prat

Senior Investigator, DESTINY-Breast04 trial and Head Medical Oncology, Hospital Clínic of Barcelona

David Fredrickson

Executive Vice President, Oncology Business

Cristian Massacesi

Chief Oncology Development Officer and Chief Medical Officer (for Q&A)

Mika Sovak

Vice President and Global Franchise Head *Enhertu,* R&D (for Q&A)

Pascal Soriot

Chief Executive Officer

Susan Galbraith

Executive Vice President, Oncology R&D

Sunil Verma

Senior Vice President, Oncology Medical (for Q&A)

Andy Barnett

VP, Head of Investor Relations

Agenda

1. AstraZeneca @ ASCO 2022
   Pascal Soriot
2. *Enhertu:* the story so far
   Susan Galbraith
3. *Enhertu* DESTINY-Breast04 trial
   Dr Aleix Prat
4. DESTINY-Breast04: redefining cancer treatment
   Dave Fredrickson
5. What's next for AZ in Oncology?
   Susan Galbraith
6. Q&A

AstraZeneca: Oncology 2025+

Delivering growth through innovation

Broad late-stage pipeline

Continued investment in clinical stage pipeline

7 Oncology NMEs
in Phase III

>90 Oncology NME or major LCM
projects in Phase II and III

Across a number of areas of high unmet need, with first or best in class potential

Innovative early-stage R&D

Using precision approaches and new modalities to create new SoCs and move earlier

- ADCs, bispecifics, PROTACs, cell therapy including T-cell engagers
- Orthogonal combinations
- Digital health
- Multi-omics led research

Strategic business development

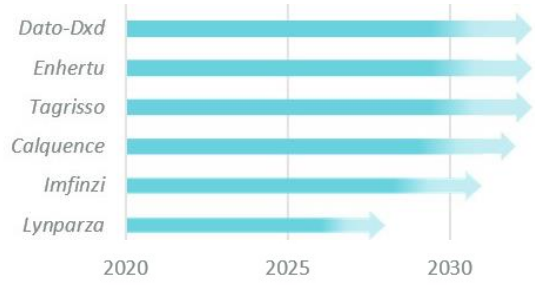
Supplementing the pipeline with smart deal making

- *Enhertu* & Dato-DXd (Daiichi Sankyo)
- CLDN18.2 (Harbour Biomed)
- Longitudinal health data (Tempus)
- Companion diagnostics (GRAIL)

Robust LCM and LoE profile

TAGRISSO® osimertinib
CALQUENCE® (acalabrutinib) 100 mg capsules
IMFINZI® durvalumab Injection for Intravenous Use 50 mg/mL
ENHERTU® fam-trastuzumab deruxtecan-nxki 20 mg/mL INJECTION FOR INTRAVENOUS USE
Lynparza™ olaparib
Orpathys® savolitinib

US LoE for selected medicines



NME = new molecular entity; LCM = life-cycle management; SoC = standard of care; ADC = antibody-drug conjugate; PROTAC = Proteolysis-targeting chimera; Dato-DXd = datopotamab deruxtecan; CLDN18.2 = isoform 2 of tight junction protein claudin-18; LoE = loss of exclusivity.

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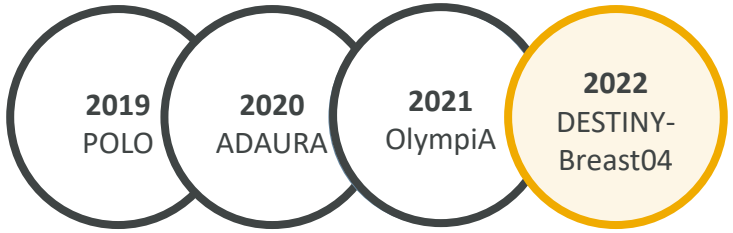
4 years of Plenary Presentations



108 abstracts with 96 presentations

- **One** plenary presentation
- **9** oral presentations
- **15** poster discussions
- **71** posters
- **12** abstracts (publication only)

2022 ASCO ANNUAL MEETING

Data highlights

- ***Enhertu* in breast cancer**
  DESTINY-Breast04
- ***Calquence* in CLL**
  Five-year follow up from ASCEND and ELEVATE-TN
- **MEDI5752 in RCC**
  First results from Phase I trial
- ***Lynparza* in prostate cancer**
  Additional safety data from PROpel

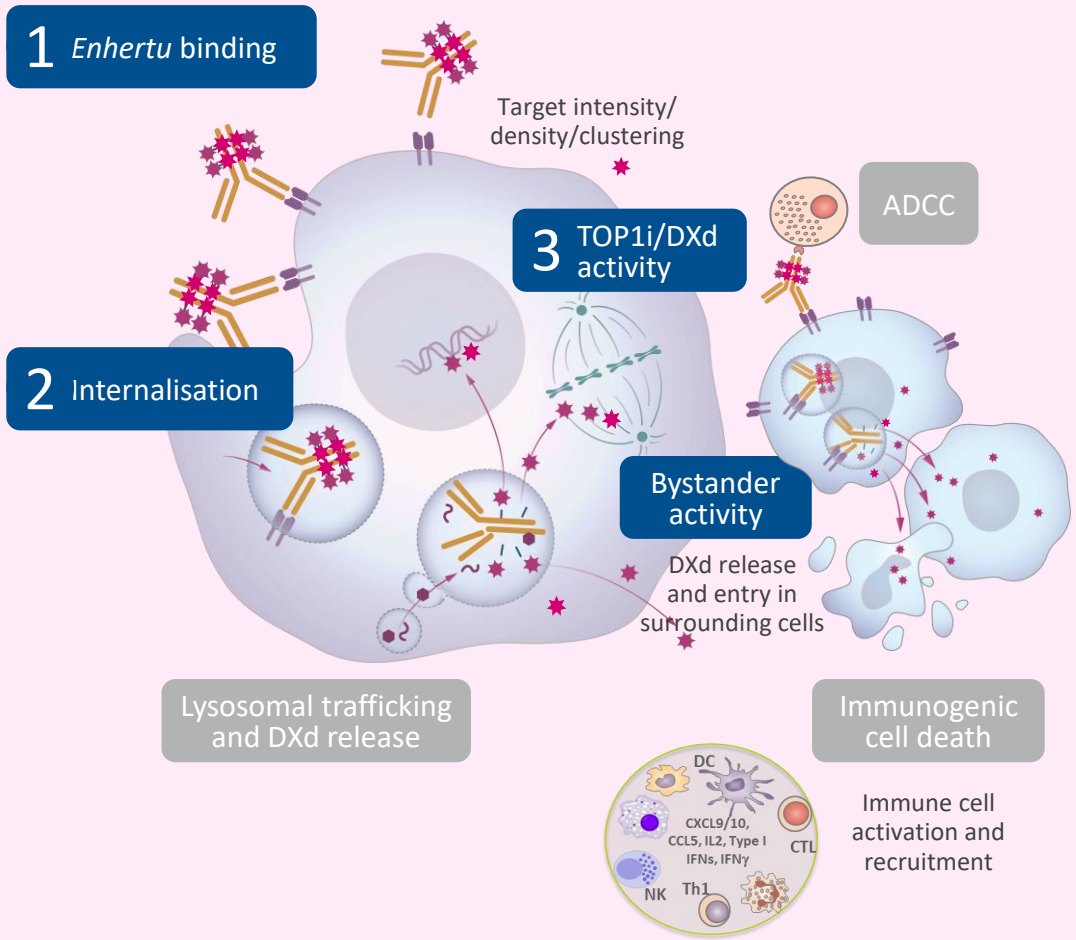
CLL = chronic lymphocytic leukaemia; RCC = renal cell carcinoma.

AstraZeneca

2. *Enhertu:* the story so far

Susan Galbraith
EVP Oncology R&D

Enhertu: best-in-class HER2-directed antibody drug conjugate



Achieved

- ☑ Improve on established **HER2+ SoC** in metastatic breast cancer
- ☑ Expand to multiple **HER2-targetable** tumour types
- ☑ **Redefine breast cancer** classification – new HER2-low segment in HR+/-

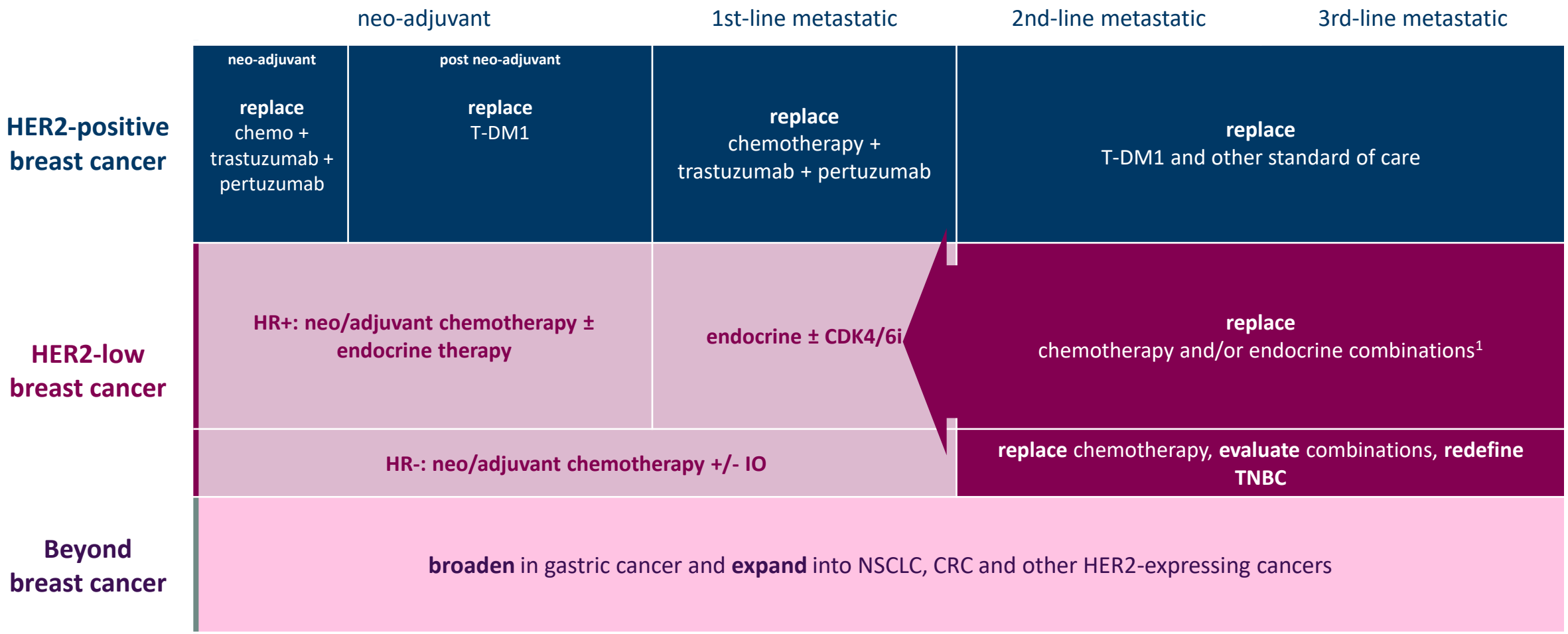
Ongoing

- ❑ Improve long term survival and cure rate in **early stage** HER2+/low disease
- ❑ **Orthogonal combinations** including IO and DDR

HER2-positive = human epidermal growth factor receptor 2 positive; T-DXd = trastuzumab deruxtecan (*Enhertu*); DXd = deruxtecan; TOP1i = topoisomerase I inhibition; ADCC = antibody dependent cell-mediated cytotoxicity; DC = dendritic cell; CTL = cytotoxic T lymphocyte; Th1 = T-cell helper 1; NK = natural killer cell; CXCL9, 10 = chemokine (CXC motif) ligand 9 and ligand 10; CCL5 = chemokine (CC motif) ligand 5; IL2 = interleukin 2; IFNs = interferons; IFNγ = interferon gamma; SoC = standard of care; HR+ = hormone-receptor positive; HR- = hormone-receptor negative; IO = immuno-oncology; DDR = DNA damage response.

