R&D Day 2019

DAIICHI SANKYO CO., LTD.

Sunao Manabe
President and CEO

December 17, 2019@Tokyo
December 19, 2019@New York
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Daiichi Sankyo’s R&D – Where We Are

- **Strength of Daiichi Sankyo’s R&D**
  - Science & technology of combined organizations

- **Sources of science & technology**
  - In-house drug creation capabilities cultivated through innovative pharmaceuticals research & development for more than 100 years
  - Culture in which individual researchers share their know-how & acquired outcomes and making improvements from there
  - Excellent assessment capability for science

**Science & Technology**

- In-house drug creation capabilities cultivated over years
- Culture of sharing know-how & outcomes and refinement
- Assessment capability for science

**Pursuing innovation**

- Delivery of new drugs with significant contribution for patients
Focusing on science & technology

Pursuing Innovation

Created DXd-ADC assets with expectations for high competitiveness

Creation of DXd-ADC assets

- DS-8201
- DS-1062
- U3-1402
CEOs Mission: (1) Realization of 2025 Vision

- Deliver DXd-ADC assets to as many patients, and as quickly as possible

Delivering DXd-ADC assets

- Enhancement of global development & commercial capabilities

- Expand Investments
  - R&D investments primary focused on 3 ADCs
  - Additional Capital expenditures 100.0 Bn JPY or more for CMC and manufacturing

As many patients as possible
As quickly as possible

Establish position as global No.1 ADC company

Realize 2025 Vision “Global Pharma Innovator with Competitive Advantage in Oncology”
CEO’s Mission: (2) Strive for Sustainable Growth

◆ Create assets Beyond DXd-ADC

Creation of Beyond DXd-ADC assets

◆ Utilize Daiichi Sankyo’s competitive new modalities and technology, expand drug creation technology platform
◆ Identify competitive assets by reliable assessment capabilities and allocate management resources

Apply Daiichi Sankyo's new modalities and technologies to delivering new drugs that are not limited to specific therapeutic areas
Key Areas for Further Growth

- Acquire world’s most cutting-edge science & technology necessary for global expansion
- Hire and develop the people who can innovate from all over the world
- Taking advantage of digital revolution (AI, Big Data, IoT etc.)
- Improve the company’s science & technology

Delivery of new drugs with significant contribution for patients
Renew Mid-to-Long-Term Vision

In parallel with the next 5-year business plan development, mid-to-long-term vision beyond 2025 will be established.

5-Year Business Plan 2021-2025
To be announced in 2021

New Vision
(Beyond 2025)

5-Year Business Plan 2016-2020
Transformation toward 2025 Vision

2025 Vision
Global Pharma Innovator with Competitive Advantage in Oncology
R&D Strategy

Junichi Koga, PhD
Global Head of R&D
Progress as Planned

CE 2025 Vision

- ADC Franchise: 3
- AML Franchise: 3
- Breakthrough Science: 1

Deliver 7 NMEs in 8 years

- Quizartinib approved in JP
- Pexidartinib approved in US

SM 2025 Vision

- Maximize near-term revenue
- Grow future franchises

- 2 NMEs in 2018-20
- 3 NMEs 2021-25

- Mirogabalin approved in JP
- Esaxerenone approved in JP
R&D Now Built on 3 Pillars

- The potential of 3 ADCs has increased enough to create a pillar from each of them
- Prioritize investments and resource allocation to 3 ADC projects

DS-8201  DS-1062  U3-1402

3 important pillars
New R&D Strategy: 3 and Alpha

3 lead ADCs

DS-8201: maximize value with co-development partnership with AZ

DS-1062: substantial opportunities across multiple indications

U3-1402: fast to market

Science-informed precision medicine: three ADCs based on the unique biology of DXd technology and the vector/receptor

Alpha

Alpha = angle of attack and speed of elevation

Alpha = Performance far exceeding benchmark index

Alpha = the cutting edge and power of true innovation delivering drugs changing SOC
Categorization of 3 and Alpha

- **3 lead ADCs**
  - DS-8201
  - DS-1062
  - U3-1402

- Alpha
  - Timely and flexible resource allocation
  - Seamless collaboration among organizations in order to further combinatorial innovation
**Drugs Changing SOC**

<table>
<thead>
<tr>
<th>First-in-class drugs</th>
<th>Best-in-class drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>having disruptive MOA</td>
<td>improved through medicinal chemistry and biology to meet unmet medical needs</td>
</tr>
<tr>
<td>Target others cannot deliver</td>
<td></td>
</tr>
</tbody>
</table>

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Daiichi Sankyo Focus on Drugs Changing SOC
Daiichi Sankyo Researchers

- Excellent junior scientists have been recruited and developed in a wide range of areas
- Resilience mindset is respected among scientists
- Disruptive thinking and approach are encouraged
- Constructive working environment regardless of expertise and hierarchy
Daiichi Sankyo's Unique Science & Technology

Outstanding medicinal chemistry, antibody engineering & discovery biology

Discovery Biology/ Med. Chem.

