AstraZeneca
What science can do

Strategic Collaboration in Oncology
Trastuzumab Deruxtecan (DS-8201)

Conference call for investors and analysts

29 March 2019

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Speakers

Pascal Soriot
Executive Director and
Chief Executive Officer

Dave Fredrickson
Executive Vice President,
Oncology

José Baselga
Executive Vice President,
R&D Oncology

Marc Dunoyer
Executive Director and
Chief Financial Officer

DS-8201: a transformative medicine

AstraZeneca & Daiichi Sankyo collaboration to maximize utility and value

- Oncology is one of our 3 core strategic TAs, Breast Cancer one of our 4 oncology pillars
- Transformative medicine for the treatment of Breast Cancer
  - Taxane free* treatment of HER2+ cancer
  - Potential use in HER2 low
  - Potential for additional tumour types e.g. Lung and Gastric
- AZ can add value to this important new medicine
  - Very experienced team in Oncology, with specific depth in Breast Cancer
  - Global footprint
- An asset with longevity that will provide strong growth to 2030+
- Transaction neutral to core earnings in 2019, growing core EPS accretion from 2020 to a significant contribution in 2023

*Notes: *non-systemic chemotherapy*

Building on our rich heritage in Breast Cancer

Adds a late stage high value asset to our innovative pipeline

1970s Nolvadex

1980s Zoladex goserelin acetate implant

1990s Arimidex anastrozole 1mg tablets

2000s FASLODEX fulvestrant injection

2010s Lynparza olaparib

2020s

Trastuzumab deruxtecan (DS-8201)

- **Imfinzi**
- **Capivasertib**
- **Oral SERD**

Sources: (1) FDA first approval history for each historical AstraZeneca asset, (2) expected 2H 2019 BLA submission to FDA for DS-8201 and (3) future BLA / sBLA / NDA submissions for other AZ pipeline assets

High unmet medical need in HER2+, HER2 low and HER2 mutant tumours across multiple cancer types

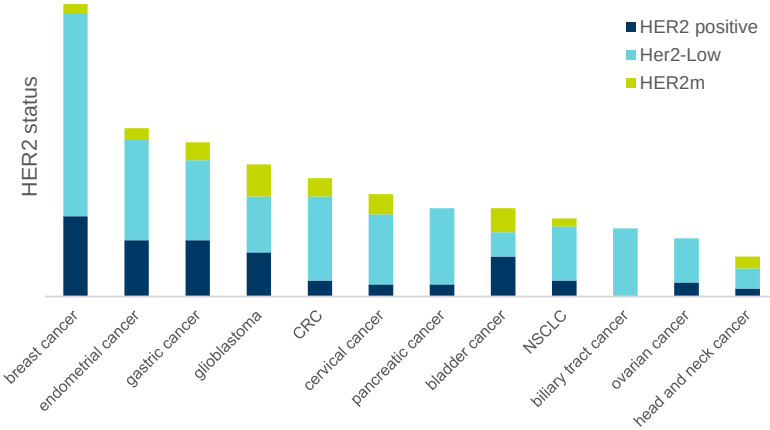
Potential transformational medicine
Innovative and highly potent ADC molecule