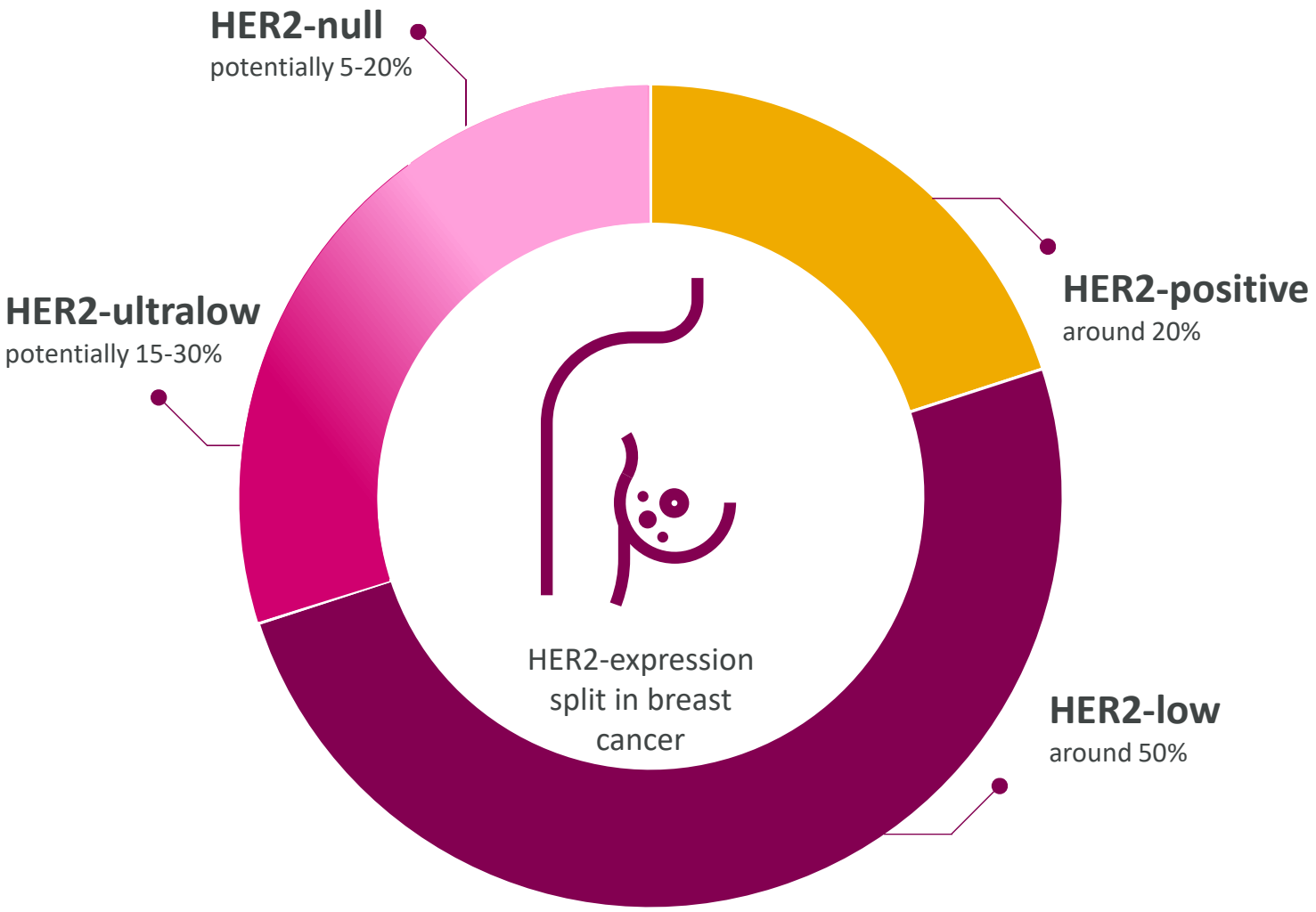
Enhertu has demonstrated efficacy across multiple cancer types

Leading data in breast and expanding into gastric, lung and colorectal

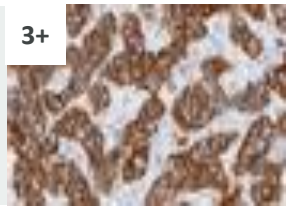


1. Ineligible to endocrine therapy and in those who are endocrine refractory/resistant. HER2-positive = human epidermal growth factor receptor 2 positive; HER2-low = human epidermal growth factor receptor 2 low; HR+ = hormone-receptor positive; HR- = hormone-receptor negative; CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; T-DM1 = trastuzumab emtansine; IO = immuno-oncology; TNBC = triple negative breast cancer; NSCLC = non-small cell lung cancer; CRC = colorectal cancer.

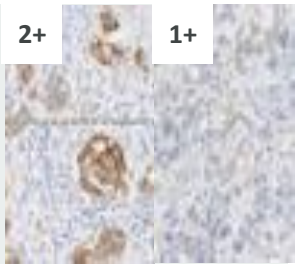
Enhertu: potential for activity across spectrum of HER2 expression



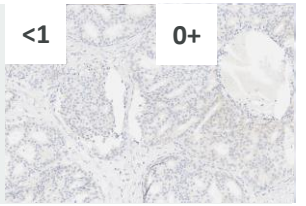
HER2-positive breast cancer
IHC 3+: ~2 million HER2 receptors per cell



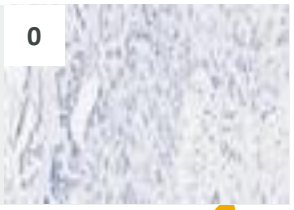
HER2-low breast cancer
IHC 2+: ~200k-500k HER2 receptors per cell
IHC 1+: ~100k-200k HER2 receptors per cell



HER2-ultralow breast cancer
IHC >0 and <1+: ~20k-100k receptors per cell



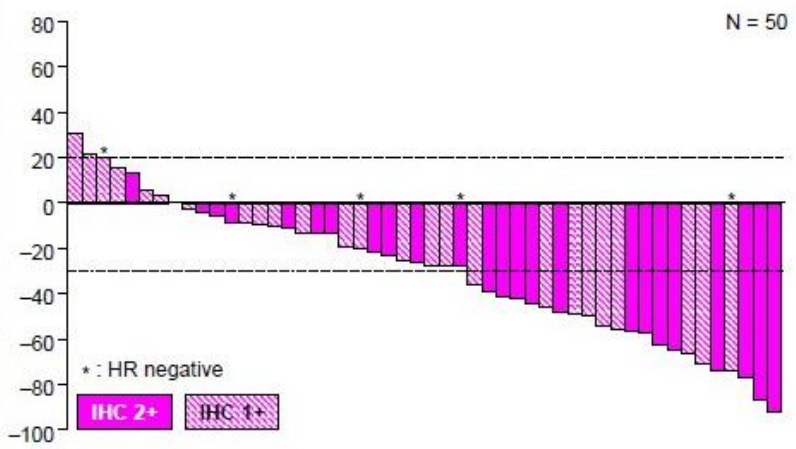
HER2-null breast cancer
IHC 0: ~20k receptors per cell



Sources: AstraZeneca data on file; Tarantino P, et al. *J Clin Oncol*. 2020; Schettini F, et al. *NPJ Breast Cancer*. 2021; Owens et al., *Clinical Breast Cancer* 2004; Lambein et al., *American Journal of Clinical Pathology* 2013, CAncerMPACT (2017); Schettini et al. ESMO BC 2020; Nuciforo et al., Molec Onc. 10, 2016; Scott et al. ASCO 2021 Abstract #1021.
HER2 = human epidermal growth factor receptor 2; IHC = immunohistochemistry.

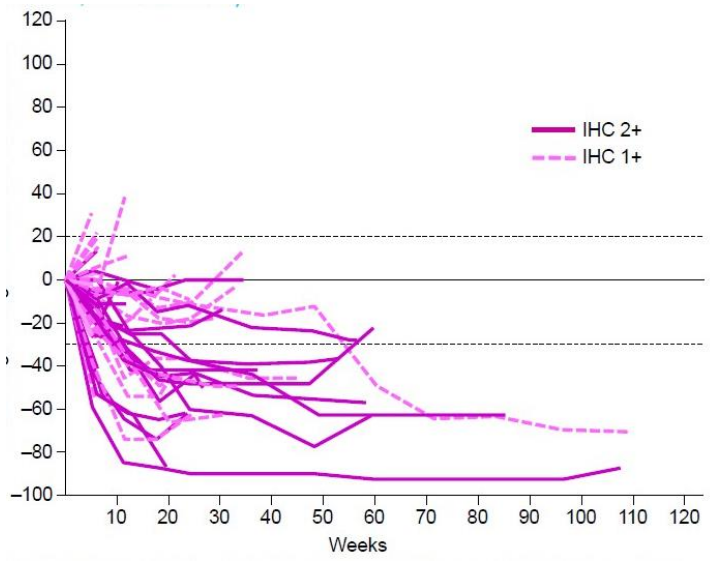
Results from the J101 Phase I trial paved the way for *Enhertu* in HER2-low breast cancer

Best percentage change in sum of target lesion size from baseline by IHC status



ORR: 44.2% | mDOR: 8.1m | mPFS 7.6m

Percentage change in sum of target lesion size from baseline by IHC status



Promising antitumor activity seen in heavily pretreated HER2-low patients

Efficacy seen in post-CDK4/6 inhibitors and IHC 1+ subgroups

Safety in HER2-low breast cancer was consistent with other *Enhertu* breast cancer trials

Source: Modi et al., SABCS 2018, Poster # P6-17-02.

HER2-low = human epidermal growth factor receptor 2 low; IHC = immunohistochemistry; HR- = hormone-receptor negative; CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; ORR = objective response rate; mDOR = median duration of response; mPFS = median progression-free survival.

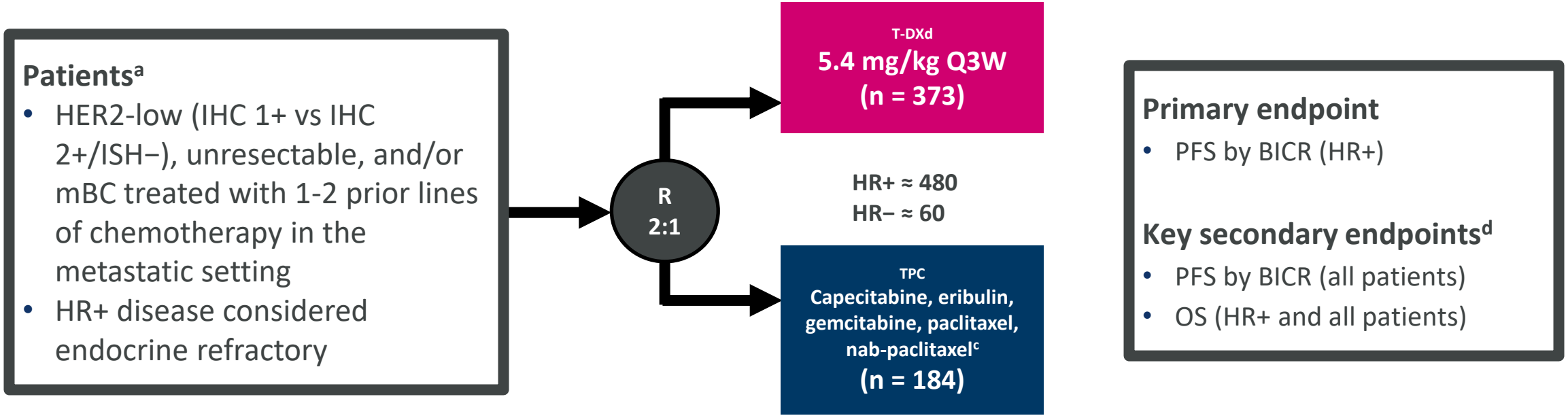
3. *Enhertu* Phase III DESTINY-Breast04 trial

Dr Aleix Prat

Senior Investigator, DESTINY-Breast04 trial, and Head Medical Oncology, Hospital Clínic of Barcelona

DESTINY-Breast04 trial design

First randomised Phase III trial of T-DXd for HER2-low mBC - An open label, multicenter trial



Stratification factors

- Centrally assessed HER2 status[b] (IHC 1+ vs IHC 2+/ISH−)
- 1 vs 2 prior lines of chemotherapy
- HR+ (with vs without prior treatment with CDK4/6 inhibitor) vs HR−

T-DXd = trastuzumab deruxtecan; HER2 = human epidermal growth factor receptor 2; HER2-low = human epidermal growth factor receptor 2 low; IHC = immunohistochemistry; ISH = in situ hybridization; mBC = metastatic breast cancer; HR+ = hormone-receptor positive; R = randomised; Q3W = every three weeks; TPC = treatment of physician's choice; PFS = progression-free survival; BICR = blinded independent central review; OS = overall survival; CDK4/6i = cyclin-dependent kinase 4/6 inhibitor.

[a]If patients had HR+ mBC, prior endocrine therapy was required. [b]Performed on adequate archived or recent tumor biopsy per ASCO/CAP guidelines using the VENTANA HER2/neu (4B5) investigational use only [IUO] Assay system. [c]TPC was administered accordingly to the label. [d]Other secondary endpoints included ORR (BICR and investigator), DOR (BICR), PFS (investigator), and safety; efficacy in the HR− cohort was an exploratory endpoint.

Baseline characteristics

	Hormone receptor-positive		All patients	
	T-DXd (n = 331)	TPC (n = 163)	T-DXd (n = 373)	TPC (n = 184)
Age, median (range), years	57 (32-80)	56 (28-80)	58 (32-80)	56 (28-80)
Female, n (%)	329 (99)	163 (100)	371 (99)	184 (100)
Region, n (%)				
Europe + Israel	149 (45)	73 (45)	166 (45)	85 (46)
Asia	128 (39)	60 (37)	147 (39)	66 (36)
North America	54 (16)	30 (18)	60 (16)	33 (18)
HER2 status (IHC), n (%)				
1+	193 (58)	95 (58)	215 (58)	106 (58)
2+/ISH−	138 (42)	68 (42)	158 (42)	78 (42)
ECOG performance status, %				
0	187 (56)	95 (58)	200 (54)	105 (57)
1	144 (44)	68 (42)	173 (46)	79 (43)
Hormone receptor[a], n (%)				
Positive	328 (99)	162 (99)	333 (89)	166 (90)
Negative	3 (1)	1 (1)	40 (11)	18 (10)
Brain metastases at baseline, n (%)	18 (5)	7 (4)	24 (6)	8 (4)
Liver metastases at baseline, n (%)	247 (75)	116 (71)	266 (71)	123 (67)
Lung metastases at baseline, n (%)	98 (30)	58 (36)	120 (32)	63 (34)

HER2 = human epidermal growth factor receptor 2; IHC = immunohistochemistry; ISH = in situ hybridization; ECOG = Eastern Cooperative Oncology Group; T-DXd = trastuzumab deruxtecan; TPC = treatment of physician's choice.

[a]Hormone receptor status is based on data collected using the interactive web/voice response system at the time of randomization, which includes mis-stratified patients.

