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

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

Notes: *non-systemic chemotherapy

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.
José Baselga
Executive Vice President, R&D Oncology
Significant survival gains in HER2+ breast cancer, but substantial unmet need persists

Metastatic Breast Cancer Survival

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**

<table>
<thead>
<tr>
<th></th>
<th>DS-8201</th>
<th>T-DM1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Payload</strong></td>
<td>Topoisomerase-1 inhibitor</td>
<td>Tubulin inhibitor</td>
</tr>
<tr>
<td><strong>Drug antibody ratio</strong></td>
<td>High: 7-8</td>
<td>Low: 3-4</td>
</tr>
<tr>
<td><strong>Payload Membrane permeability</strong></td>
<td>Highly membrane permeable → &quot;bystander effect&quot;</td>
<td>Membrane impermeable → no bystander effect</td>
</tr>
</tbody>
</table>

**Clinical Implications**

- **Validated topo-1 mechanism**
- **More drug delivery, greater tumor cell killing**
- **Kills neighboring heterogenous non-HER2 tumor cells (pH dependent topo-1 potency)**

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

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

<table>
<thead>
<tr>
<th>Pertuzumab + trastuzumab + chemo (1L)</th>
<th>T-DM1 (1L, failed)</th>
<th>T-DM1 (2L)</th>
<th>T-DM1 (3L+)</th>
<th>DS-8201 (Aug '18 DCO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS</td>
<td>18.5m</td>
<td>14.1m</td>
<td>9.6m</td>
<td>6.2m</td>
</tr>
<tr>
<td>DoR</td>
<td>20.2m</td>
<td>20.7m</td>
<td>12.6m</td>
<td>9.7m</td>
</tr>
<tr>
<td>ORR</td>
<td>80.2%</td>
<td>59.7%</td>
<td>43.6%</td>
<td>31.3%</td>
</tr>
<tr>
<td>Median prior LoT for adv. disease</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

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

**Stage I – IIIa BC**
- Neoadjuvant Tx

**Stage IIIb – IV BC**
- Neoadjuvant Tx

**Post Neoadj**
- Adjuvant Tx

**1L Metastatic**
- 19.5K patients*

**2L Metastatic**

**3L Metastatic**

**3L+ Metastatic**

**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**

### Confirmed ORR, mDoR, mPFS

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

*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

<table>
<thead>
<tr>
<th></th>
<th>Palbociclib + ET</th>
<th>Endocrine</th>
<th>Alpelisib 1L/2L PIK3CAm</th>
<th>Chemo 3L+ (4 studies)</th>
<th>DS-8201 3L+ (n=22*, IHC2+)</th>
<th>DS-8201 3L+ (n=21*, IHC1+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS</td>
<td>25m</td>
<td>10m</td>
<td>5m</td>
<td>11m (Positive Ph3)</td>
<td>~4m</td>
<td>13.6m</td>
</tr>
<tr>
<td>ORR</td>
<td>42%</td>
<td>19%</td>
<td>6%</td>
<td>36%</td>
<td>5-27%</td>
<td>54.5%</td>
</tr>
<tr>
<td>Median prior LoT for adv. disease</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0-1</td>
<td>2+</td>
<td>5</td>
</tr>
</tbody>
</table>


*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

<table>
<thead>
<tr>
<th></th>
<th>Trastuzumab + chemo</th>
<th>Ramucirumab + chemo</th>
<th>T-DM1 (Failed)</th>
<th>DS-8201</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS</td>
<td>6.7m</td>
<td>4.4m</td>
<td>2.7m</td>
<td>5.6m</td>
</tr>
<tr>
<td>ORR</td>
<td>47%</td>
<td>28%</td>
<td>21%</td>
<td>43%</td>
</tr>
<tr>
<td>Median prior LoT</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

### HER2+ & HER2\textsuperscript{mut} NSCLC

<table>
<thead>
<tr>
<th></th>
<th>Osimertinib EGFRm\textsuperscript{6}</th>
<th>Alectinib ALK+\textsuperscript{7}</th>
<th>Pembrolizumab + Ctx Non-EGFR/ALK\textsuperscript{8}</th>
<th>T-DM1 HER2\textsuperscript{mut}</th>
<th>DS-8201 HER2\textsuperscript{mut}</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS</td>
<td>18.9m</td>
<td>34.8m</td>
<td>8.8m</td>
<td>5m</td>
<td>14.1m</td>
</tr>
<tr>
<td>ORR</td>
<td>80%</td>
<td>83%</td>
<td>48%</td>
<td>44%</td>
<td>73%</td>
</tr>
<tr>
<td>Median prior LoT</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

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

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**N=44**

Exon 20 insertion
Single base pair substitution
Not examined/missing

Data cutoff, August 10, 2018.
DS-8201: ILD to be reduced by dose, less prior treatment, earlier diagnosis and proactive management

### ILD in Phase 1/2 studies

<table>
<thead>
<tr>
<th></th>
<th>All-grade</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>All subjects N=665</td>
<td>9.9%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Breast cancer, any dose N=510</td>
<td>10.6%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Breast cancer, 5.4 mg/kg N=269</td>
<td>5.6%</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

### Conclusions

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

Source: ¹Powell 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.

Source: AZ Full Year 2018 Results Presentation

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1. Mantle cell lymphoma.
2. Chronic lymphocytic leukaemia.
HER2+ market today: $11bn in breast & gastric cancer

HER2+ patients (2018)

- Neo/Adj BC
- mBC
- Gastric

0k 50k 100k 150k

HER2+ Sales (2018, $bn)

- Trastuzumab
- Pertuzumab
- T-DM1

Gastric
Breast

Epi source: Kantar CancerM pact 2018 drug treated patients in first line in metastatic (unless otherwise specified), for US, EUS & Japan; Prevalence sources: Literature; Sales source: Evaluate Pharma, worldwide sales
DS-8201: Potential to expand HER2 market today

Current HER2+ Treatments

G7 treated patients (2018)

- Neo/Adj BC
- mBC
- Gastric
- CRC
- Non-Sq NSCLC
- Pancreatic
- Biliary Tract*
- Bladder
- Ovarian
- Head & Neck*
- Cervical

HER2+
HER2 Low
HER2^{mut}

Epi source: Kantar CancerM pact 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

<table>
<thead>
<tr>
<th></th>
<th>Neoadjuvant / adjuvant</th>
<th>1L metastatic</th>
<th>2L metastatic</th>
<th>3L metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HER2+ Breast</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post neoadj:</td>
<td>Replace T-DM1</td>
<td>Replace trastuzumab + pertuzumab + chemo</td>
<td>Replace T-DM1</td>
<td>Post T-DM1</td>
</tr>
<tr>
<td>trastuzumab + pertuzumab + chemo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HER2 Low Breast</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR+:</td>
<td>Endocrine ± chemo</td>
<td>Endocrine ± CDK4/6i</td>
<td></td>
<td>Post CDK4/6i</td>
</tr>
<tr>
<td>HR-:</td>
<td>Chemotherapy</td>
<td></td>
<td>Replace 1L chemo</td>
<td></td>
</tr>
</tbody>
</table>

**Beyond Breast**

Expand into other tumour types: Gastric, NSCLC, CRC and others

*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

Breast cancer
Ovarian cancer
Lung cancer
Haematology

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**

- Investment in the business
- Progressive dividend policy
- Strong, investment-grade credit rating
- Immediately earnings accretive

**DS-8201 collaboration**

- Accelerates Oncology strategy
- Supportive
- Concurrent equity placing strengthens credit profile
- Neutral to core EPS 2019, growing accretion from 2020 to a significant contribution in 2023*

*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