1 Taxane free* treatment in HER2+ breast & gastric cancer

2 Expand to HER2 low breast cancer

3 Move to early disease & explore in other HER2 expressing tumours

Prevalence of HER2 status across cancer types

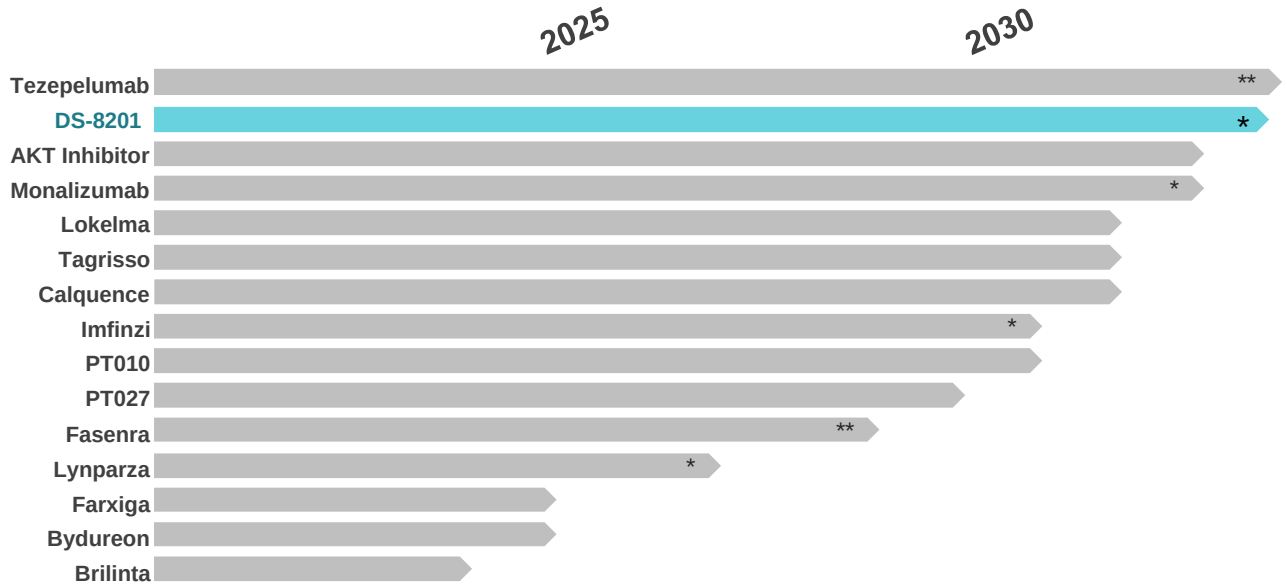


Current HER2+ breast, gastric market
Opportunity in HER2 low

*Notes: *non-systemic chemotherapy*

Source: (1) Literature review including Yan et al, 2014 & 2015, Connell et al, 2017, Peters et al, 2014, Sienna et al, 2018 and (2) Kantar CancerMpact database

Trastuzumab deruxtecan (DS-8201)
An innovative asset with longevity beyond 2030

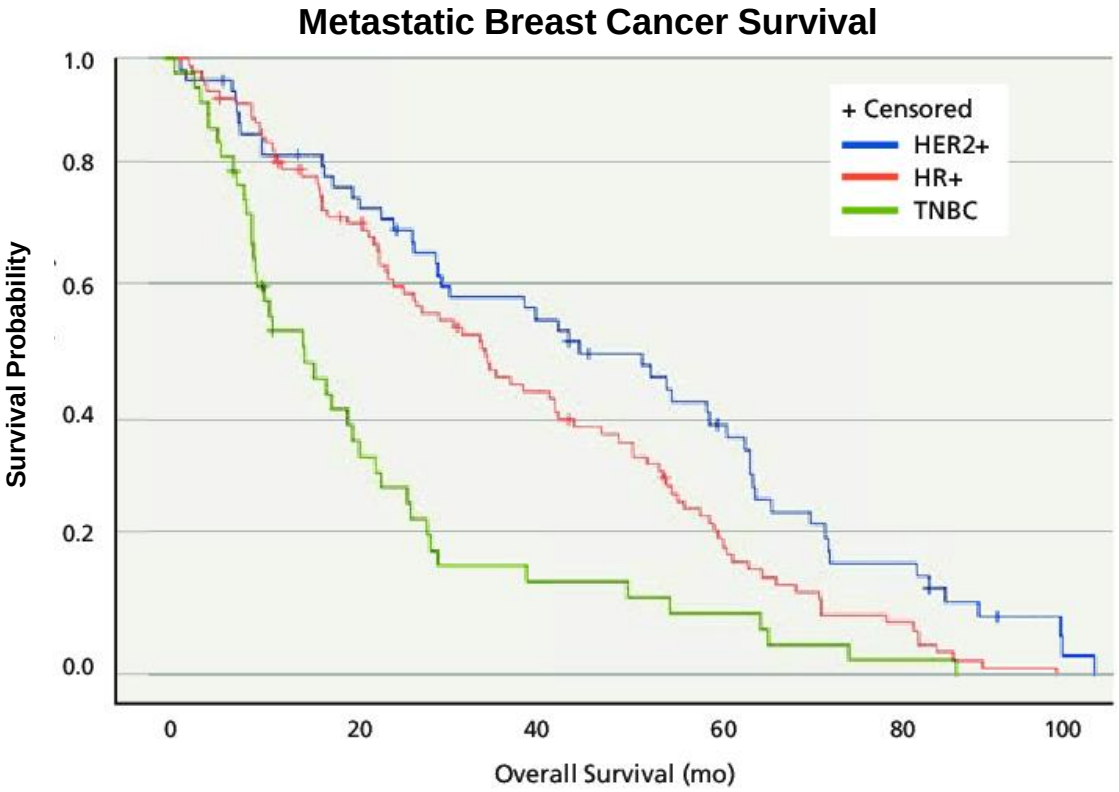


*Notes: *Exclusivity period projected to extend beyond patent expiry due to patent restoration; ** Data exclusivity exceeds patent expiry.*

Speakers

José Baselga
Executive Vice President,
R&D Oncology

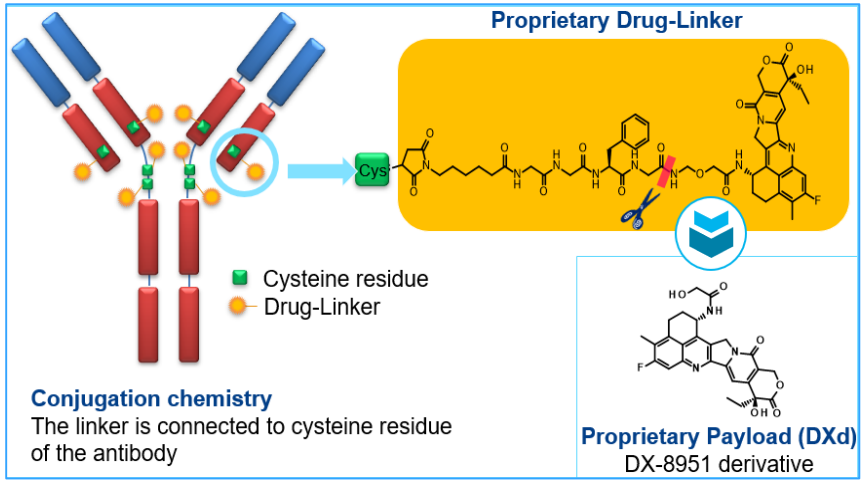
Significant survival gains in HER2+ breast cancer, but substantial unmet need persists