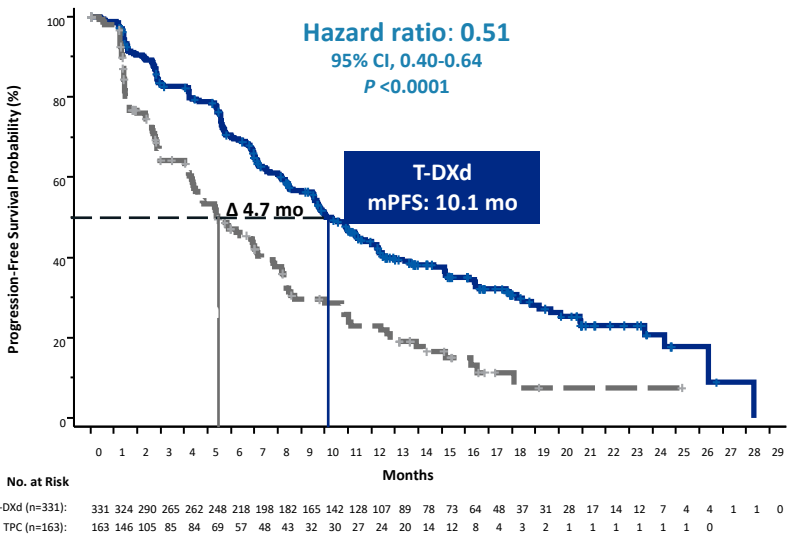
Prior therapies

	Hormone receptor-positive		All patients	
	T-DXd (n = 331)	TPC (n = 163)	T-DXd (n = 373)	TPC (n = 184)
Lines of systemic therapy (metastatic setting)				
Median number of lines (range)	3 (1-9)	3 (1-8)	3 (1-9)	3 (1-8)
Number of lines, n (%)				
1	23 (7)	14 (9)	39 (10)	19 (10)
2	85 (26)	41 (25)	100 (27)	53 (29)
≥3	223 (67)	108 (66)	234 (63)	112 (61)
Lines of chemotherapy (metastatic setting)				
Median number of lines (range)	1 (0-3)	1 (0-2)	1 (0-3)	1 (0-2)
Number of lines, n (%)				
0	1 (0.3)	1 (0.6)	1 (0.3)	1 (0.5)
1	203 (61.3)	93 (57.1)	221 (59.2)	100 (54.3)
2	124 (37.5)	69 (42.3)	145 (38.9)	83 (45.1)
≥3	3 (0.9)	0	6 (1.6)	0
Lines of endocrine therapy (metastatic setting)				
Median number of lines (range)	2 (0-7)	2 (0-6)	2 (0-7)	2 (0-6)
Number of lines, n (%)				
0	28 (8)	17 (10)	60 (16)	34 (18)
1	105 (32)	49 (30)	108 (29)	51 (28)
2	110 (33)	53 (33)	115 (31)	54 (29)
≥3	88 (27)	44 (27)	90 (24)	45 (24)
Prior targeted cancer therapy, n (%)				
Targeted therapy	259 (78)	132 (81)	279 (75)	140 (76)
CDK4/6 inhibitor	233 (70)	115 (71)	239 (64)	119 (65)

CDK4/6 = cyclin-dependent kinase 4/6; T-DXd = trastuzumab deruxtecan; TPC = treatment of physician's choice.

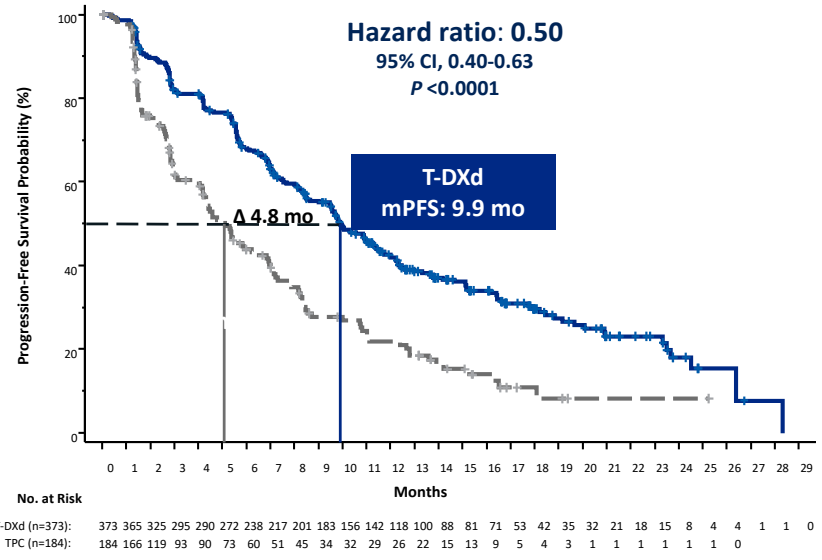
Progression-free survival by blinded independent central review

Hormone receptor positive



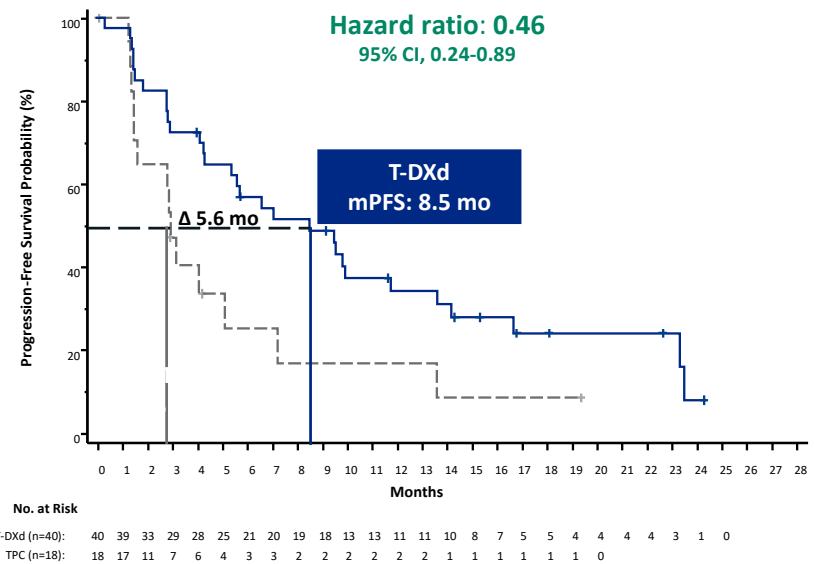
	T-DXd	TPC
mPFS, mo	10.1 mo	5.4 mo
HR (95% CI)	**0.51 (0.40-0.64)**	
	***P* <0.0001**	

Intention to treat



	T-DXd	TPC
mOS, mo	9.9 mo	5.1 mo
HR (95% CI)	**0.50 (0.40-0.63)**	
	***P* <0.0001**	

Hormone receptor negative

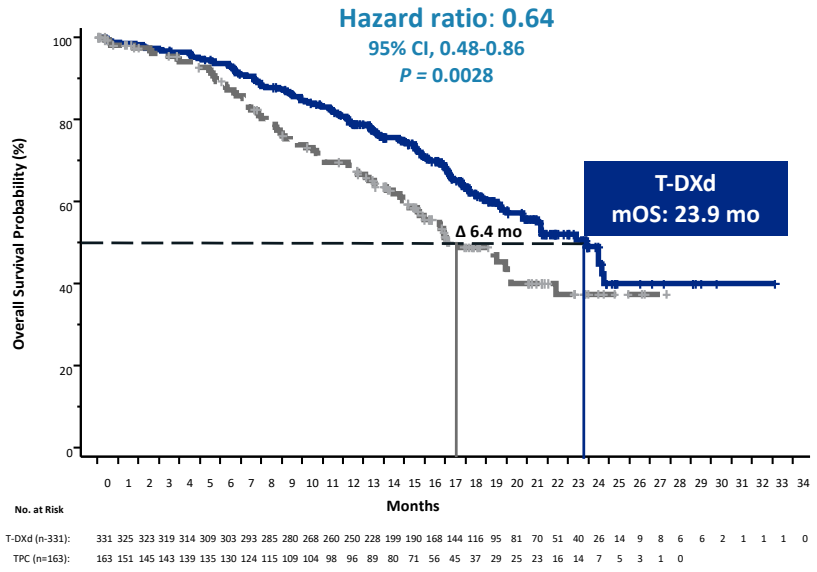


	T-DXd	TPC
mOS, mo	8.5 mo	2.9 mo
HR (95% CI)	**0.46 (0.24-0.89)**	
	(Exploratory endpoint)	

PFS by blinded independent central review.
CI = confidence interval; T-DXd = trastuzumab deruxtecan; TPC = treatment of physician's choice; mPFS = median progression-free survival.

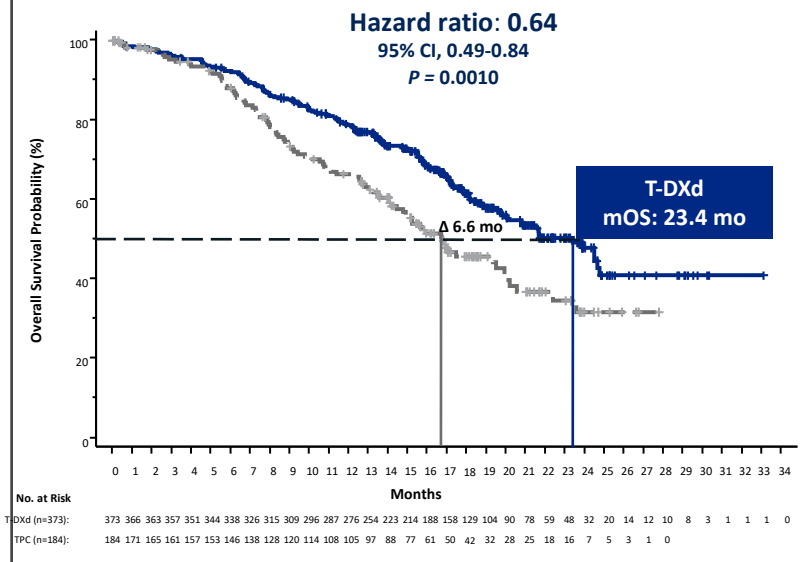
Overall survival by blinded independent central review

Hormone receptor positive



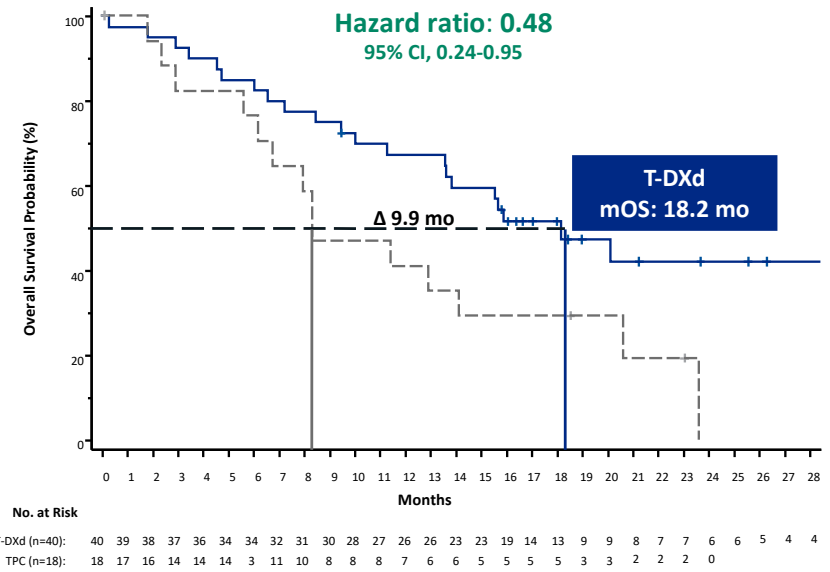
	T-DXd	TPC
mOS, mo	23.9 mo	17.5 mo
HR (95% CI)	**0.64 (0.48-0.86)**	
	***P* <0.0001**	

Intention to treat



	T-DXd	TPC
mOS, mo	23.4 mo	16.8 mo
HR (95% CI)	**0.64 (0.49-0.84)**	
	***P* <0.0010**	

Hormone receptor negative



	T-DXd	TPC
mOS, mo	18.2 mo	8.3 mo
HR (95% CI)	**0.48 (0.24-0.95)**	
	(Exploratory endpoint)	

CI = confidence interval; T-DXd = trastuzumab deruxtecan; TPC = treatment of physician's choice; mOS = median overall survival.

PFS subgroup analysis in HR+ cohort

	No. of Events/No. of Patients		mPFS, months (95% CI)		Hazard Ratio for Disease Progression or Death (95% CI)
	T-DXd	TPC	T-DXd	TPC	
Prior CDK4/6 inhibitors					
Yes	149/233	74/115	10.0 (8.3-11.4)	5.4 (4.0-7.8)	0.55 (0.42-0.73)
No	60/96	35/47	11.7 (9.5-17.7)	5.9 (4.3-8.2)	0.42 (0.28-0.64)
IHC status					
IHC 1+	119/192	66/96	10.3 (8.6-12.3)	5.3 (4.1-7.8)	0.48 (0.35-0.65)
IHC 2+/ISH−	92/139	44/67	10.1 (8.2-12.2)	5.9 (4.3-7.9)	0.55 (0.38-0.80)
Prior lines of chemotherapy					
1	129/203	63/93	10.9 (8.5-12.3)	6.8 (4.5-8.2)	0.54 (0.40-0.73)
≥2	81/127	47/69	9.9 (8.3-11.7)	4.6 (2.8-6.2)	0.47 (0.33-0.68)
Age					
<65 years	170/260	79/120	9.8 (8.4-11.3)	5.4 (4.1-7.8)	0.51 (0.39-0.67)
≥65 years	41/71	31/43	12.0 (9.5-14.7)	5.6 (4.3-10.8)	0.47 (0.29-0.77)
Race					
White	100/156	43/78	10.0 (8.5-12.2)	7.1 (4.0-10.0)	0.64 (0.44-0.91)
Asian	83/131	54/66	11.0 (8.4-13.8)	4.8 (4.2-6.4)	0.40 (0.28-0.56)
Other	25/37	11/16	6.0 (5.4-10.5)	7.0 (1.4-11.0)	0.83 (0.41-1.69)
Region					
Asia	81/128	48/60	10.9 (8.4-14.7)	5.3 (4.2-6.8)	0.41 (0.28-0.58)
Europe and Israel	90/149	44/73	10.8 (8.5-13.0)	7.1 (3.0-10.7)	0.62 (0.43-0.89)
North America	40/54	18/30	8.5 (6.3-11.3)	4.5 (2.9-8.2)	0.54 (0.30-0.97)
ECOG performance status					
0	116/187	55/95	10.9 (9.5-13.0)	7.0 (4.2-8.5)	0.56 (0.40-0.77)
1	95/144	55/68	9.7 (7.3-11.5)	4.6 (2.9-6.2)	0.45 (0.32-0.64)
Visceral disease at baseline					
Yes	196/298	100/146	9.8 (8.5-11.1)	5.8 (4.4-7.1)	0.54 (0.42-0.69)
No	15/33	10/17	17.9 (10.9-26.4)	4.5 (1.6-12.4)	0.23 (0.09-0.55)

PFS by blinded independent central review. Based on derived data, which includes protocol deviations.