Modality

Technology

Organically work together

Discovery of drugs changing SOC
Technology Portfolio in Daiichi Sankyo

- **Antibody**
- **Next Generation ADC**
- **Genetic/Orphan Disease**
- **Inflammation/Immunology**
- **Cardio-renal diseases**
- **Neurology/Neuroscience**
- **Vaccine**
- **Gene Therapy**
- **Scaffold**
- **Cell Therapy**
- **MED & ENA Nucleotide**
- **LNP/mRNA**
- **Bispecific**
- **Sugar chain modification**
- **Cyclic peptide Peptide drug**

Next Generation

ADC
DS-Original Lipid Nanoparticle (LNP)

- Efficient encapsulation of nucleic acids
- High nucleic acid delivery ability
- Wide safety margin due to metabolizable cationic lipid
- Suitable to clinical development

Particle size ~100nm

Therapeutic application research (cancer, genetic disease etc.) are on-going.

Nucleic acids
- single- or double-strand DNA and RNA, modified oligonucleotides (e.g. MED-siRNA, mRNA)
**DS-Original Small Interfering RNA: MED-siRNA**

**MED-siRNA** modified with alternately combined 2’-O-methyl RNA and DNA

- Comparable Kd activity with natural siRNA
- Low cost & easy manufacture
- RNase resistance
- Reduction of IFN induction
- Avoidance of off-target

**Key Points**

- Natural siRNA
- MED-siRNA
- Chemical modification
- Transfection into cells
- RNAi activity

**Symbols**

- RNA
- DNA
- 2’-OMe RNA
- p: phosphate
Embrace our Differences

Mindsets & Behaviors which Nourish

World Class Science & Technology

Serve Patients Globally

Trust

Collaboration

Blend the Best of East and West

Create Unity

Embrace our Differences

Appreciate Disruptive Mindset

Transparency
R&D Day 2019
Progress Report

Antoine Yver, MD, MSc
Executive VP & Global Head R&D Oncology
Today’s Agenda

1 Introduction

2 DS-8201: The Data

3 DS-8201: The Collaboration

4 ADC Portfolio: Data and CDP Updates

5 DXd ADC ILD

6 “3 and Alpha”

7 News Flow and Future Events
Today Marks A Critical Step on Our Journey

2016

Cancer Enterprise Strategy
- Accelerated DS-8201 and scale of manufacturing (300M$ CAPEX)
- Predicted 2019 crunch point for CE, needing ~100% RD Unit Budget

2017

R&D Strategy and Cancer Enterprise 2025
- ‘7 in 8’ CE 2025
- Enhanced CE allocation of R&D resources

2018

ADC Franchise Strategy
- Highlighted the scope of opportunity offered by the DXd platform
- Defined choices for operating model to maximize the ADC franchise value
- Validated ADC strategy with AZ agreement

2019

“3 and Alpha” Strategy

2019
# History of Antibody Drug Conjugates (ADCs)

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1913</td>
<td>Paul Ehrlich described the concept of a “magic bullet” and drug targeting (i.e. a ‘haptophore’ that can deliver a ‘toxophore’ selectively to a tumor)</td>
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<tr>
<td>1958</td>
<td>MTX* linked to an antibody directed toward leukemia cells</td>
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<tr>
<td>1967</td>
<td>ADCs proposed; immunoradioactive agent disclosed</td>
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<tr>
<td>1972</td>
<td>Noncovalent linked ADC tested in animal models</td>
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<tr>
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<td>Noncovalent linked ADC tested in animal models</td>
</tr>
<tr>
<td>1975</td>
<td>Production of mABs using hybridoma-based technology</td>
</tr>
<tr>
<td>1975</td>
<td>Production of mABs using hybridoma-based technology</td>
</tr>
<tr>
<td>1978</td>
<td>Humanized mAbs reported</td>
</tr>
<tr>
<td>1978</td>
<td>Humanized mAbs reported</td>
</tr>
<tr>
<td>1983</td>
<td>Clinical trials w/ ADC vindesine-αCEA</td>
</tr>
<tr>
<td>1983</td>
<td>Clinical trials w/ ADC vindesine-αCEA</td>
</tr>
<tr>
<td>1988</td>
<td>First FDA approved ADC (Mylotarg®)</td>
</tr>
<tr>
<td>1988</td>
<td>First FDA approved ADC (Mylotarg®)</td>
</tr>
<tr>
<td>2000</td>
<td>Production of mAbs using hybridoma-based technology</td>
</tr>
<tr>
<td>2000</td>
<td>Production of mAbs using hybridoma-based technology</td>
</tr>
<tr>
<td>2011</td>
<td>Adcetris® approved</td>
</tr>
<tr>
<td>2011</td>
<td>Adcetris® approved</td>
</tr>
<tr>
<td>2013</td>
<td>Kadcyla® approved</td>
</tr>
<tr>
<td>2013</td>
<td>Kadcyla® approved</td>
</tr>
<tr>
<td>2014</td>
<td>Mylotarg® withdrawn from market</td>
</tr>
<tr>
<td>2014</td>
<td>Mylotarg® withdrawn from market</td>
</tr>
</tbody>
</table>

*MTX = methotrexate

Adapted from *Drug Discovery Today*
History of ADCs

From a brilliant concept to DXd break-through technology

Ehrlich’s early (1900) views “on cellular metabolism, and the mode of toxin action and antitoxin formation during the process of immunization” (Courtesy of the Royal Society)

1913 Nobel Prize

DS-8201
2019
Daiichi Sankyo has created seven major technologies on two critical components of the ADC: payload and linker.