Source: Seah et al. JNCCN 2014

DS-8201: A State of the Art Second Generation ADC

Designing Better Characteristics for Potentially Enhanced Clinical Benefit



Drug Design Attributes

	DS-8201	T-DM1	Clinical Implications
Payload	Topoisomerase-1 inhibitor	Tubulin inhibitor	Validated topo-1 mechanism
Drug antibody ratio	High: 7-8	Low: 3-4	More drug delivery, greater tumor cell killing
Payload Membrane permeability	Highly membrane permeable → "bystander effect"	Membrane impermeable → no bystander effect	Kills neighboring heterogenous non-HER2 tumor cells (pH dependent topo-1 potency)

Sources: (1) Daiichi Sankyo's R&D Day December 2018, (2) T-DM1 FDA label and (3) Ogitani et al, 2016, Cancer Science for DS-8201 Bystander Killing effect

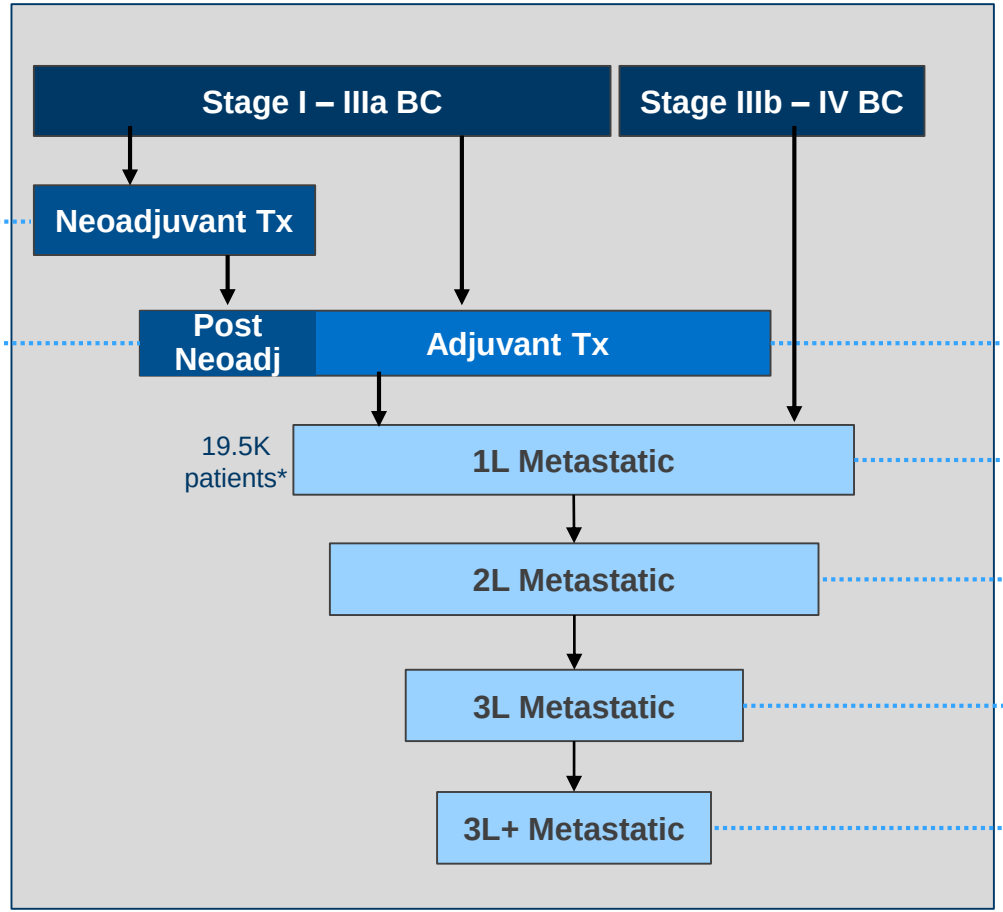
Notes: T-DM1 = trastuzumab emtansine; DS-8201 = trastuzumab deruxtecan

DS-8201: Unprecedented efficacy in late line HER2+ metastatic breast cancer

	Pertuzumab + trastuzumab + chemo (1L)[2]	T-DM1 (1L, failed)[3]	T-DM1 (2L)[4]	T-DM1 (3L+)[5]	DS-8201 (Aug '18 DCO)[1]
mPFS	18.5m	14.1m	9.6m	6.2m	**Not published**
DoR	**20.2m**	**20.7m**	**12.6m**	**9.7m**	**20.7m**
ORR	**80.2%**	**59.7%**	**43.6%**	**31.3%**	**59.5%**
Median prior LoT for adv. disease	0	0	1	4	7[6] 100% prior T-DM1 88% prior pertuzumab

Sources: [1]DS data on file, N=111 (R&D Day Dec 2018) [2]CLEOPATRA (NEJM 2012) [3]MARIANNE [4]EMILIA [5]TH3RESA [6]Iwata et al ASCO2018, April 2018 data cut off, N=111 includes neoadjuvant and/or adjuvant therapies, J101 study, https://clinicaltrials.gov/ct2/show/NCT02564900

