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**

### Prevalence of HER2 status across cancer types

**Current HER2+ breast, gastric market**

**Opportunity in HER2 low**

**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.
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

<table>
<thead>
<tr>
<th></th>
<th>DS-8201</th>
<th>T-DM1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Payload</td>
<td>Topoisomerase-1 inhibitor</td>
<td>Tubulin inhibitor</td>
</tr>
<tr>
<td>Drug antibody ratio</td>
<td>High: 7-8</td>
<td>Low: 3-4</td>
</tr>
<tr>
<td>Payload Membrane permeability</td>
<td>Highly membrane permeable → “bystander effect”</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)

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

<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

**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 CancerM pact 2018, G7 (US, EU5, Japan)
## DS-8201: Breakthrough efficacy in HER2 low breast cancer

**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*
## Palbociclib + ET

<table>
<thead>
<tr>
<th></th>
<th>1L¹</th>
<th>2L²</th>
<th>Endocrine 2L²</th>
<th>Alpelisib 1L/2L PIK3CAm³</th>
<th>Chemo 3L+ (4 studies)⁴</th>
<th>DS-8201 3L+ (n=22*, IHC2+)</th>
<th>DS-8201 3L+ (n=21*, IHC1+)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>mPFS</strong></td>
<td>25m</td>
<td>10m</td>
<td>5m</td>
<td>11m (Positive Ph3)</td>
<td>~4m</td>
<td>13.6m</td>
<td>5.7m</td>
</tr>
<tr>
<td><strong>ORR</strong></td>
<td>42%</td>
<td>19%</td>
<td>6%</td>
<td>36%</td>
<td>5-27%</td>
<td>54.5%</td>
<td>33.3%</td>
</tr>
<tr>
<td><strong>Median prior LoT for adv. disease</strong></td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0-1</td>
<td>2+</td>
<td>5 (8 incl. neo/adj)</td>
<td></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 + chemo³</th>
<th>Ramucirumab + chemo⁴</th>
<th>T-DM1 (Failed)⁵</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+&HER2mut NSCLC**

<table>
<thead>
<tr>
<th></th>
<th>Osimertinib EGFRm⁶</th>
<th>Alectinib ALK⁺⁷</th>
<th>Pembrolizumab+Ctx Non-EGFR/ALK⁸</th>
<th>T-DM1 HER2mut⁹</th>
<th>DS-8201 HER2mut</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: ¹Iwata et al, ASCO 2018 Abstract #2501 ²Tsurutani et al, WCLC 2018 Abstract #13325; ³ToGA ⁴RAINBOW ⁵GATSBY ⁶FLAURA ⁷ALEX ⁸KEYNOTE-189 ⁹Li 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

<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

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

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

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

Source: AZ Full Year 2018 Results Presentation

1. Mantle cell lymphoma.
2. Chronic lymphocytic leukaemia.
HER2+ patients (2018)

- Neo/Adj BC
- mBC
- Gastric

HER2+ Sales (2018, $bn)

- Trastuzumab
- Pertuzumab
- T-DM1

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

G7 treated patients (2018)

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

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

<table>
<thead>
<tr>
<th>HER2+ Breast</th>
<th>Neoadjuvant / adjuvant</th>
<th>1L metastatic</th>
<th>2L metastatic</th>
<th>3L metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post neoadj: Replace T-DM1</td>
<td>trastuzumab + pertuzumab + chemo</td>
<td>Replace trastuzumab + pertuzumab + chemo retreatment</td>
<td>Replace T-DM1</td>
<td>Post T-DM1</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Beyond Breast</th>
<th>Neoadjuvant / adjuvant</th>
<th>1L metastatic</th>
<th>2L metastatic</th>
<th>3L metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

- **Beyond Breast**: Expand into other tumour types: Gastric, NSCLC, CRC and others

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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: Faslodex, Lynparza
Ovarian cancer: Lynparza
Lung cancer: Tagrisso, Imfinzi, Iressa
Haematology: 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

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

*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