**Seven major innovations**

**PAYLOAD**
- A novel MOA of cytotoxic Topoisomerase 1 inhibitor
- 10 times more potent than SN38
- A high cell membrane cross-penetration that creates a “bystander effect” to kill neighboring tumor cells
- Short systemic half-life of released payload

**LINKER**
- High stability, sparing non-cancerous normal tissue from exposure to toxicity
- Selectively cleaved by lysosomal enzymes that tend to be upregulated in tumors
- High number of payload molecules per antibody (Drug-Antibody Ratio; DAR)
**Additional Technology for DXd ADCs**

**Drug Antibody Ratio (DAR) 4 Conjugation**

### DAR8: DS-8201, U3-1402

**High Drug Antibody Ratio Compared to T-DM1**

<table>
<thead>
<tr>
<th></th>
<th>T-DM1</th>
<th>DS-8201</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibody</td>
<td>Trastuzumab</td>
<td>Anti-HER2 Ab</td>
</tr>
<tr>
<td>Payload</td>
<td>Tubulin inhibitor (DM1)</td>
<td>DNA Topoisomerase I inhibitor (DXd)</td>
</tr>
<tr>
<td>DAR</td>
<td>3.5</td>
<td>7-8</td>
</tr>
</tbody>
</table>


### DAR4: DS-1062, DS-7300

**D4-enriched DAR4**

![Diagram showing DAR values and intensity plots for DAR8 and DAR4 conjugates.](image)
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Trastuzumab Deruxtecan (DS-8201) in HER2-Positive Metastatic Breast Cancer Previously Treated With T-DM1: DESTINY-Breast01 Study

Ian Krop, Cristina Saura, Toshinari Yamashita, Yeon Hee Park, Sung-Bae Kim, Kenji Tamura, Fabrice André, Hiroji Iwata, Yoshinori Ito, Junji Tsurutani, Joohyuk Sohn, Neelima Denduluri, Christophe Perrin, Kenjiro Aogi, Eriko Tokunaga, Seock-Ah Im, Keun Seok Lee, Sara Hurvitz, Javier Cortes, Caleb Lee, Shuquan Chen, Lin Zhang, Javad Shahidi, Antoine Yver, Shanu Modi

On behalf of the DESTINY-Breast01 investigators

These data are published simultaneously in NEJM on Dec 11, 2019  Link to NEJM
DESTINY-Breast01 Study Design:
An Open-Label, Multicenter, Phase 2 Study

**Population**
- ≥18 years of age
- Unresectable and/or metastatic BC
- HER2-positive (centrally confirmed on archival tissue)
- Prior T-DM1
- Stable, treated brain metastases were allowed

**T-DM1 Resistant/Refractory** (n=249)

**T-DM1 Intolerant** (n=4)

**Endpoints**
- **Primary:** confirmed ORR by independent central imaging facility review per RECIST v1.1
- **Secondary:** investigator-assessed ORR, DCR, DOR, CBR, PFS, OS, PK and safety

**PART 1**
- **PK Stage** (n=65)
  - 5.4 mg/kg (n=22)
  - 6.4 mg/kg (n=22)
  - 7.4 mg/kg (n=21)

**Dose-Finding Stage** (n=54)
- 5.4 mg/kg (n=28)
- 6.4 mg/kg (n=26)

**PART 2**
- **Continuation Stage** (n=134)
  - PART 2a 5.4 mg/kg (n=130)
  - PART 2b 5.4 mg/kg (n=4)

**PART 2a**
- 5.4 mg/kg (n=130)
- 6.4 mg/kg (n=26)

**PART 2b**
- 5.4 mg/kg (n=4)

**Data Cutoff:** August 1, 2019
- **79 patients** (42.9%) are ongoing
- **105 patients** (57.1%) discontinued, primarily for progressive disease (28.8%)

184 patients enrolled at 5.4 mg/kg
## Patient Baseline Characteristics

| Characteristics                                      | Patients T-DXd 5.4 mg/kg (N=184)
|------------------------------------------------------|----------------------------------
| Age, median (range), years                           | 55.0 (28-96)                     |
| Female, %                                            | 100                              |
| Region, %                                            |                                   |
| Asia / North America / Europe                        | 34.2 / 28.8 / 37.0               |
| ECOG performance status 0 / 1 / 2, %                 | 55.4 / 44.0 / 0.5                |
| Hormone receptor positive / negative / unknown, %    | 52.7 / 45.1 / 2.2                |
| HER2 expression, %                                   |                                   |
| IHC 3+                                               | 83.7                             |
| IHC 2+; ISH+ / IHC 1+; ISH+                          | 15.2 / 1.1                       |
| Presence of visceral disease, %                      | 91.8                             |
| History of brain metastases, %                       | 13.0                             |