HER2+ breast cancer: Patient flow and landmark studies



NeoSphere (Neoadjuvant)
Pertuzumab + trastuzumab + CTX
46% pCR

KATHERINE (Post Neoadjuvant)
T-DM1
88% 3-yr iDFS

APHINITY (Adjuvant)
Pertuzumab + trastuzumab + CTX
94% 3-yr iDFS

CLEOPATRA (1L)
Pertuzumab + trastuzumab + CTX;
18.5m mPFS

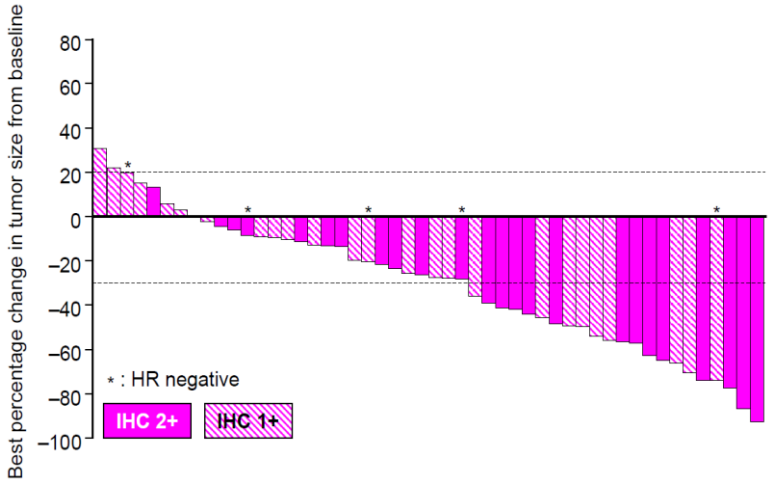
EMILIA (2L)
T-DM1
9.6m mPFS

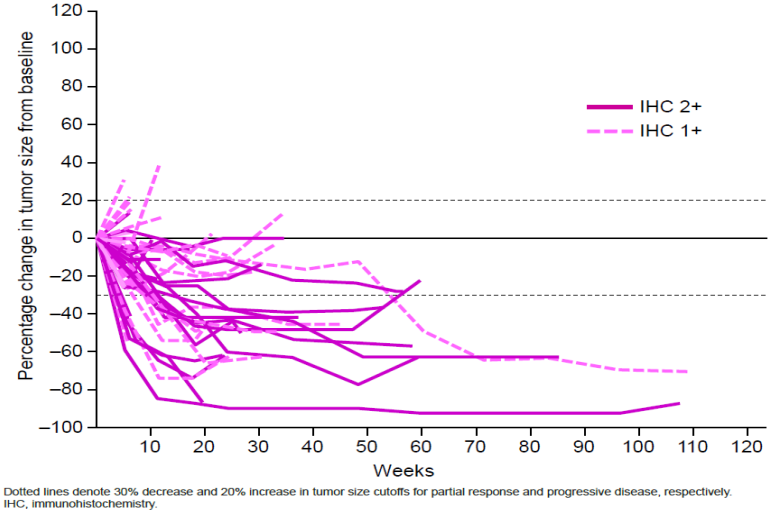
TH3RESA (3L)
T-DM1
6.2m mPFS

J101
DS-8201
20.7m mDOR

**Source: Kantar CancerMpact 2018, G7 (US, EU5, Japan)*

DS-8201: Breakthrough efficacy in HER2 low breast cancer





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

	Confirmed ORR	mDoR	mPFS
All (N = 51)	44.2% (N=43)	9.4m	7.6m
IHC 2+ (n = 24)	54.5% (N=22)	11.0m	13.6m
IHC 1+ (n = 27)	33.3% (N=21)	7.9m	5.7m
HR+ (n = 45)	47.4% (N=38)	11.0m	7.9m
Prior CDK4/6 inhibitor (n = 15)	33.3% (N=12)	NR	7.1m

Source: SABCS Dec 2018, Modi et al; Poster # p6-17-02, Abstract #486. October 12th, 2018 data cut off

DS-8201 in HER2 low: Compelling data vs benchmarks in hormone receptor positive (HR+) breast cancer

	Palbociclib + ET		Endocrine	Alpelisib	Chemo	DS-8201	DS-8201
	1L[1]	2L[2]	2L[2]	1L/2L PIK3CAm[3]	3L+ (4 studies)[4]	3L+ (n=22*, IHC2+)	3L+ (n=21*, IHC1+)
mPFS	25m	10m	5m	11m (Positive Ph3)	~4m	13.6m	5.7m
ORR	**42%**	**19%**	**6%**	**36%**	**5-27%**	**54.5%**	**33.3%**
Median prior LoT for adv. disease	0	1	1	0-1	2+	5 (8 incl. neo/adj)	