CDK4/6 = cyclin-dependent kinase 4/6; IHC = immunohistochemistry; ISH = in situ hybridization; ECOG = Eastern Cooperative Oncology Group; T-DXd = trastuzumab deruxtecan; TPC = treatment with physician's choice; mPFS = median progression-free survival; CI = confidence interval.

Safety and tolerability

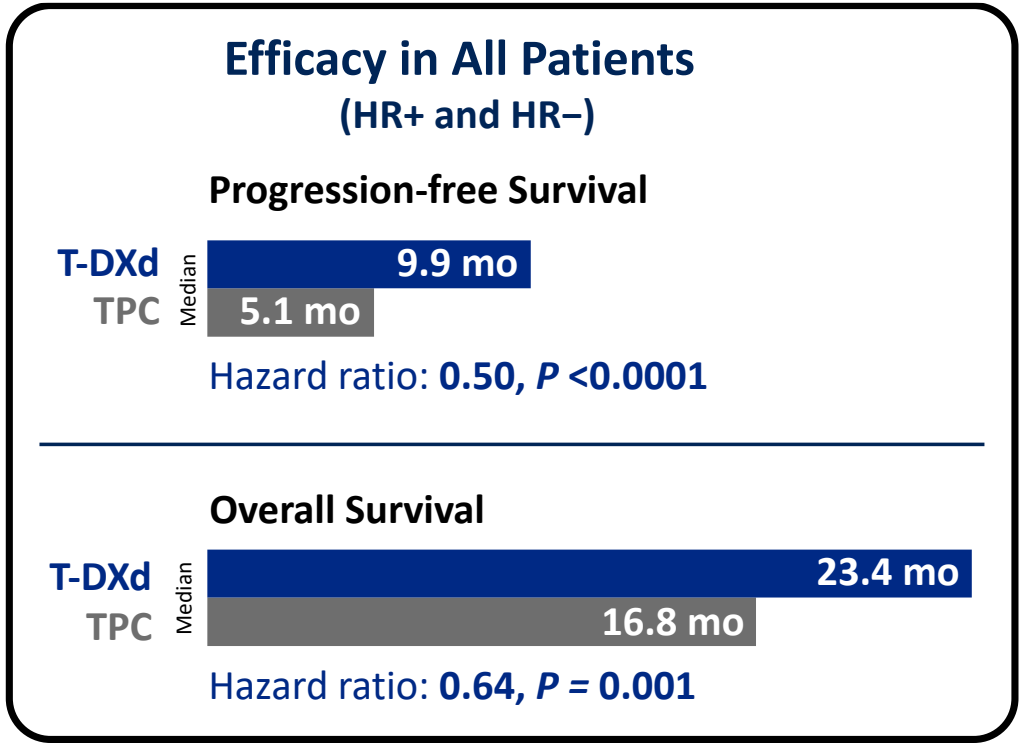
n (%)	Safety analysis set	
	T-DXd (n = 371)	TPC (n = 172)
Total patient-years of exposure, years[a]	283.55	63.59
TEAEs	369 (99)	169 (98)
Grade ≥3	195 (53)	116 (67)
Serious TEAEs	103 (28)	43 (25)
TEAEs associated with dose discontinuations	60 (16)	14 (8)
TEAEs associated with dose interruptions	143 (39)	72 (42)
TEAEs associated with dose reductions	84 (23)	66 (38)
TEAEs associated with deaths	14 (4)	5 (3)

- **Median treatment duration**
  - **T-DXd: 8.2 months (range, 0.2-33.3)**
  - **TPC: 3.5 months (range, 0.3-17.6)**
- Most common TEAE associated with treatment discontinuation
  - T-DXd: 8.2%, ILD/pneumonitis[b]
  - TPC: 2.3%, peripheral sensory neuropathy
- Most common TEAE associated with dose reduction
  - T-DXd: 4.6%, nausea and fatigue
  - TPC: 14.0%, neutropenia[c]
- T-DXd drug related ILD/pneumonitis AEs
  - Grade 3: 8 (2.1%)
  - Grade 5: 3 (0.8%)
- Total on-treatment deaths[d]
  - T-DXd: 3.8%
  - TPC: 4.7%

TEAE = treatment-emergent adverse event; T-DXd = trastuzumab deruxtecan; TPC = treatment with physician's choice; ILD = interstitial lung disease.
[a]Patient years of exposure are the treatment duration with year as unit. [b]Grouped term. [c]Fatigue includes the preferred terms fatigue, malaise and asthenia; neutropenia included the preferred terms of neutropenia and neutrophil count decreased. [d]On-treatment death was defined as any death that occurred from the date of the first dose to 47 days after the last dose of study drug irrespective of the cause, the TEAEs associated with deaths represent subset of on-treatment deaths reported by the investigators as adverse events.

DESTINY-Breast04 establishes T-DXd as the new standard of care in HER2-low, HR+/HR- mBC

- T-DXd is the first HER2-targeted therapy to demonstrate unprecedented statistically significant and clinically meaningful improvement in PFS and OS versus TPC
- Similar magnitude of benefit across all subgroups, including HER2 IHC status and prior CDK4/6i use
- Safety is consistent with the known safety profile and showed an overall positive benefit-risk
- DESTINY-Breast04 establishes HER2-low (IHC 1+, IHC 2+/ISH−) mBC as a new targetable patient population with T-DXd as a new standard of care



T-DXd = trastuzumab deruxtecan; HER2-low = human epidermal growth factor receptor 2 low; HR+ = hormone-receptor positive; HR- = hormone-receptor negative; mBC = metastatic breast cancer; PFS = progression-free survival; OS = overall survival; TPC = treatment with physician's choice; IHC = immunohistochemistry; CDK4/6i = cyclin-dependent kinase 4/6 inhibitors.

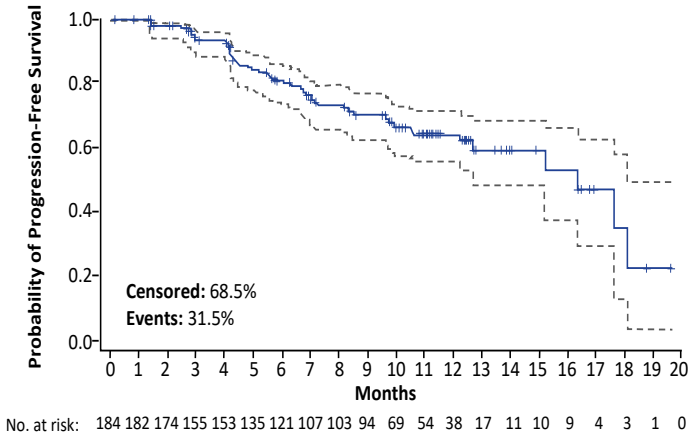
AstraZeneca

3. DESTINY-Breast04: redefining cancer treatment

Dave Fredrickson
EVP Oncology Business

Enhertu: continuing to transform breast cancer

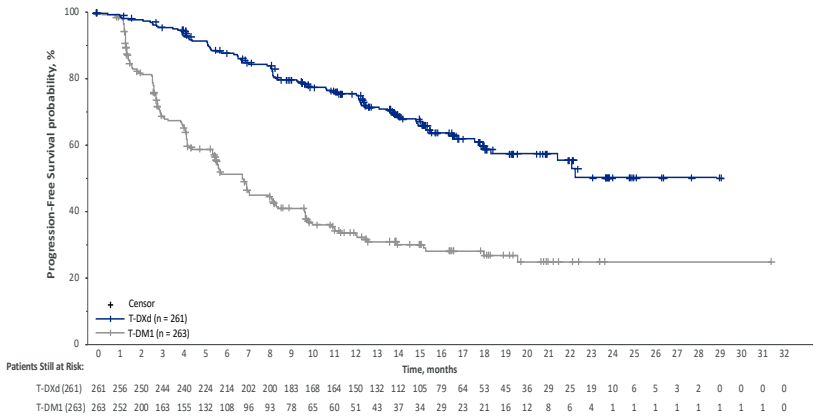
2019: DESTINY-Breast01[1]



mPFS: 16.4m

From compelling Phase II data in 3rd line+ HER2-positive breast cancer…

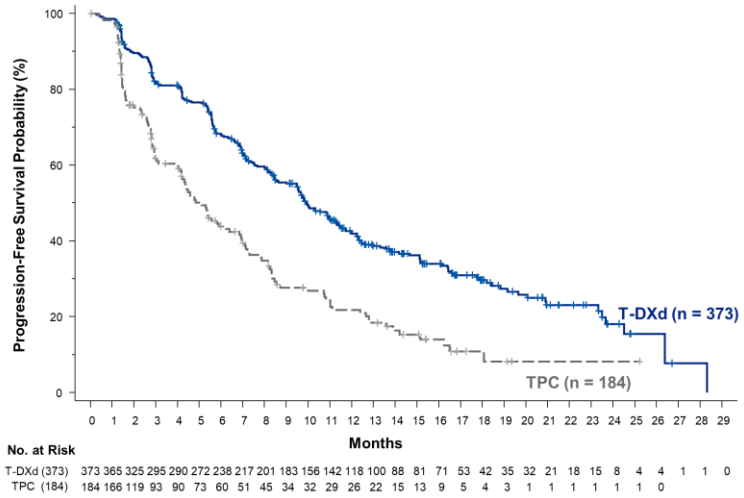
2021: DESTINY-Breast03[2]



mPFS: not reached

…to redefining expectations in 2nd line HER2-positive breast cancer…

2022: DESTINY-Breast04



mPFS 9.9m

…to now reaching more than half of all breast cancer patients

1. Krop SABCS 2019 Abstract #GS1-03. 2. Cortes ESMO 2021 Abstract #LBA1

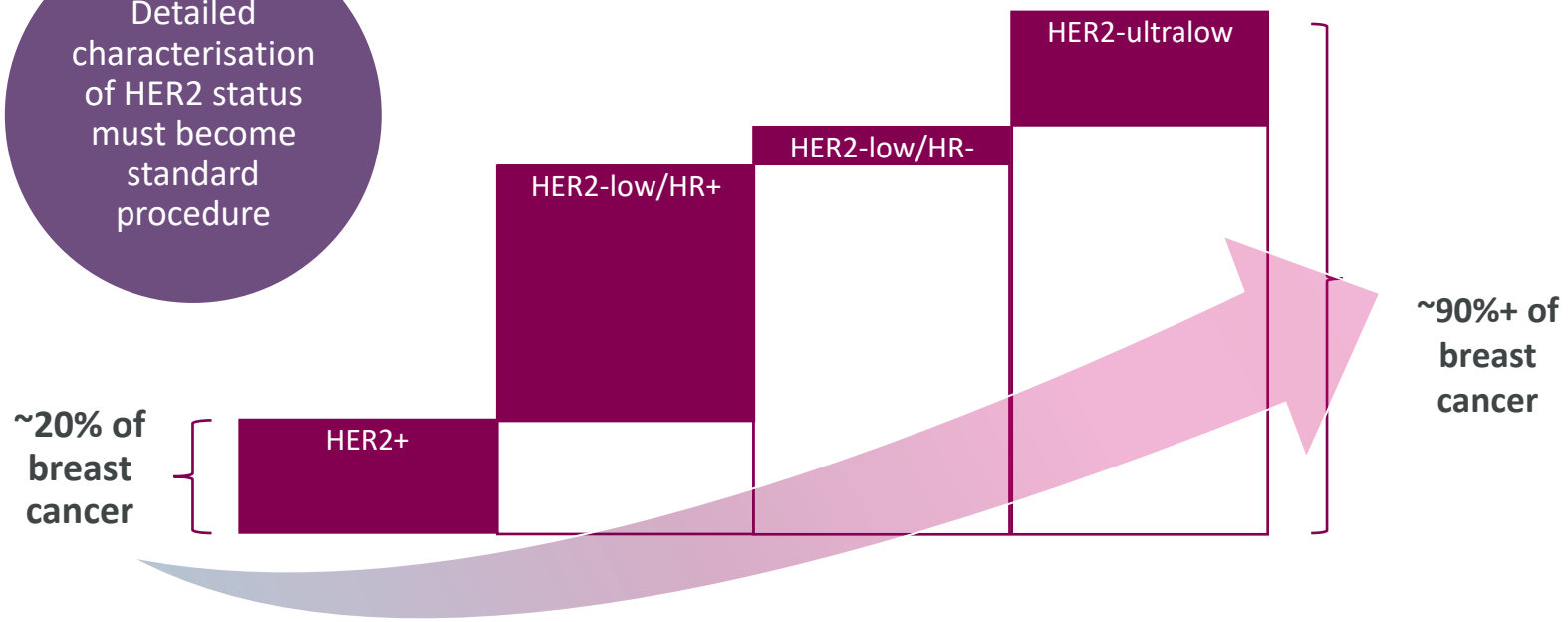
HER2 = human epidermal growth factor receptor 2; T-DXd = trastuzumab deruxtecan; TPC = treatment of physician's choice; mPFS = median progression-free survival.