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*All 184 patients received ≥1 dose of T-DXd. HER2 status was centrally assessed on archival tissue according to guidelines of the American Society of Clinical Oncology–College of American Pathologists.*

ECOG, Eastern Cooperative Oncology Group; IHC, immunohistochemistry; ISH, in situ hybridization.
**Patient Baseline Characteristics (cont’d)**

**Median prior lines of cancer therapy: 6 (range 2-27)**

<table>
<thead>
<tr>
<th>Prior Treatment</th>
<th>Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-DXd 5.4 mg/kg (N=184)</td>
<td></td>
</tr>
<tr>
<td><strong>Trastuzumab</strong></td>
<td>100</td>
</tr>
<tr>
<td><strong>T-DM1</strong></td>
<td>100</td>
</tr>
<tr>
<td><strong>Pertuzumab</strong></td>
<td>65.8</td>
</tr>
<tr>
<td>Other anti-HER2 therapies</td>
<td>54.3</td>
</tr>
<tr>
<td>Hormone therapy</td>
<td>48.9</td>
</tr>
<tr>
<td>Other systemic therapy</td>
<td>99.5</td>
</tr>
</tbody>
</table>

*Therapies for locally advanced or metastatic breast cancer, including hormone therapy.*
Primary Endpoint: Overall Response Rate

<table>
<thead>
<tr>
<th>Intent-to-treat analysis</th>
<th>Patients T-DXd 5.4 mg/kg (N = 184)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Confirmed ORR by ICR</strong></td>
<td><strong>60.9% (n = 112)</strong> (95% CI, 53.4%-68.0%)</td>
</tr>
<tr>
<td>CR</td>
<td>6.0% (n = 11)</td>
</tr>
<tr>
<td>PR</td>
<td>54.9% (n = 101)</td>
</tr>
<tr>
<td>SD</td>
<td>36.4% (n = 67)</td>
</tr>
<tr>
<td>PD</td>
<td>1.6% (n = 3)</td>
</tr>
<tr>
<td>Not evaluable</td>
<td>1.1% (n = 2)</td>
</tr>
<tr>
<td>DCR</td>
<td>97.3% (95% CI, 93.8%-99.1%)</td>
</tr>
<tr>
<td>CBR × 6 months</td>
<td>76.1% (95% CI, 69.3%-82.1%)</td>
</tr>
<tr>
<td><strong>Duration of response, median</strong></td>
<td>14.8 months (95% CI, 13.8-16.9)</td>
</tr>
</tbody>
</table>

- Median time to response was 1.6 months (95% CI, 1.4-2.6 months)

CBR, clinical benefit rate (SD for ≥6 mo + CR + PR); CR, complete response; DCR, disease control rate (CR + PR + SD); ICR, independent central review; ORR, objective response rate (CR + PR); PD, progressive disease; PR, partial response; SD, stable disease.
Best Change in Tumor Size

**Confirmed ORR: 60.9%**

(95% CI, 53.4%–68.0%)

11 CRs

The line at 20% indicates progressive disease; the line at −30% indicates partial response.

*Includes all patients who received T-DXd 5.4 mg/kg (intent-to-treat analysis; N=184).
# Overall Response Rate by Subgroup

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>N</th>
<th>ORR, %</th>
<th>[95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients*</td>
<td>184</td>
<td>60.9</td>
<td>[53.4-68.0]</td>
</tr>
<tr>
<td>Prior pertuzumab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (n=121)</td>
<td></td>
<td>64.5</td>
<td>[55.2-73.0]</td>
</tr>
<tr>
<td>No (n=63)</td>
<td></td>
<td>54.0</td>
<td>[40.9-66.6]</td>
</tr>
<tr>
<td>Hormone receptors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive (n=97)</td>
<td></td>
<td>57.7</td>
<td>[47.3-67.7]</td>
</tr>
<tr>
<td>Negative (n=83)</td>
<td></td>
<td>66.3</td>
<td>[55.1-76.3]</td>
</tr>
<tr>
<td>Brain metastasis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (n=24)</td>
<td></td>
<td>58.3</td>
<td>[36.6-77.9]</td>
</tr>
<tr>
<td>No (n=160)</td>
<td></td>
<td>61.3</td>
<td>[53.2-68.8]</td>
</tr>
<tr>
<td>Presence of visceral disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (n=169)</td>
<td></td>
<td>60.4</td>
<td>[52.6-67.8]</td>
</tr>
<tr>
<td>No (n=15)</td>
<td></td>
<td>66.7</td>
<td>[38.4-88.2]</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asia (n=63)</td>
<td></td>
<td>58.7</td>
<td>[45.6-71.0]</td>
</tr>
<tr>
<td>North America (n=53)</td>
<td></td>
<td>62.3</td>
<td>[47.9-75.2]</td>
</tr>
<tr>
<td>Europe (n=68)</td>
<td></td>
<td>61.8</td>
<td>[49.2-73.3]</td>
</tr>
<tr>
<td>ECOG performance status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 (n=102)</td>
<td></td>
<td>65.7</td>
<td>[55.6-74.8]</td>
</tr>
<tr>
<td>1 (n=81)</td>
<td></td>
<td>55.6</td>
<td>[44.1-66.6]</td>
</tr>
<tr>
<td>HER2 positive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IHC 3+ (n=154)</td>
<td></td>
<td>63.0</td>
<td>[54.8-70.6]</td>
</tr>
<tr>
<td>IHC 1+/2+ (n=28)</td>
<td></td>
<td>46.4</td>
<td>[27.5-66.1]</td>
</tr>
</tbody>
</table>