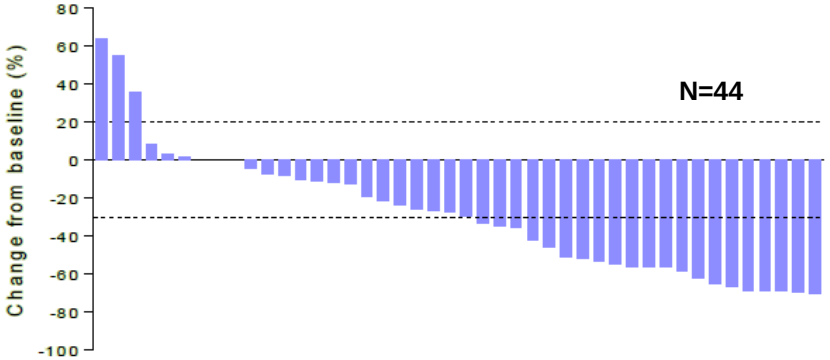
Sources: [1]PALOMA-2 [2]PALOMA-3 [3]SOLAR-1 [4]Cortes et al. Lancet 2011; Kaufman et al. J Clin Oncol. 2015; Rha et al. Breast Cancer Res Treat. 2005.; Gradishar et al. J Clinical Oncol. 2005

**Includes up to N=5 TNBC patients (1 response), split by IHC status not available*
SABCS Dec 2018, Modi et al; Poster # p6-17-02, Abstract #486. October 12th, 2018 data cut off

DS-8201: Compelling efficacy in other tumor types

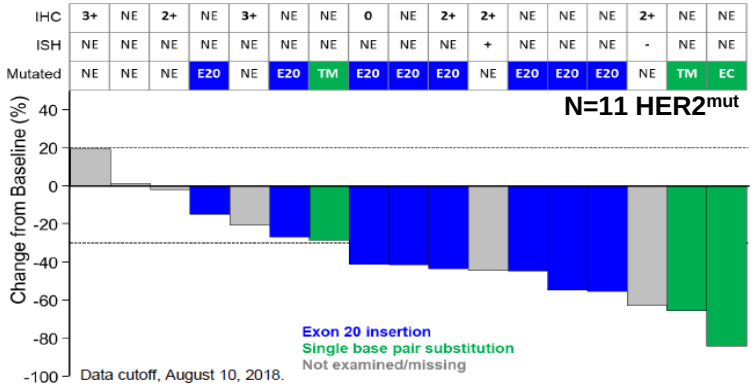
HER2 expression and HER2 mutation

HER2+ Gastric Cancer[1]



	Trastuzumab + chemo[3]	Ramucirumab + chemo[4]	T-DM1 *(Failed)*[5]	DS-8201
mPFS	6.7m	4.4m	2.7m	5.6m
ORR	**47%**	**28%**	**21%**	**43%**
Median prior LoT	0	1	1	3

HER2+ & HER2^{mut} NSCLC[2]



	Osimertinib EGFRm[6]	Alectinib ALK+[7]	Pembrolizumab + Ctx Non-EGFR/ALK[8]	T-DM1 HER2^{mut}[9]	DS-8201 HER2^{mut}
mPFS	18.9m	34.8m	8.8m	5m	14.1m
ORR	**80%**	**83%**	**48%**	**44%**	**73%**
Median prior LoT	0	0	0	2	3

Sources: [1]Iwata et al, ASCO 2018 Abstract #2501 [2]Tsurutani et al, WCLC 2018 Abstract #13325; [3]ToGA [4]RAINBOW [5]GATSBY [6]FLAURA [7]ALEX [8]KEYNOTE-189 [9]Li et al, JCO 2018, N=18

DS-8201: ILD to be reduced by dose, less prior treatment, earlier diagnosis and proactive management

ILD in Phase 1/2 studies[1]

	All-grade	Grade 5
All subjects N=665	9.9%	0.8%
Breast cancer, any dose N=510	10.6%	0.8%
Breast cancer, 5.4 mg/kg N=269	5.6%	0.4%

Conclusions

- **Higher likelihood of developing ILD associated with[1]:**
  - **Higher dose (≥6.4 mg/kg)**
  - **Japanese origin:** *Japanese patients 49% of N=665 sample*
  - **Number of prior therapies:** *Many patients in Phase1/2 have multiple prior lines of therapy*
- **Median 149 days (~6 months) to onset[1] allows for monitoring & intervention**
- **Education and guidelines implementation underway**

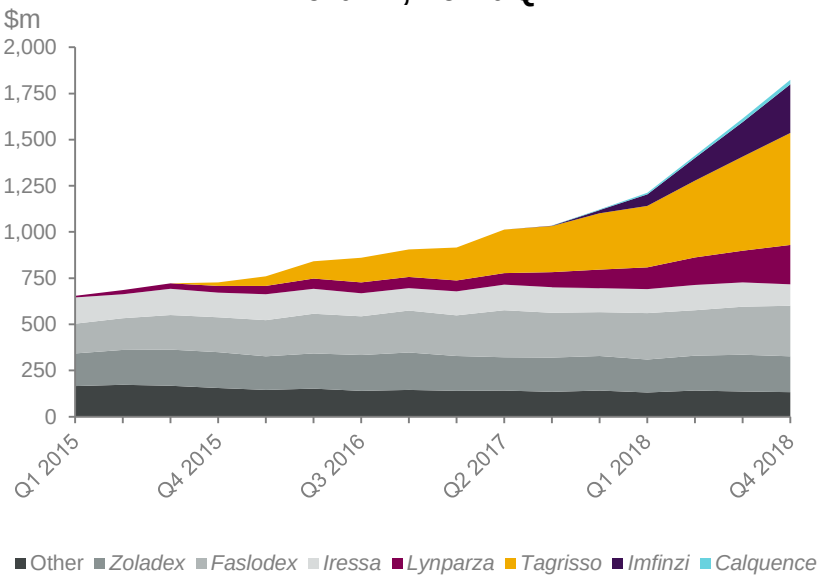
Source: [1]Powell et al, SABCS 2018; Poster #P6-17-06, Abstract #979