HER2-low breast cancer: visible, but underserved

Patients are numerous

and ready to be identified

Detailed characterisation of HER2 status must become standard procedure



Outcomes are currently poor

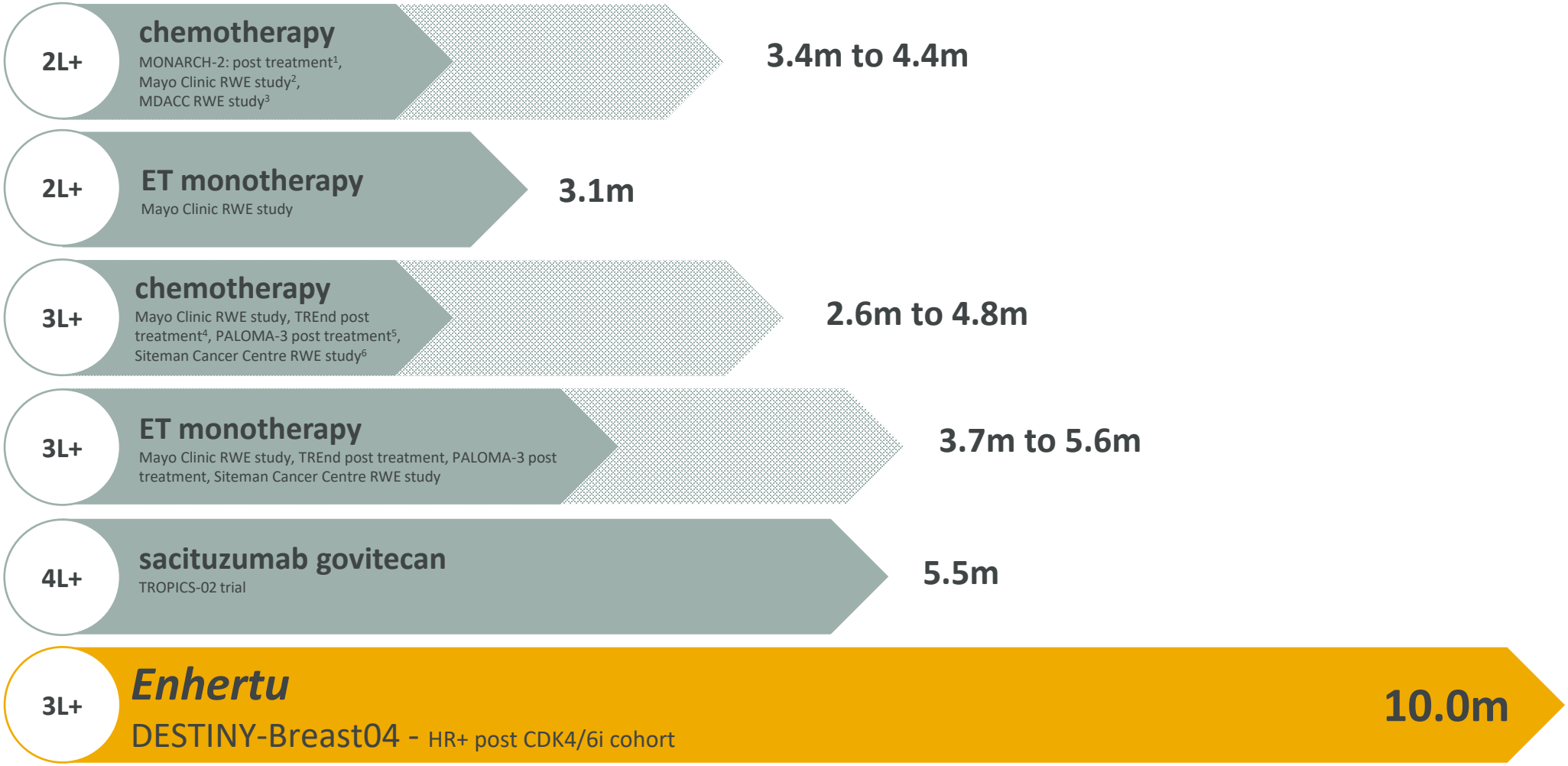
~32% 5-year survival for **metastatic, HR+ breast cancer** in the US[2]

~12% 5-year survival for metastatic, **triple negative breast cancer** in the US[2]

1. AstraZeneca data on file. 2. NIH NCI SEER data.
HR+ = Hormone receptor positive (cancer that is driven by oestrogen and/or progesterone) . TNBC = triple negative breast cancer is both HR- and HER2-. CDK4/6i Cyclin-dependent kinase 4,6 inhibitors such as palbociclib, target the mechanisms of uncontrolled growth of HR+ cancer cells. Endocrine therapies target the hormones that drive HR+ cancer and include SoC SERDs *Faslodex* (fulvestrant) and aromatase inhibitors like *Arimidex* (anastrozole)

Enhertu transforms the treatment paradigm

for HR+ metastatic patients who see limited benefit from current standards of care



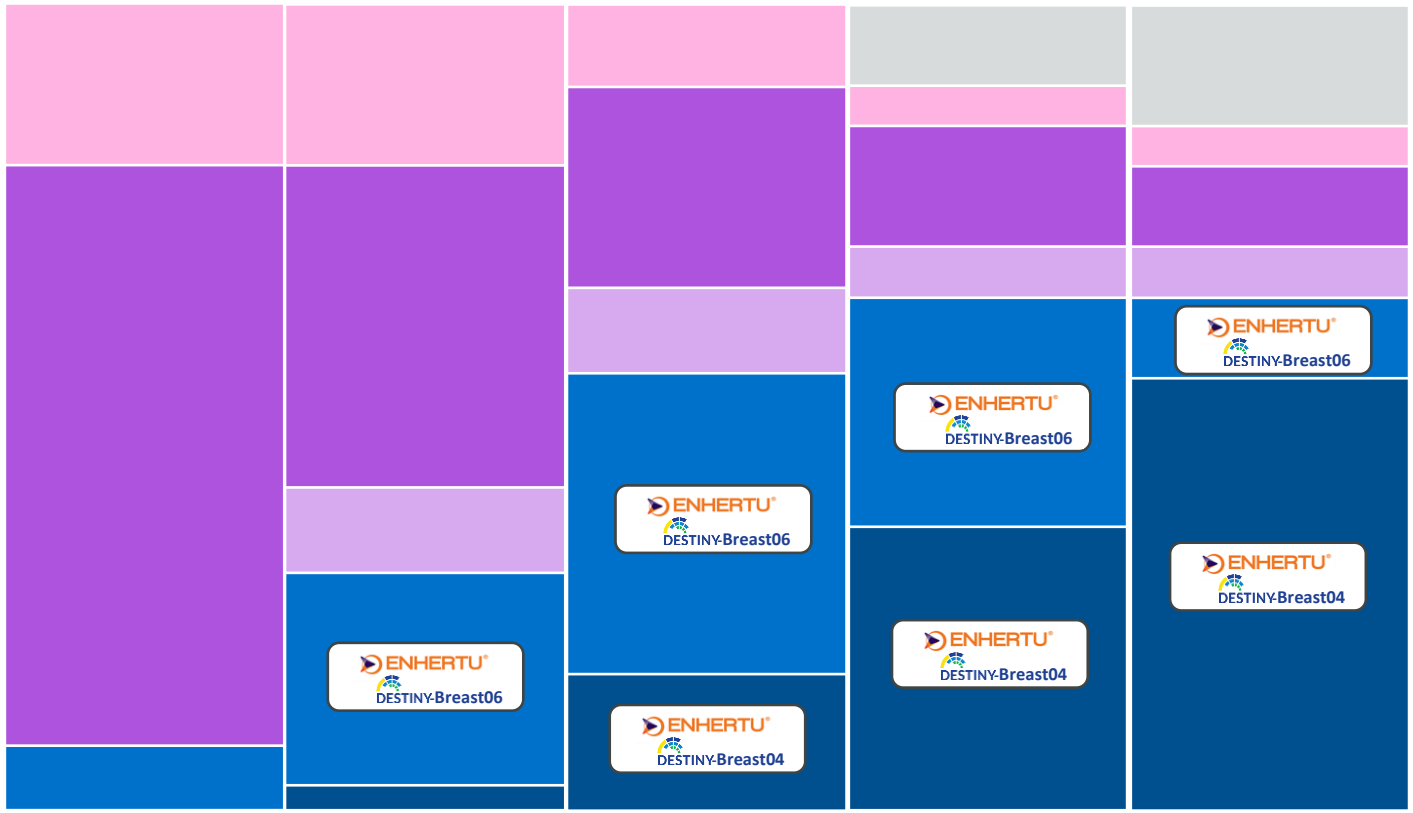
1. Sledge GW. et al., JAMA Oncol 2020.6(1) 116-124. 2. Giridhar GV., SABCS 2018 Abstract #P6-18-09. 3. Chainitikun S. et al., *Breast Cancer Research and Treatment* 2020. 4. Rossi L et al., Breast Cancer Res 21, 71(2019). 5. Turner NC. Et al., 2018 Nov 15,379(30) 1925-1936. 6. Xi j. et al., *JNCCN* 2019.

HR+ = hormone-receptor positive; RWE = real-world evidence; ET = endocrine therapy; CDK4/6i = cyclin-dependent kinase 4/6 inhibitors; MDACC = MD Anderson Cancer Center.

Establishing a new standard of care

Enhertu set to deliver greater benefit than all current therapies beyond second line

~60k HR+ patients in US, EU and Japan



Source: AstraZeneca data on file.

HR+ = hormone-receptor positive; ET = endocrine therapy; CDK4/6i = cyclin-dependent kinase 4/6 inhibitors.

AstraZeneca

5. What's next for AstraZeneca in Oncology?

Susan Galbraith
EVP Oncology R&D

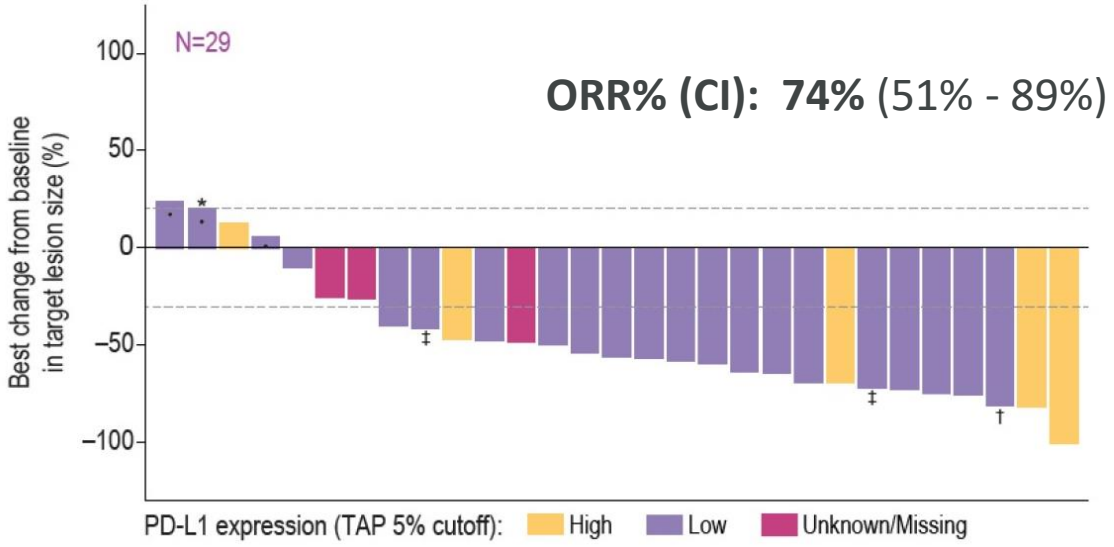
Dato-DXd could address "triple negative" patients

TROPION-Breast02 Phase III in HER2-negative/HR-negative breast cancer

ESMO BREAST CANCER 2022 data recap

BEGONIA Arm 7

(Dato-DXd + *Imfinzi*)



HER2-low/HER2-null tumour cells could have around five times more TROP2 receptors per cell versus HER2

TROPION-Breast02

TROP2 targeting in order to redefine TNBC

Key eligibility criteria:

- Locally recurrent inoperable or metastatic TNBC
- No prior chemo or targeted systemic therapy for mBC
- Not a candidate for PD-1 / PD-L1 inhibitor therapy
- Measurable disease as defined by RECIST v1.1
- ECOG PS 0 or 1

n=300 **n=300**

1:1 randomisation

Dato-DXd

Investigators' choice of chemotherapy

Dual primary endpoints:
PFS (BICR) and OS
Secondary endpoints:
PFS (inv), ORR, DoR, safety

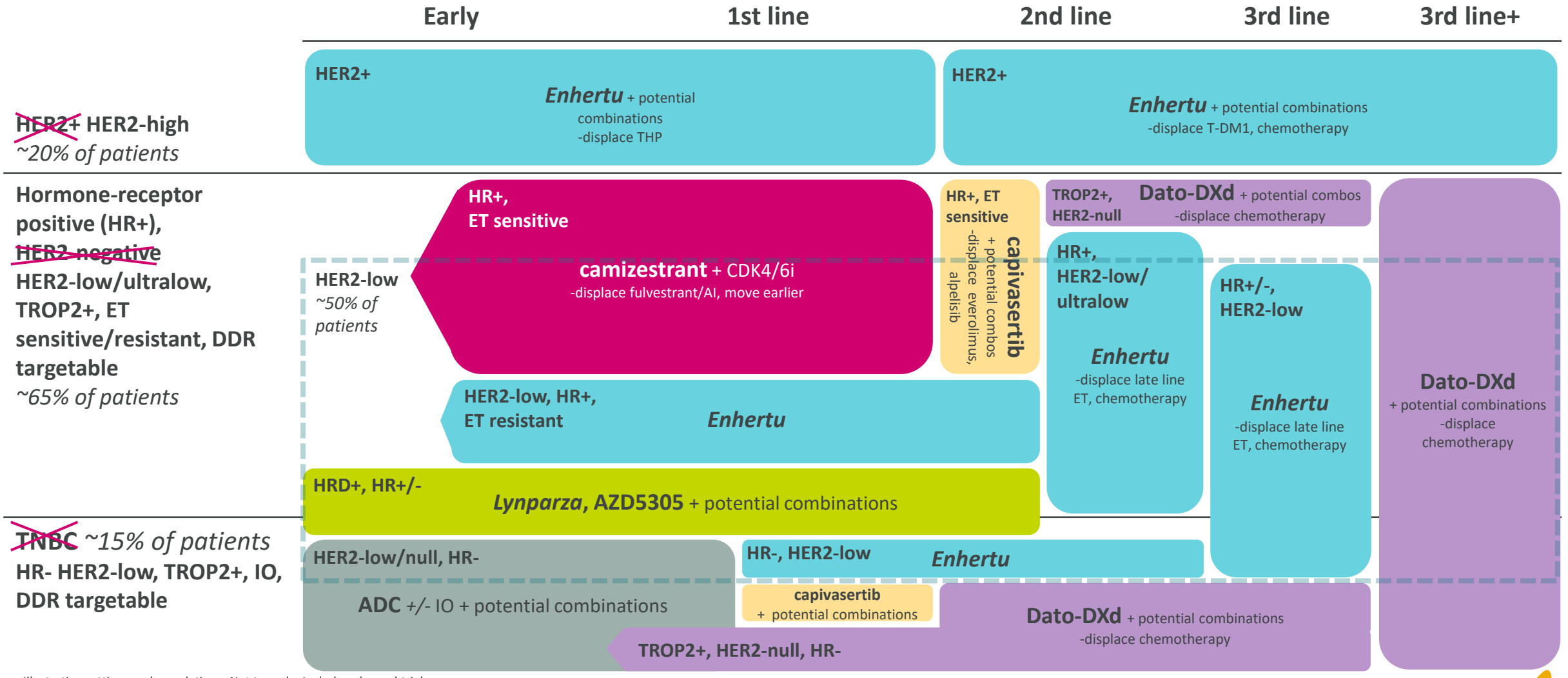
Data readout: >2023

Source: Schmid ESMO Breast 2022, Abstract #166MO.