*Patients who received T-DXd 5.4 mg/kg.
Progression-Free and Overall Survival

Progression-Free Survival

Median: 16.4 months (95% CI, 12.7-NE)

Overall Survival

Median: Not reached (95% CI, NE-NE)

- Median follow-up, 11.1 months (range, 0.7-19.9 months)
- Median PFS in the 24 patients with brain metastases was 18.1 months (95% CI, 6.7-18.1 months)\(^a\)

Patients who received T-DXd 5.4 mg/kg.
CI, confidence interval; NE, not estimable.

\(^a\)Patients who received T-DXd 5.4 mg/kg.
Treatment-emergent Adverse Events in >15% of Patients

- Nausea
- Fatigue
- Alopecia
- Vomiting
- Constipation
- Neutropenia
- Decreased appetite
- Anemia
- Diarrhea
- Decreased WBC count
- Thrombocytopenia
- Headache
- Cough

Grade 1 or 2
Grade ≥3

Serious TEAEs, 22.8% (drug related, 12.5%)
TEAEs associated with discontinuation, 15.2% (drug related, 14.7%); the majority were due to pneumonitis/ILD (8.7%)

Patients who received T-DXd 5.4 mg/kg.
## Adverse Events of Special Interest: LVEF

### Patients who received T-DXd 5.4 mg/kg (N=184)

<table>
<thead>
<tr>
<th>Preferred Term, n (%)</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
<th>Any Grade/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac failure</td>
<td>1 (0.5)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Cardiac failure congestive</td>
<td>0</td>
<td>1 (0.5)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>Ejection fraction decreased(^a)</td>
<td>0</td>
<td>2 (1.1)</td>
<td>1 (0.5)^b</td>
<td>0</td>
<td>0</td>
<td>3 (1.6)</td>
</tr>
</tbody>
</table>

- No events of cardiac failure with LVEF decline were reported
- No patients had an LVEF of <40% or a decrease of ≥20% at any timepoint
- 4 out of the 5 subjects continued on treatment for 2–18 cycles

\(^a\)All patients were asymptomatic and recovered/recovering after interruption of study treatment.

\(^b\)LVEF was >55% during treatment.

LVEF, left ventricular ejection fraction.
### Adverse Events of Special Interest: Interstitial Lung Disease (ILD)

#### Patients who received T-DXd 5.4 mg/kg (N=184)

<table>
<thead>
<tr>
<th>Preferred Term, n (%)</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
<th>Any Grade/Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interstitial lung disease</td>
<td>5 (2.7)</td>
<td>15 (8.2)</td>
<td>1 (0.5)</td>
<td>0</td>
<td>4 (2.2)</td>
<td>25 (13.6)</td>
</tr>
</tbody>
</table>

Drug related; ILD was determined by the Independent ILD Adjudication Committee based on 44 preferred terms.

Among the 25 total events:
- Median time to investigator-reported onset was 193 days (range, 42-535 days)
- 13 of 20 patients with grade ≥2 ILD received corticosteroids
- 7 patients recovered, 2 were recovering, 12 were either outcome unknown or not followed until resolution, and 4 died
- Of the 4 fatal cases, onset was from 63-148 days, 3 received steroids as part of treatment, and death occurred 9-60 days after ILD diagnosis

Recommendations: Monitor for symptoms. Hold T-DXd and start steroids as soon as ILD is suspected.
How does it compare vs historical HER2 agents in HER2 metastatic breast cancer?

<table>
<thead>
<tr>
<th></th>
<th>Pertuzumab + trastuzumab + docetaxel (1L)¹</th>
<th>T-DM1 (1L, failed study)²</th>
<th>T-DM1 (2L)³</th>
<th>T-DM1 (3L+)⁴</th>
<th>DS-8201⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPFS</td>
<td>18.5m</td>
<td>14.1m</td>
<td>9.6m</td>
<td>6.2m</td>
<td>16.4m</td>
</tr>
<tr>
<td>DoR</td>
<td>20.2m</td>
<td>20.7m</td>
<td>12.6m</td>
<td>9.7m</td>
<td>14.8m</td>
</tr>
<tr>
<td>OS</td>
<td>56.5m</td>
<td>53.7m</td>
<td>30.9m</td>
<td>22.7m</td>
<td>NE</td>
</tr>
<tr>
<td>ORR</td>
<td>80%</td>
<td>60%</td>
<td>43.6%</td>
<td>31%</td>
<td>60.9%</td>
</tr>
<tr>
<td>Median prior Rx for adv. disease</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

³CLEOPATRA (NEJM 2012), ²MARIANNE (J Clin Oncol 2017), ³EMILIA (NEJM 2012), ⁴TH3RESA (Lancet Oncol 2017), ⁵Lancet Oncology, April 29, 2019, m: Month, NR:Not Reached

*DS-8201 is an investigational agent; efficacy and safety have not been established.
So what have we seen so far.....?