Speakers

Dave Fredrickson
Executive Vice President,
Oncology

AstraZeneca Oncology building on strong growth

Total Oncology sales
+49% FY; +61% Q4



New medicines *Lynparza*, *Tagrisso*, *Imfinzi* and *Calquence* added $1.9bn

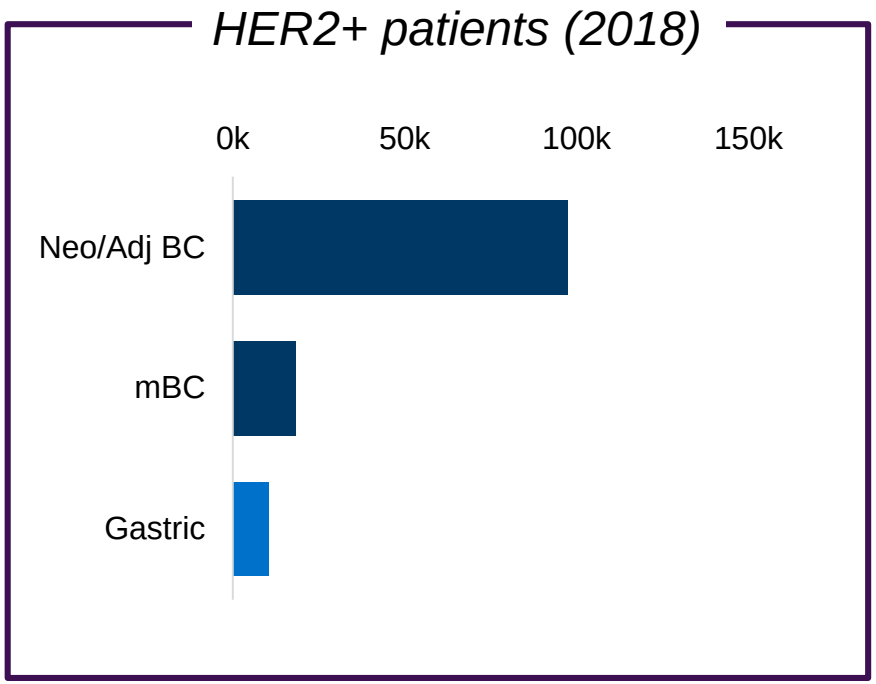
- ***Tagrisso*** quickly moving ahead to become the no. 1 AstraZeneca medicine in 2019
- ***Imfinzi*** strong US uptake; ex-US opportunity underway
- ***Lynparza***, leading PARP in ovarian and breast cancers
- ***Calquence*** first ex-US approvals in MCL[1]; CLL[2] Phase III data in H2 2019
- ***Faslodex*** became $1bn blockbuster

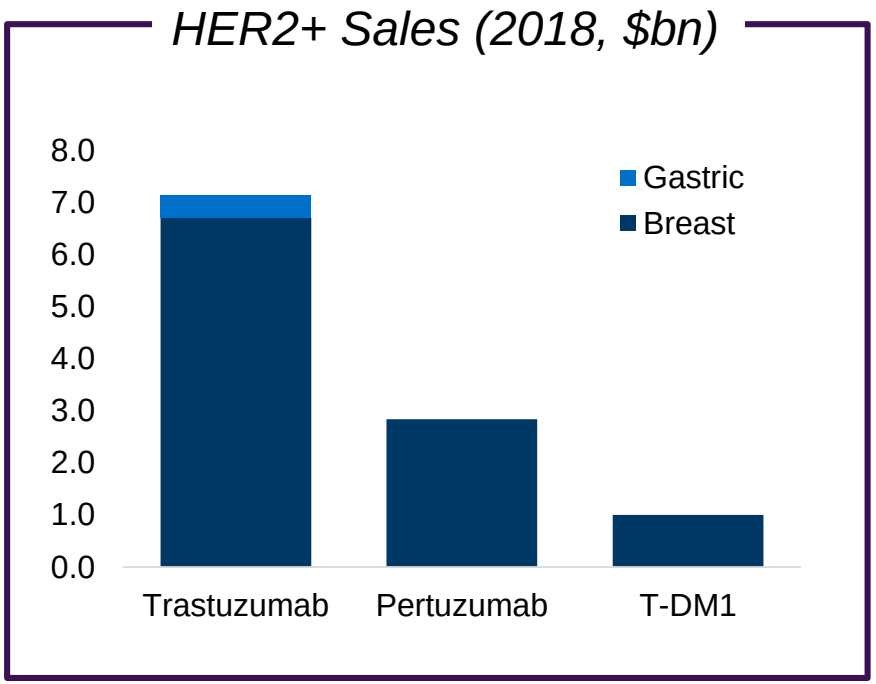
Absolute values and changes at CER and for FY 2018, unless otherwise stated.