Dato-DXd = datopotamab deruxtecan; HER2-negative = human epidermal growth factor receptor 2 negative; HR- = hormone-receptor negative; PD-L1 = programmed death-ligand 1; ORR = objective response rate; CI = confidence interval; TROP2 = trophoblast antigen 2; TNBC = triple negative breast cancer; mBC = metastatic breast cancer; PD-1 = programmed cell death protein 1; ECOG = Eastern Cooperative Oncology Group; PS = performance status; PFS = progression-free survival; OS = overall survival; DoR = duration of response.

Positioned to address the full spectrum of breast cancer

with potential for at least seven medicines in monotherapy and combinations

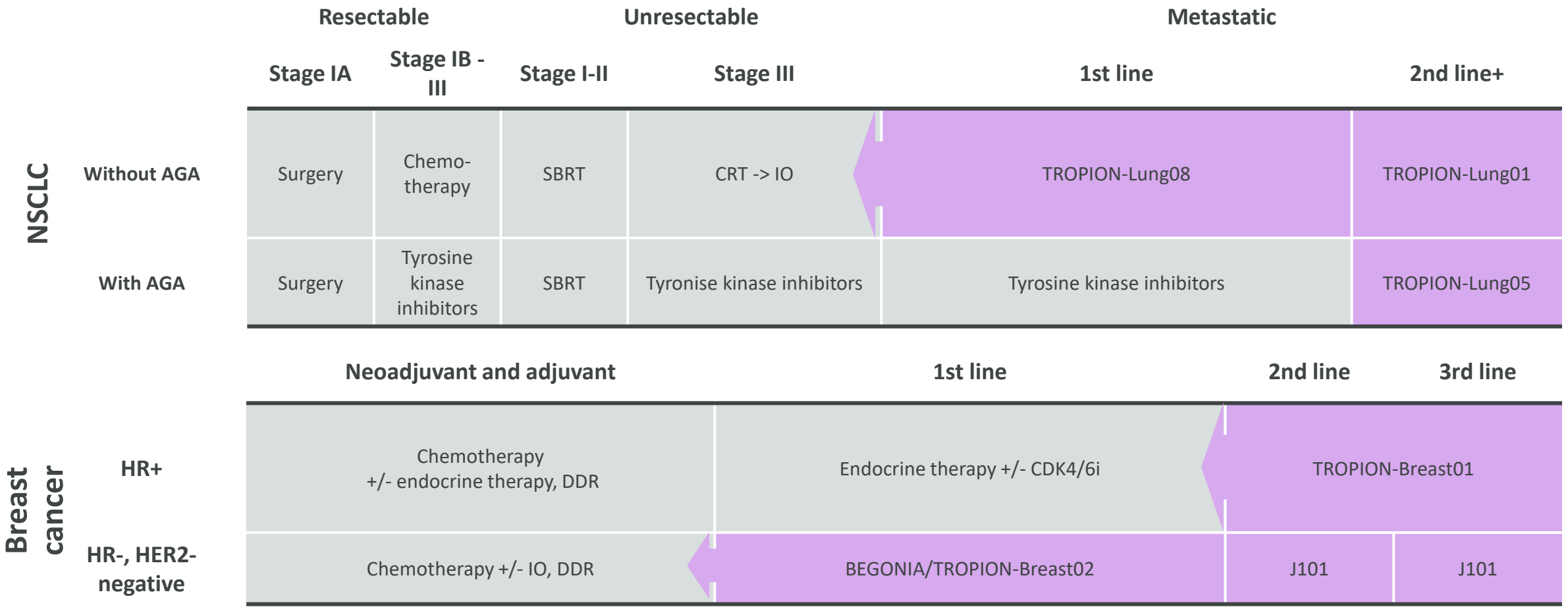


Illustrative settings and populations. Not to scale. Includes planned trials.

HER2 = human epidermal growth factor receptor 2; HER2-low = human epidermal growth factor receptor 2 low; HR+ = hormone-receptor positive; HR- = hormone-receptor negative; TNBC = triple negative breast cancer; TROP2+ = trophoblast antigen 2 positive; IO = immuno-oncology; DDR = DNA damage response; CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; ET = endocrine therapy; HRD+ = homologous recombination deficiency positive; ADC = antibody-drug conjugate; THP = paclitaxel , trastuzumab and pertuzumab; T-DM1 = trastuzumab emtansine; AI = aromatase inhibitor.

Dato-DXd: initial TROP2 opportunities

At least five new Phase III trials planned to commence in the next 18 months

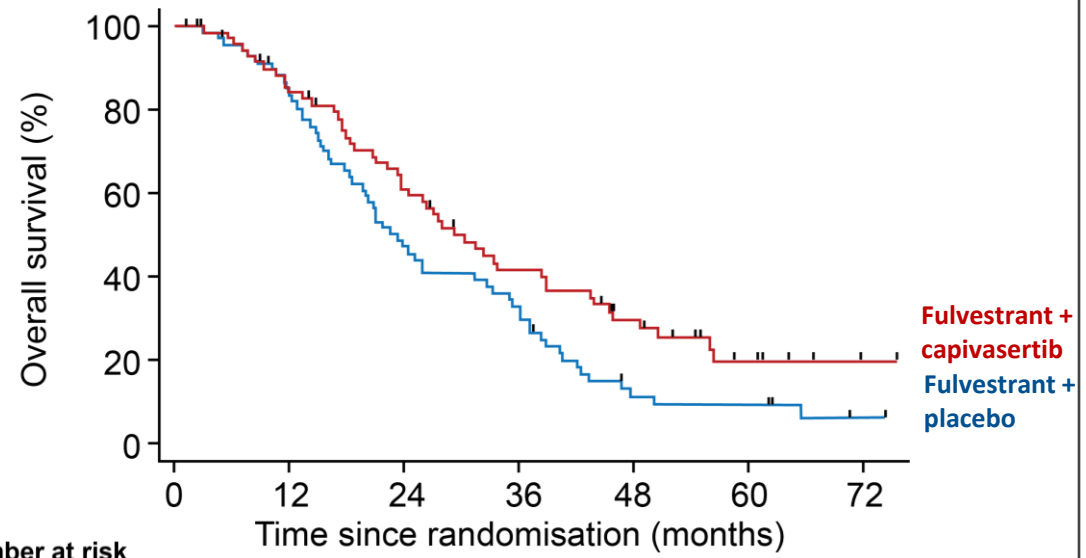


NSCLC = non-small cell lung cancer; AGA = actionable genomic alterations; HR+ = hormone-receptor positive; HER2-negative = human epidermal growth factor receptor 2 negative; SBRT = stereotactic body radiotherapy; CRT = chemoradiation therapy; IO = immuno-oncology; DDR = DNA damage response; CDK4/6i = cyclin-dependent kinase 4/6 inhibitor.

Capivasertib: oral, potent and selective pan-AKT inhibitor

Updated overall survival data from Phase II trial that supported CAPItello-291

FAKTION Phase II trial



	Fulvestrant + capivasertib (n = 69)	Fulvestrant + placebo (n = 71)
OS events	49	59
Median OS (95% CI)	**29.3 months (23.7–39.0)**	**23.4 months (18.7–32.7)**
Adjusted HR	**0.66 (95% CI 0.45–0.97); *p* = 0.035**	

CAPItello-291 Phase III trial

Key eligibility criteria:

- post-menopausal women with metastatic ER+ BC
- suitable for ET.
- < three lines of prior ET and up to one line of chemo in metastatic setting
- Progressive disease during treatment with an aromatase inhibitor

n=350 | **n=350**

1:1 randomisation

capivasertib + fulvestrant

Placebo + fulvestrant

Primary endpoint: PFS

Targeting the PI3K/AKT pathway as a common mechanism of resistance to endocrine therapy

AKT = protein kinase B; OS = overall survival; HR = hazard ratio; ER+ = oestrogen receptor positive; BC = breast cancer; ET = endocrine therapy; PFS = progression-free survival; PI3K = phosphoinositide 3-kinase.

AZD8205: ADC targeting B7-H4 protein

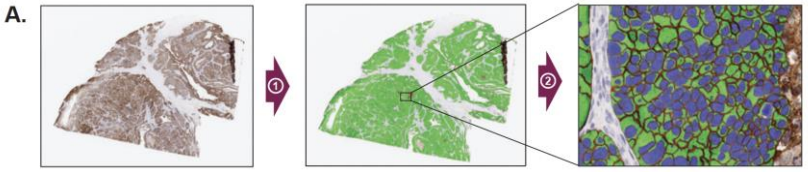
The first ADC engineered with AstraZeneca's novel linker-warhead technology

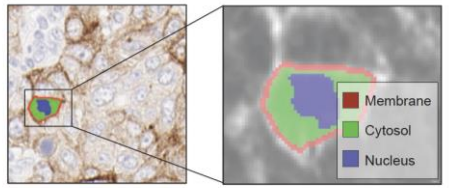
AACR ANNUAL MEETING 2022 data recap

From histology to histogram:

quantitative continuous score-based image analysis for B7-H4

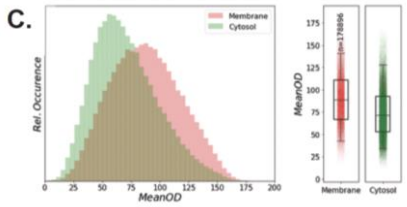
A: AI-based identification of tumour epithelial region and segmentation into cells





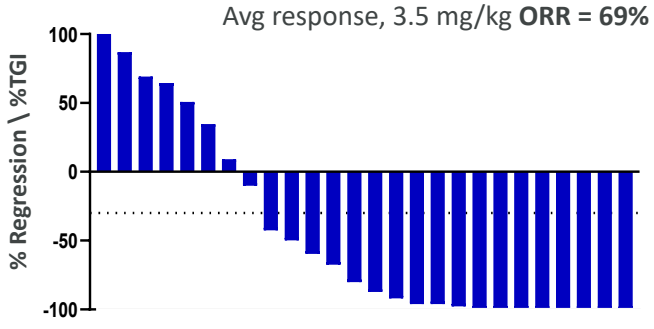
B: Target expression quantified for nucleus, cytosol and membrane from stain isolation layer based on Hue-Saturation-Density transform

C: Mean target expression per cell membrane/cytosol is analysed at whole slide image level



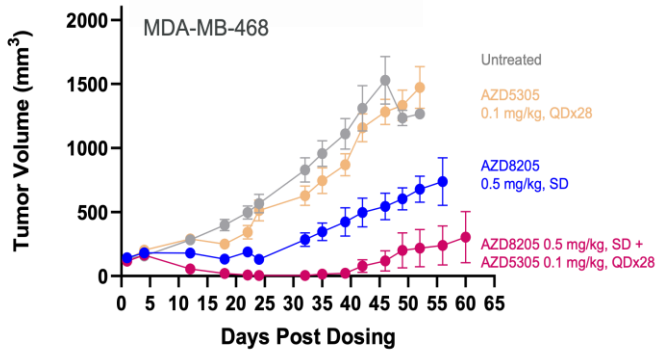
Encouraging preclinical efficacy

and PARPi-selective combination data



Robust efficacy *in vivo* of 26 TNBC PDX tumours

Significant combination benefit seen in preclinically with AZD5305



Kinneer et al AACR. Wortmann P, et al. "Development and implementation of image analysis-based Quantitative Continuous Score (QCS) for B7-H4 IHC to understand AZD8205 pharmacodynamics". AACR 2022; Abstract 452/3.