◆ ADC concept was first described in 1913, and it took until now to really break through

◆ **DS-8201 is**, first and foremost, a massively advanced technological breakthrough
  - It was designed to achieve best-in-class technology
  - It delivers unique practice-changing evidence

◆ **Breast cancer doctors don’t ‘think’ ILD**
  - We do not shy away from discussing the importance of monitoring, and actively screening and treating any suspicion of ILD
DS-8201 | Remarkable Speed in Development & Manufacturing Scale up

Keytruda® is 2nd fastest US biologics ever: FTIH to US market 4.5 years... so DS-8201 can possibly break this precedent

Japan NDA submitted & accepted 09 Sep. 2019; EU MAA tracking to plan
Today’s Agenda

1. Introduction
2. DS-8201: The Data
3. DS-8201: The Collaboration
4. ADC Portfolio: Data and CDP Updates
5. DXd ADC ILD
6. “3 and Alpha”
7. News Flow and Future Events
Opportunity for strategic collaboration with excellent partner with a rich heritage in breast cancer

Accelerate building in-house oncology business infrastructure, while optimizing resources

Maximize product value oncology products
- Earlier penetration in global market
- Expand to new indications
Together, we have achieved much!

**Optimized Resources with Accelerated Development**
- Regulatory submissions on time with joint review and rapid alignment
- Joint clinical operations working group to accelerate study initiation
- Leverage AZ’s ongoing platform studies (HUDSON/BEGONIA) with DS-8201 cohort
- Joint IT working group to support upcoming DS-8201 studies

**Maximizing Product Value**
- Joint Clinical Development Plan (CDP) updated with 26 new studies
- Multiple indications studied in parallel
- Joint Translational / CDx Working Group to optimize patient selection and execution across the program
- Collaboration with ex-US development teams to penetrate global markets
- Partnerships with patient advocacy groups in support of ongoing DESTINY trials

DS-8201 | Immediate Benefits of the Collaboration
DS AZ Collaboration Fully Finances ADC’s Development

- At a speed and scale DS alone could not have supported
- Whilst preserving DS’ ability to progress the rest of our portfolio

- Next fiscal year 2020, we’ll spend externally
  - DS-8201: ~175% of current DS-8201 FY2019 spend (Daiichi Sankyo part)
  - DS-1062 and U3-1402: ~175% of current FY2019 spend on these 2 assets
Transform treatment for HER2 tumors, as they will newly be defined

<table>
<thead>
<tr>
<th>HER2+ met BC</th>
<th>Establish DS-8201 as the new SoC in HER2+ BC</th>
<th>2020-2022:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>• Establish DS-8201 as SOC in 3L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Move quickly into 2L based on head-to-head data</td>
</tr>
<tr>
<td>HER2+ early BC</td>
<td></td>
<td>• Optimize opportunity in earlier settings</td>
</tr>
<tr>
<td>HER2 Low met BC</td>
<td>Redefine the BC treatment paradigm</td>
<td>Disrupt the current BC treatment paradigm with new HER2 Low characterization</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Optimize testing and access as the first targeted agent for HER2 Low patients</td>
</tr>
<tr>
<td>Other tumors</td>
<td>Expand leadership across other tumors</td>
<td>Transform treatment across HER2 tumors (NSCLC, GC, CRC)</td>
</tr>
</tbody>
</table>
Changing the Breast Cancer Clinical Paradigm

Breaking swim lanes

**Traditional Paradigm**
Patients and treatments defined by few segments...

**HER2+**
Current treatments

**HR+**
Current treatments

**TNBC**
*(Not HER2+/HR+)*
Current treatments

**Future Paradigm**
Define new biology-driven characterization

**HER2+**

**HR+**

**TNBC**

**DS-8201**
Starting 16 studies in next 18 months

- Extend use of DS-8201 to GC, NSCLC and CRC
  - Develop **combination strategy** / Explore tumor-agnostic opportunities
  - **Start 6 Registration & 4 Ph2 studies in next 18 mo**

- Expand leadership across HER2 expressing tumors

- Create a **new treatment paradigm** in HER2low mBC
  - **Shape a new CDx framework** in mBC
  - **Start 2 Registration studies & 1 Ph2 study in the next 18 mo**

- Redefine Breast Cancer treatment paradigm

- Build on unprecedented data in HER2+
  - **Start 2 Registration & 1 Ph2 studies in next 18 mo**

- Establish DS-8201 as the new SOC in HER2+ Breast Cancer
### Summary of CDP of DS-8201: directional view