1. Mantle cell lymphoma.
2. Chronic lymphocytic leukaemia.

Source: AZ Full Year 2018 Results Presentation

HER2+ market today: $11bn in breast & gastric cancer

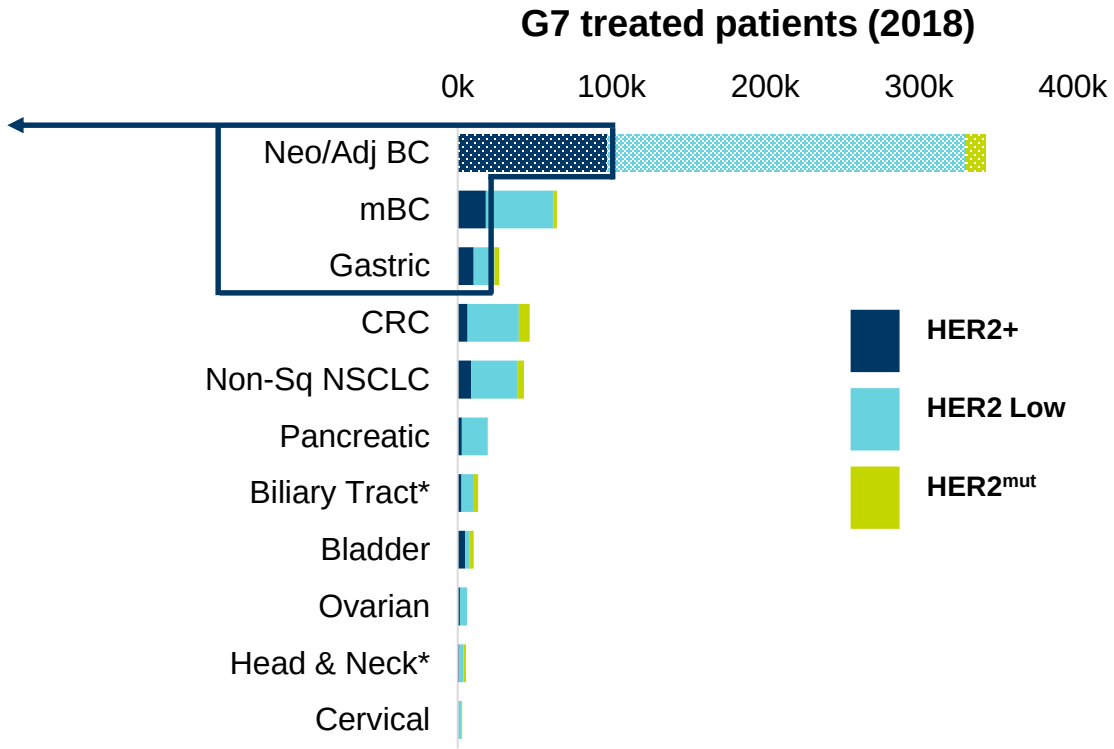




Epi source: Kantar CancerMpact 2018 drug treated patients in first line in metastatic (unless otherwise specified), for US, EU5 & Japan; Prevalence sources: Literature; Sales source: Evaluate Pharma, worldwide sales

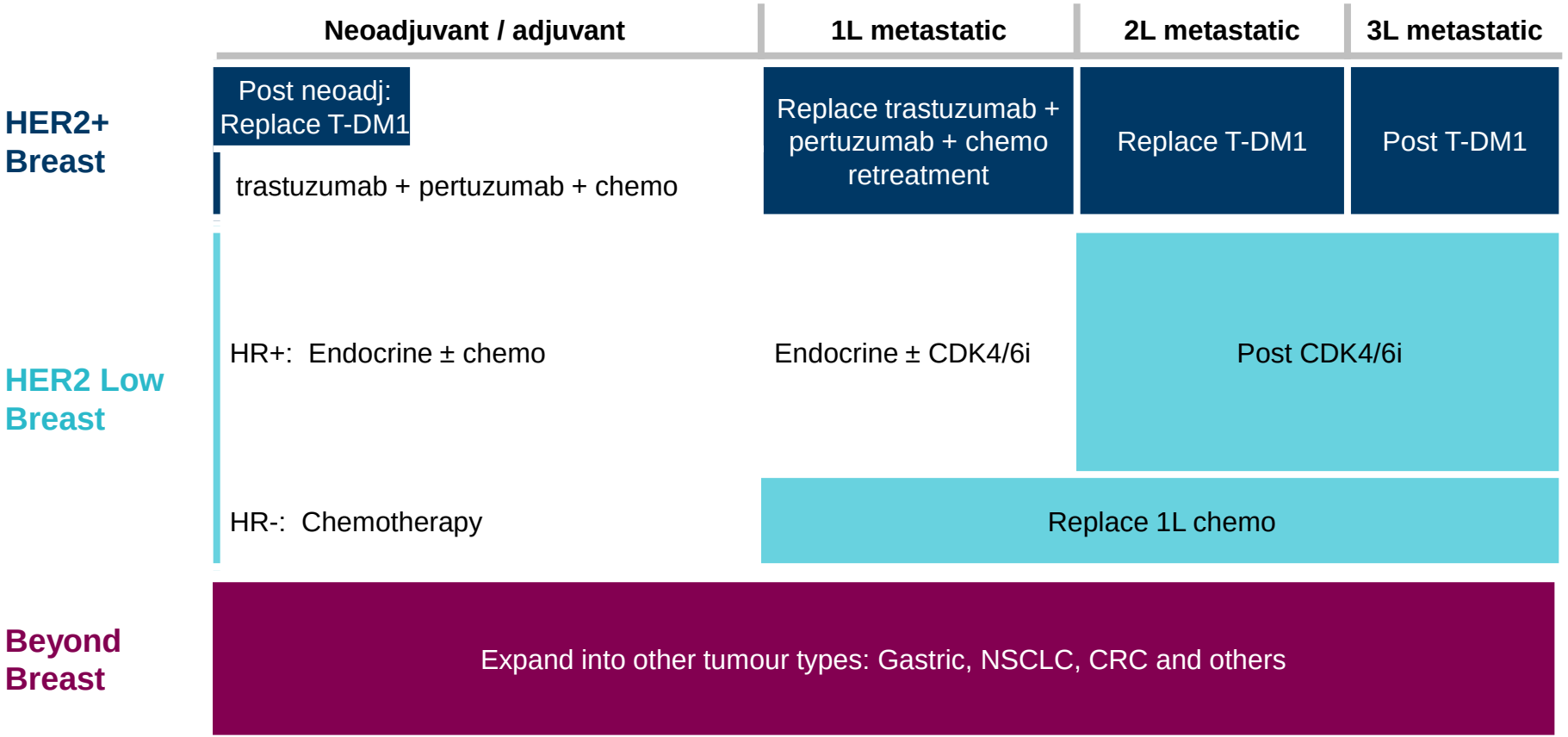
DS-8201: Potential to expand HER2 market today