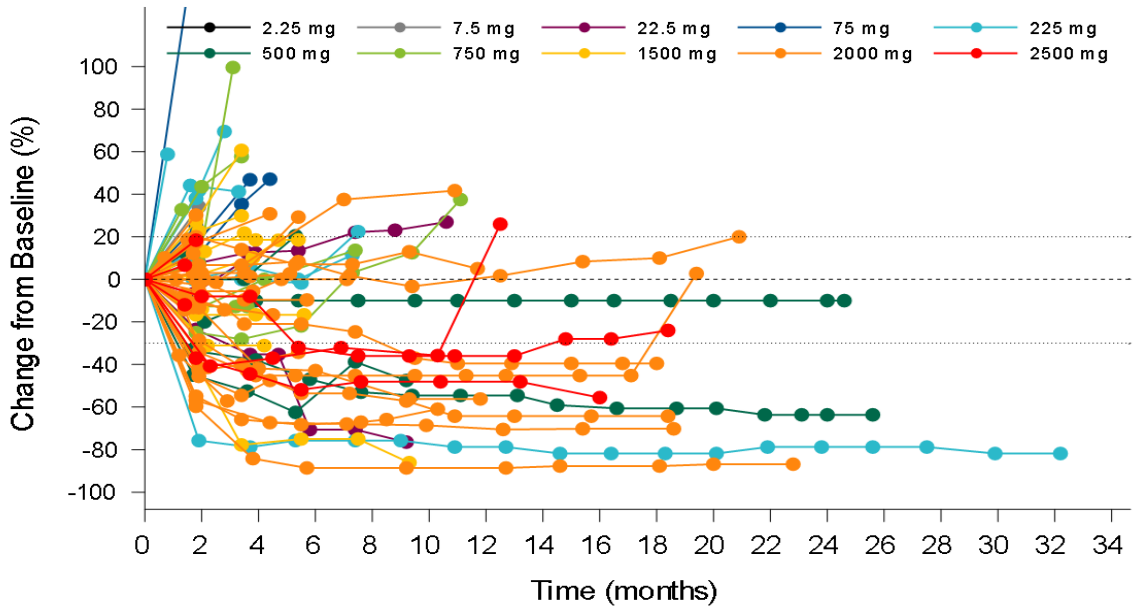
ADC = antibody-drug conjugate; B7-H4 = immune co-regulatory ligand of the B7 family; AI = artificial intelligence; OD = once daily; PARPi = poly ADP ribose polymerase inhibitor; ORR = objective response rate; TGI = tumour growth inhibition; TNBC = triple negative breast cancer; PDX = patient-derived xenografts; QDx28 = every 28 days; SD = single dose.

MEDI5752: a novel PD-1/CTLA-4 bispecific

Potential for improved therapeutic index versus components

AACR ANNUAL MEETING 2022 data recap

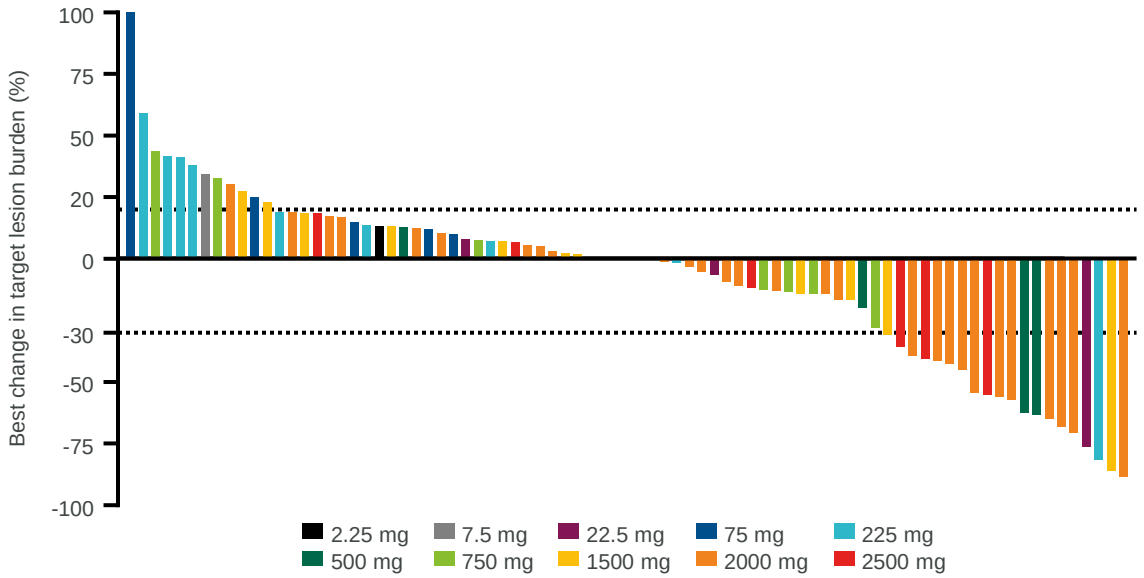
Durable clinical response in Phase I trial



mDOR: 17.5 months (95% CI: 5.7 – NE)

Deep responses seen across a range of tumours

including RCC, TNBC, PDL1-low NSCLC, gastric, bladder and colorectal cancer



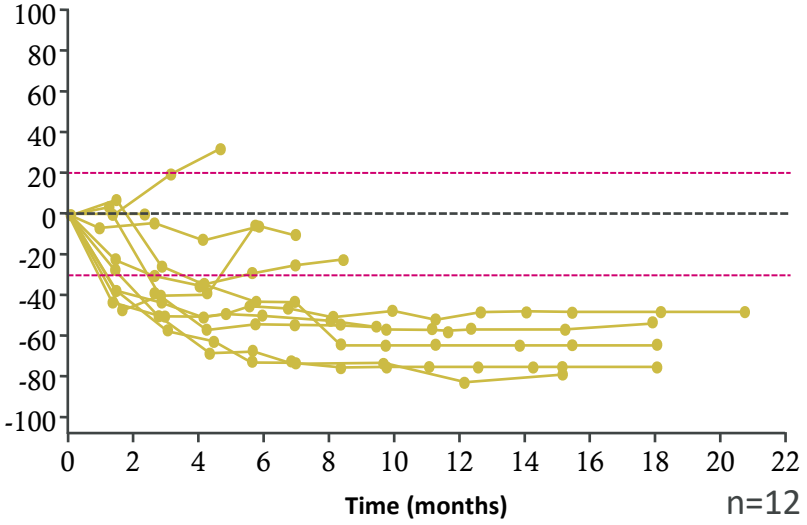
PD-1 = programmed cell death protein 1; CTLA-4 = cytotoxic T-lymphocyte–associated antigen 4; mDOR = median duration of response; CI = confidence interval; RCC = renal cell carcinoma; TNBC = triple negative breast cancer; PD-L1-low = programmed death-ligand 1 low; NSCLC = non-small cell lung cancer.

MEDI5752 in advanced renal cell carcinoma

Deep and durable responses in immunotherapy-naïve patients

1500 mg dose expansion responses

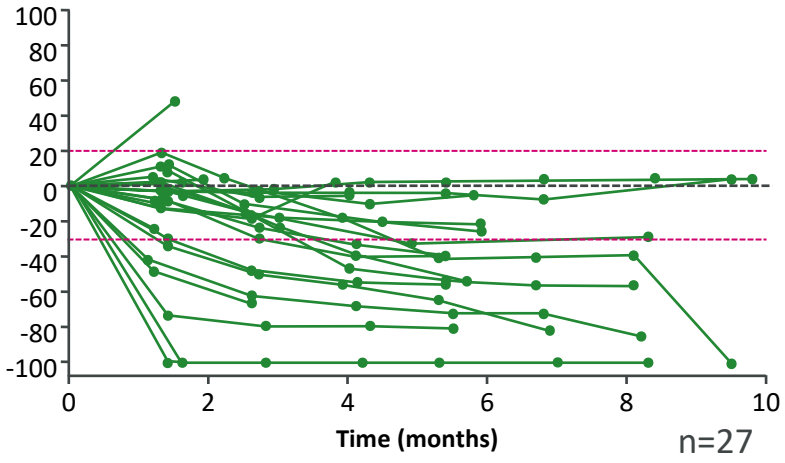
Change from baseline (%)



Median DoR, months (95% CI)	16.2 (4.1–NE)
Median PFS, months (95% CI)	16.1 (4.6–NE)
Median duration of follow-up, months (range)	18.4 (0.5-23.6)

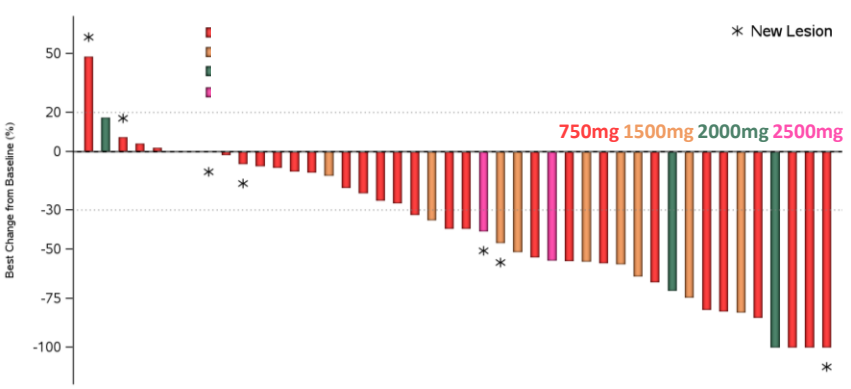
750 mg dose expansion responses

Change from baseline (%)



Median DoR, months (95% CI)	Data immature
Median PFS, months (95% CI)	Data immature
Median duration of follow-up, months (range)	6.9 (1.4-10.9)

Emerging efficacy at 750mg looks similar to 1500mg monotherapy



Across all cohorts in 1st line RCC:
ORR 51% (25/49)

Improved toxicity, fewer treatment discontinuations and similar efficacy for 750mg dose compared to higher dose

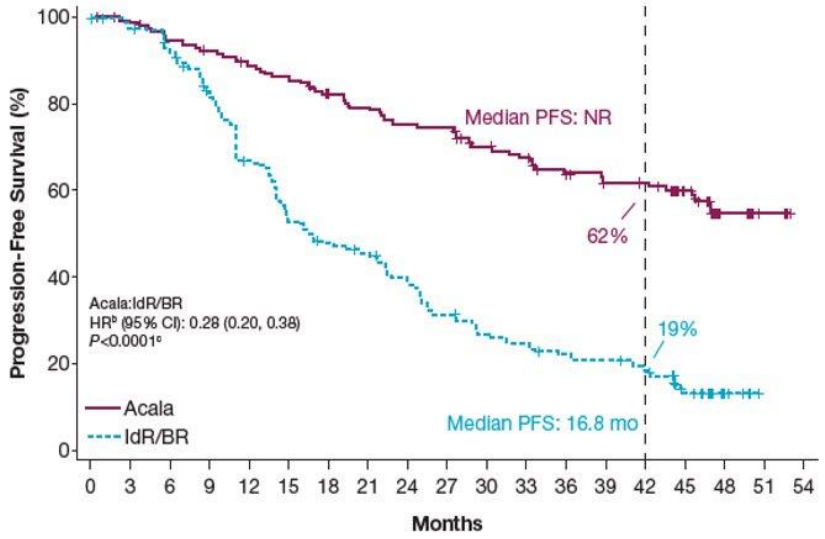
Source: Tran et al., AACR 2022, Abstract #CT016

IO = immuno-oncology; RCC = renal cell carcinoma; Q3W = every three weeks; DoR = duration of response; PFS = progression-free survival; CI = confidence interval.

Calquence: best-in-class BTK inhibitor

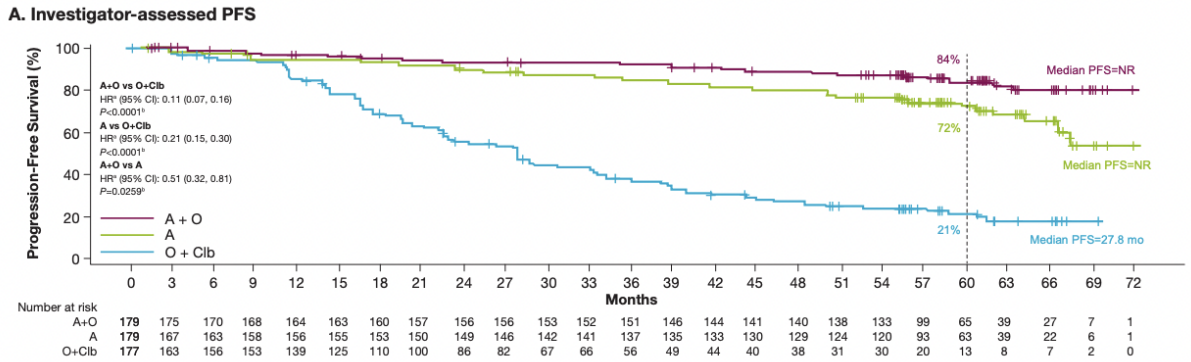
Superior, durable efficacy and tolerability profile supports long-term use