**Green: Today’s focus (Studies newly aligned with AZ)**

### Total 43 studies

<table>
<thead>
<tr>
<th>Tumors</th>
<th># of studies</th>
<th>Deal defined Studies</th>
<th>Added Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breast Cancer HER2+</strong></td>
<td>9</td>
<td>4 studies (3 DS ongoing studies, 1 new registrational study)</td>
<td>5 studies (4 Registrational intent &amp; 1 Platform)</td>
</tr>
<tr>
<td><strong>Breast Cancer HER2 Low</strong></td>
<td>7</td>
<td>2 studies (1 DS ongoing studies, 1 new registrational study)</td>
<td>5 Studies (3 Registrational intent &amp; 2 Platform)</td>
</tr>
<tr>
<td><strong>Lung</strong></td>
<td>7</td>
<td>2 studies (1 DS ongoing studies, 1 new Ph2 study)</td>
<td>5 Studies (4 Registrational intent &amp; 1 Ph1/2)</td>
</tr>
<tr>
<td><strong>Gastric</strong></td>
<td>5</td>
<td>2 studies (2 DS ongoing studies)</td>
<td>3 studies (2 Registrational intent &amp; 1 Ph1/2)</td>
</tr>
<tr>
<td><strong>Colorectal Cancer</strong></td>
<td>6</td>
<td>1 Studies (1 DS ongoing studies)</td>
<td>5 Studies (4 Registrational intent &amp; 1 Ph1/2)</td>
</tr>
<tr>
<td><strong>Tumor Agnostic</strong></td>
<td>3</td>
<td>N/A</td>
<td>3 studies (1 Registrational intent &amp; 2 Ph1/2)</td>
</tr>
<tr>
<td><strong>I/O Combination</strong> (other partners)</td>
<td>2</td>
<td>2 Studies (2 DS ongoing studies)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Multiple tumors (FIH)/Clin pharm/Safety</strong></td>
<td>4</td>
<td>4 Studies (completed or ongoing)</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Transform treatment for HER2 Tumors

Our obligation to patients is beyond what one company can achieve alone.
Today’s Agenda

1 Introduction

2 DS-8201: The Data

3 DS-8201: The Collaboration

4 ADC Portfolio: Data and CDP Updates

5 DXd ADC ILD

6 “3 and Alpha”

7 News Flow and Future Events
TROP2 ADC is designed to be best in class

**Antibody**
Humanized anti-TROP2 monoclonal antibody (hIgG1)

**Payload**
Topoisomerase I inhibitor

**Cys conjugation**
GGFG

**D4-enriched to protect safety margin**

**Non-selective DAR4**

**Optimized conjugation method**

**D4-enriched DAR4**
**DS-1062 | Phase 1 Study Design (NCT03401385)**

- Ongoing first-in-human, US and Japan dose escalation and expansion phase 1 study of DS-1062 in unselected pts with unresectable advanced NSCLC relapsed/refractory to SOC
  - Male (57.7%)
  - Stage IV disease (88.5%)
  - Adenocarcinoma histology (73.1%)
  - ECOG PS 1 (80.8%)
  - Failed prior immune checkpoint inhibitors (86.5%)

**DLT, dose-limiting toxicity; ECOG PS, Eastern Cooperative Oncology Group performance status; NSCLC, non-small cell lung cancer; Pt, patient; Q3W, every 3 weeks; RDE, recommended dose for expansion; SOC, standard of care; TROP2, trophoblast cell-surface antigen 2.**

Data cut-off 03Jul2019

Source: Heist-R et al., Abstract #MA25.10, WCLC 2019
12 PRs (10 confirmed; 2 too early to confirm) across all doses in dose escalation

- At the 8-mg/kg dose there were 5/7 PRs and 2/7 SDs, and 6/7 pts are ongoing

Data cut-off: July 3, 2019.

ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor, HER2; human epidermal growth factor receptor 2; PD, progressive disease; PR, partial response; Pt, patient; SD, stable disease.

Source: Heist-R et al., Abstract #MA25.10, WCLC 2019
Clear dose-effect on frequency of response

Data cut-off: July 3, 2019.
ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; HER2, human epidermal growth factor receptor 2; PD, progressive disease; PR, partial response; Pt, patient; SD, stable disease.