Current HER2+ Treatments



Epi source: Kantar CancerMpact 2018 drug treated patients in first line in metastatic (unless otherwise specified), for US, EU5 & Japan; Prevalence sources: Literature
**Biliary Tract includes Cholangiocarcinoma & Gallbladder, AZ estimate for patients; Head & Neck includes Salivary Gland cancer*

Building DS-8201 in Breast Cancer and beyond



Source: AZ strategy for DS-8201 in context of standard of care regimens based upon NCCN Guidelines

AZ oncology capabilities and scale strengthen DS-8201

AstraZeneca Oncology

- **Clinical operations:** >80 ongoing, clinical development projects*
- **Regulatory affairs:** 28 major market filings for 4 key brands**
- **Sales, marketing, diagnostics:** Launch experienced, breast cancer teams in 80+ countries
- **Manufacturing**: Biologics manufacturing scale up expertise

Opportunities

- **Accelerate & expand development program**
  - ➢ New indications & combinations
- **Broaden global commercial reach**
  - ➢ AZ presence in China & beyond
- **Mitigate commercial execution risk with deep oncology expertise**
  - ➢ Leverage filing and launch experience

Source: AstraZeneca Annual Report
*Notes: **Major markets: US, EU, Japan, China; 4 key brands: Imfinzi, Lynparza, Calquence & Tagrisso (since 2014)*

Building our Oncology franchises

Significantly accelerates and expands AZ oncology portfolio

Faslodex, *Lynparza*

Lynparza

Tagrisso, *Imfinzi*, *Iressa*

Calquence

Four disease areas with first or best-in-class cornerstone medicine

Source: Various AZ investor presentations

Speakers

Marc Dunoyer
Executive Director and
Chief Financial Officer

Key transaction terms

- **Territory:** Worldwide excluding Japan
- **Structure:** co-development and co-commercialisation, 50/50 cost and profit split (ex Japan)
- **Supply:** Daiichi Sankyo will manufacture and supply product for the collaboration
- **Consideration:**
  - Non-contingent upfront cash fee of $1.35bn (split evenly across 2019 & 2020)
  - Regulatory and other contingent payments (up to $3.8bn), sales-related milestones (up to $1.75bn)
  - AZ receives royalties on Japan sales
- **Closing:** 29 March, 2019. No shareholder or regulatory approval required
- **Financing: ~**$3.5bn of new ordinary shares
- **Financial impact*:** neutral in 2019, growing accretion from 2020 to a significant contribution in 2023 - 2019 guidance reconfirmed

*Note: * financial impact with respect to core earnings per share, post equity placing*

Capital allocation priorities unchanged

Capital allocation priorities	DS-8201 collaboration
Investment in the business	*Accelerates Oncology strategy*
Progressive dividend policy	*Supportive*
Strong, investment-grade credit rating	*Concurrent equity placing strengthens credit profile*
Immediately earnings accretive	*Neutral to core EPS 2019, growing accretion from 2020 to a significant contribution in 2023**

*Note: * financial impact with respect to core earnings per share, post equity placing*

Equity placing demonstrates commitment to credit rating

Equity placing to fund near-term transaction requirements and strengthen balance sheet:

- Meet upfront and near term DS-8201 funding requirements
  - $1.35bn upfront non-contingent payment (split evenly across 2019 & 2020)
  - ~$1bn approval and sales-related contingent payments from 2020 to 2022
- Increase overall balance sheet strength and liquidity
  - Repay $1bn bond maturing September 2019

2019 guidance reconfirmed

Product sales

A high single-digit percentage increase

Core EPS

$3.50 to $3.70

Guidance at CER, post equity placing


Q&A