ASCEND
relapsed/refractory CLL



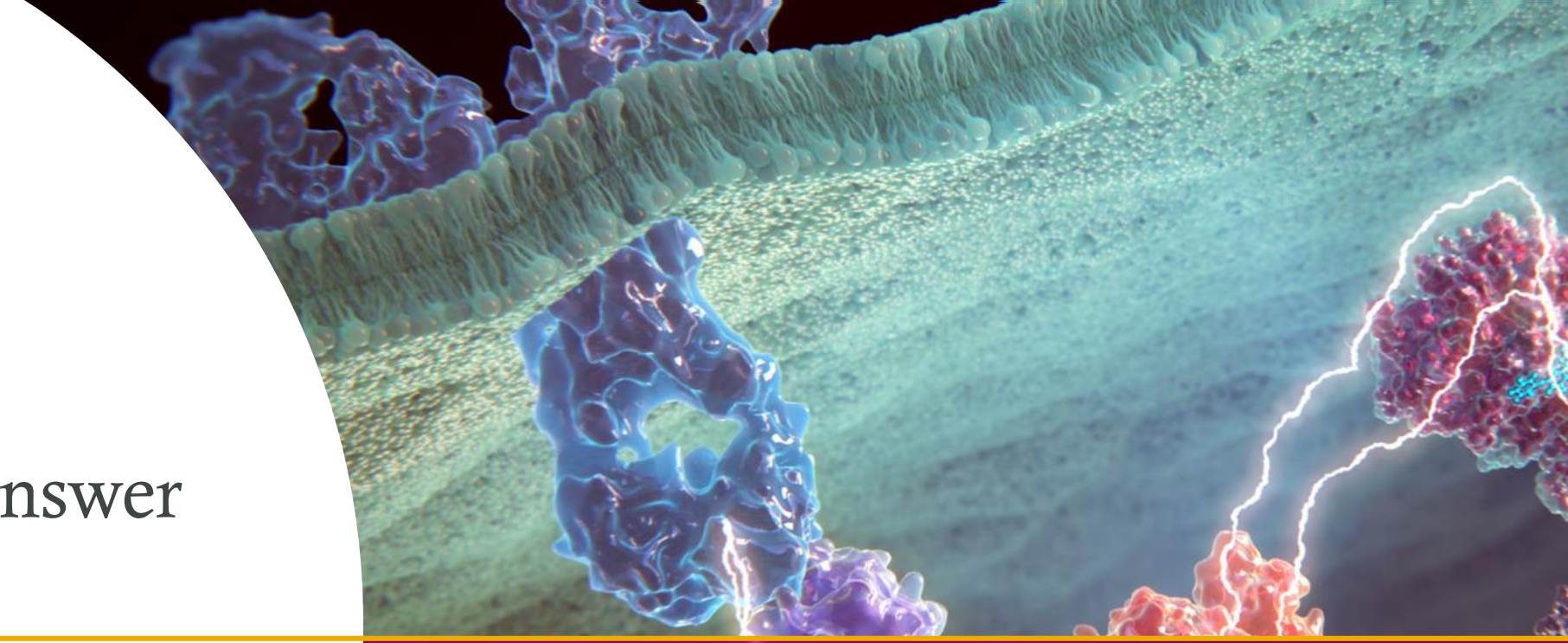
Calquence sees **62%** PFS benefit at **four years**

ELEVATE-TN
treatment naïve CLL



Calquence + obintuzumab sees strong **84%** PFS benefit at **five years**

6. Question and Answer session



Panel

Dr Aleix Prat

Senior Investigator, DESTINY-Breast04 trial and Head Medical Oncology, Hospital Clínic of Barcelona

David Fredrickson

Executive Vice President, Oncology Business

Cristian Massacesi

Chief Oncology Development Officer and Chief Medical Officer (for Q&A)

Mika Sovak

Vice President and Global Franchise Head *Enhertu,* R&D (for Q&A)

Pascal Soriot

Chief Executive Officer

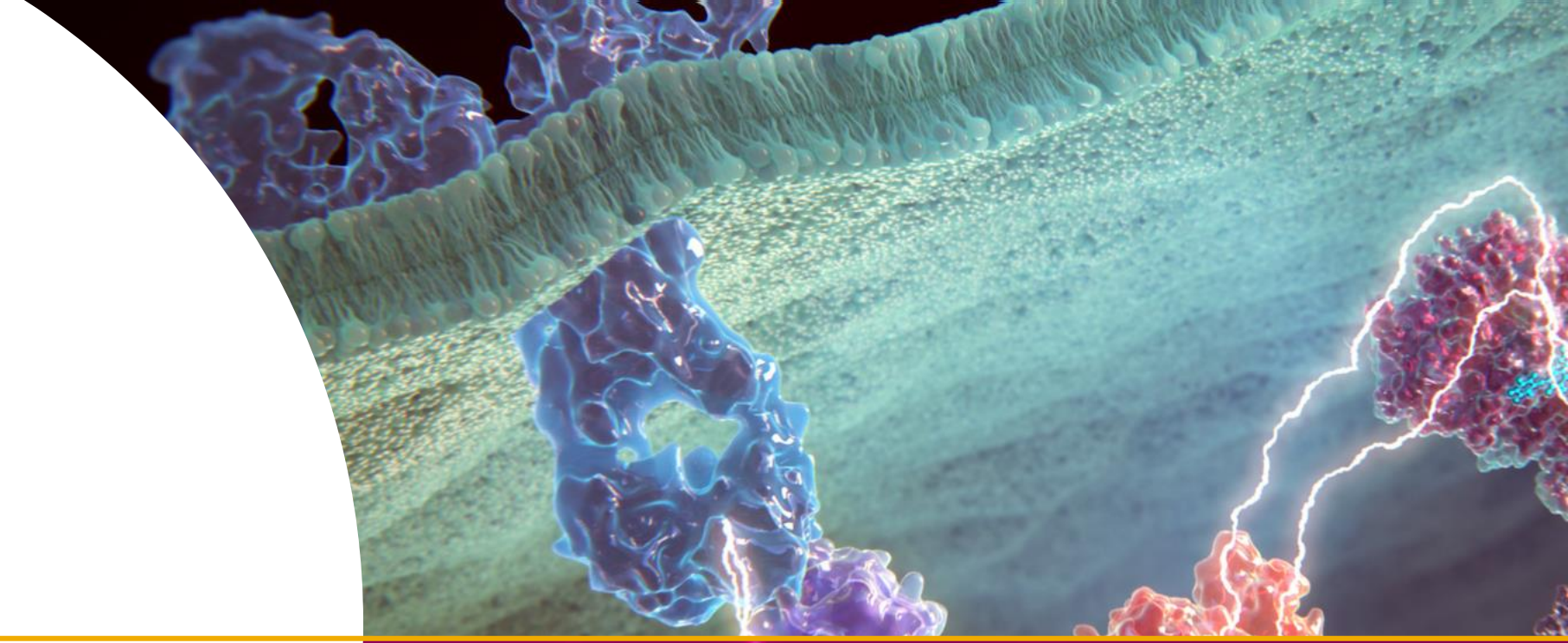
Susan Galbraith

Executive Vice President, Oncology R&D

Sunil Verma

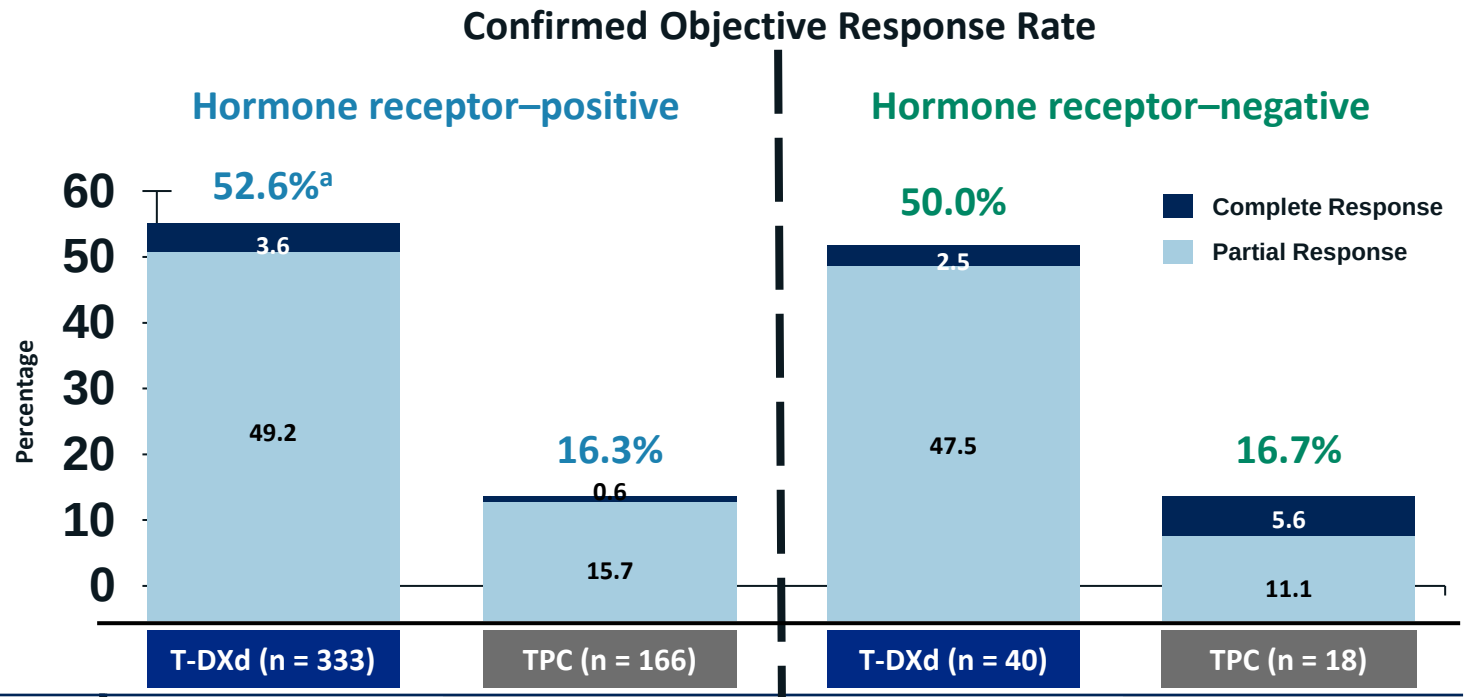
Senior Vice President, Oncology Medical (for Q&A)

7. Appendix



DESTINY-Breast04

Confirmed objective response rate



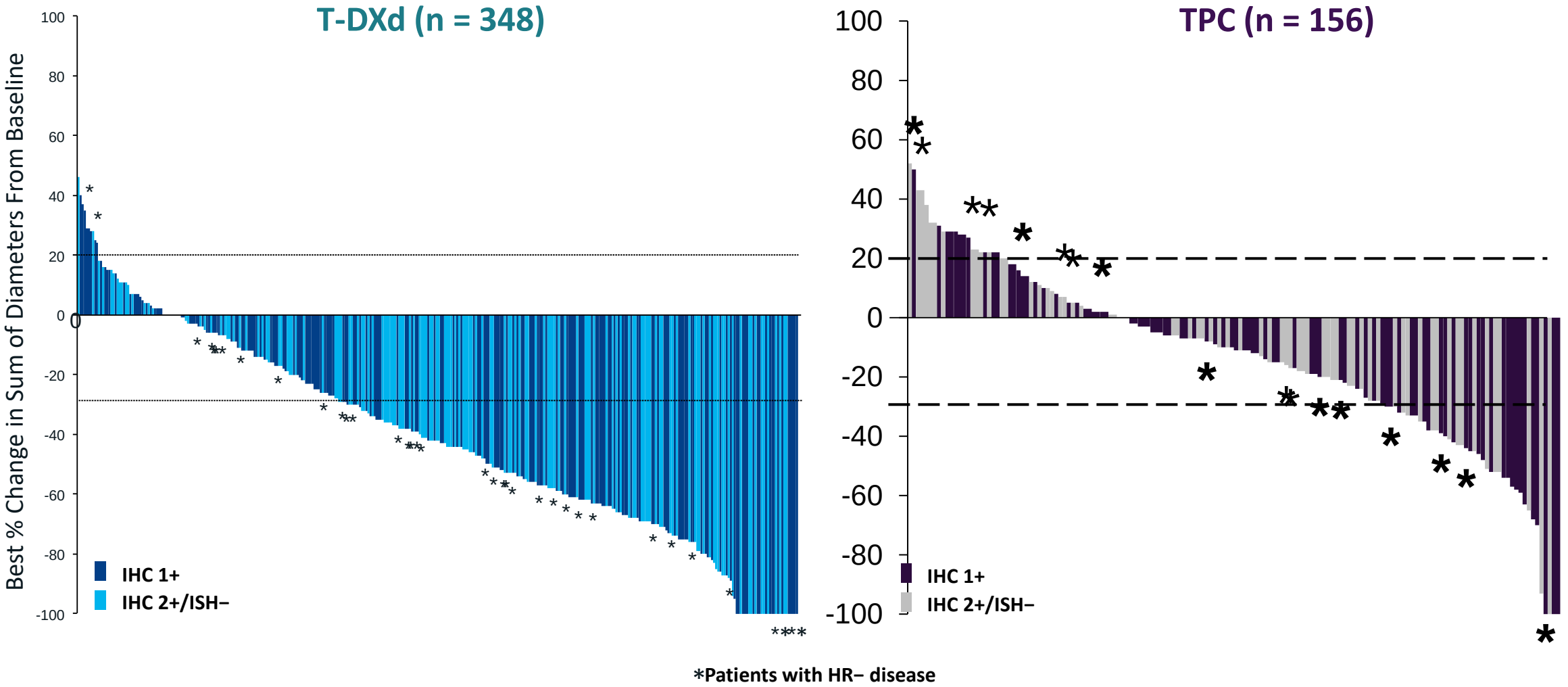
	T-DXd (n = 333)	TPC (n = 166)	T-DXd (n = 40)	TPC (n = 18)
Progressive disease, %	7.8	21.1	12.5	33.3
Not evaluable, %	4.2	12.7	7.5	5.6
Clinical benefit rate,[b] %	71.2	34.3	62.5	27.8
Duration of response, months	10.7	6.8	8.6	4.9

Hormone receptor status is based on data from the electronic data capture corrected for misstratification.

ORR, objective response rate; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

[a]The response of 1 patient was not confirmed. [b]Clinical benefit rate is defined as the sum of complete response rate, partial response rate, and more than 6 months' stable disease rate, based on blinded independent central review.

Best change in target lesions (all patients)



Shown are the best percentage changes from baseline in the sum of the largest diameters of measurable tumors in patients for whom data from both baseline and postbaseline assessments of target lesions by independent central review were available. The upper dashed horizontal line indicates a 20% increase in tumor size in the patients who had disease progression, and the lower dashed line indicates a 30% decrease in tumor size (partial response).

HR, hormone receptor; IHC, immunohistochemistry; ISH, in situ hybridization; T-DXd, trastuzumab deruxtecan; TPC, treatment of physician's choice.

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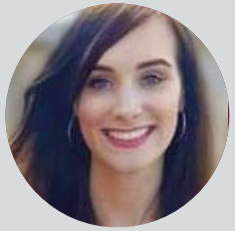

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