Source: Heist-R et al., Abstract #MA25.10, WCLC 2019
## DS-1062 | Safety

<table>
<thead>
<tr>
<th>TEAEs, regardless of causality, (in ≥10% of pts), n (%) (N=52)</th>
<th>All Grades</th>
<th>Grade ≥3</th>
<th>All grades</th>
<th>Grade ≥3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAE</td>
<td>48 (92.3)</td>
<td>22 (42.3)</td>
<td>7 (13.5)</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>19 (36.5)</td>
<td>2 (3.8)</td>
<td>7 (13.5)</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>19 (36.5)</td>
<td>0</td>
<td>7 (13.5)</td>
<td>0</td>
</tr>
<tr>
<td>Alopecia</td>
<td>15 (28.8)</td>
<td>0</td>
<td>6 (11.5)</td>
<td>0</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>14 (26.9)</td>
<td>0</td>
<td>6 (11.5)</td>
<td>0</td>
</tr>
<tr>
<td>Anemia</td>
<td>12 (23.1)</td>
<td>0</td>
<td>5 (9.6)</td>
<td>0</td>
</tr>
<tr>
<td>Stomatitis/mucosal inflammation</td>
<td>12 (23.1)</td>
<td>2 (3.8)</td>
<td>5 (9.6)</td>
<td>1 (1.9)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>12 (23.1)</td>
<td>0</td>
<td>5 (9.6)</td>
<td>0</td>
</tr>
<tr>
<td>Infusion related reaction</td>
<td>11 (21.2)</td>
<td>0</td>
<td>5 (9.6)</td>
<td>1 (1.9)</td>
</tr>
<tr>
<td>Rash</td>
<td>8 (15.4)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Any TEAE**
  - **All Grades**: 48 (92.3%)
  - **Grade ≥3**: 22 (42.3%)
  - **Any Grade**: 7 (13.5%)
  - **Grade ≥3**: 0

- **Fatigue**
  - **All Grades**: 19 (36.5%)
  - **Grade ≥3**: 2 (3.8%)
  - **Any Grade**: 7 (13.5%)
  - **Grade ≥3**: 0

- **Nausea**
  - **All Grades**: 19 (36.5%)
  - **Grade ≥3**: 0
  - **Any Grade**: 7 (13.5%)
  - **Grade ≥3**: 0

- **Alopecia**
  - **All Grades**: 15 (28.8%)
  - **Grade ≥3**: 0
  - **Any Grade**: 6 (11.5%)
  - **Grade ≥3**: 0

- **Decreased appetite**
  - **All Grades**: 14 (26.9%)
  - **Grade ≥3**: 0
  - **Any Grade**: 6 (11.5%)
  - **Grade ≥3**: 0

- **Anemia**
  - **All Grades**: 12 (23.1%)
  - **Grade ≥3**: 0
  - **Any Grade**: 5 (9.6%)
  - **Grade ≥3**: 0

- **Stomatitis/mucosal inflammation**
  - **All Grades**: 12 (23.1%)
  - **Grade ≥3**: 2 (3.8%)
  - **Any Grade**: 5 (9.6%)
  - **Grade ≥3**: 1 (1.9%)

- **Vomiting**
  - **All Grades**: 12 (23.1%)
  - **Grade ≥3**: 0
  - **Any Grade**: 5 (9.6%)
  - **Grade ≥3**: 0

- **Infusion related reaction**
  - **All Grades**: 11 (21.2%)
  - **Grade ≥3**: 0
  - **Any Grade**: 5 (9.6%)
  - **Grade ≥3**: 1 (1.9%)

- **Rash**
  - **All Grades**: 8 (15.4%)
  - **Grade ≥3**: 0

### Key Points

- **DLT at 10 mg/kg**: Median exposure duration was 10.6 weeks (range 3.0–43.1 weeks).
- **Serious TEAEs**: In 14 (26.9%) pts and death in 3 (5.8%) pts; no deaths were related to study drug.
- **TEAEs associated with dose reduction, interruption, or discontinuation**: In 5 (9.6%), 5 (9.6%), and 2 (3.8%) pts, respectively.
- **One pt (1.9%)** with disease progression treated with the 6.0 mg/kg dose developed a pulmonary adverse event of special interest of respiratory failure (grade 5), adjudicated as not an ILD.

  - Including cases post-data cutoff, 4 not-yet adjudicated possible ILD reports were observed (1 grade 2 pneumonitis [6.0 mg/kg], 1 grade 2 organizing pneumonia [8 mg/kg], 1 grade 2 pneumonitis [8 mg/kg], and 1 grade 5 [respiratory failure in a pt with disease progression; 8.0 mg/kg]).

---

Source: Heist-R et al., Abstract MA25.10, WCLC 2019
Dose dependent increase in tumor response in heavily pretreated, unselected NSCLC patients having progressed on standard of care, including immune checkpoint inhibitors, EGFR inhibitors, and ALK inhibitors

- 6/8 10mg/kg subjects discontinued quickly due to AEs
- 83% of patients received a prior immune checkpoint inhibitor

*Source: Internal data on file at Daiichi Sankyo.
DS-1062 appears to have the characteristics of a “drug-to-be”
Early clinical results indicate that DS-1062 maintains clear activity, dose effect, durability and tolerability – ILD to watch

**DXd portability** further established, added technology of **D4-enriched DAR4 conjugation** validated

Driven by emergent NSCLC data, **differentiation vs IMMU-132** appears credible

**Fast-to-market** US path emerging in NSCLC
# DS-1062 | NSCLC Development Plan

## NSCLC without actionable mutations, post IO/Platinum

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSCLC Expand</td>
<td>DS-1062 at 2 doses</td>
<td>Randomized DS-1062 vs. DTX ± ramucirumab</td>
</tr>
</tbody>
</table>

## NSCLC with actionable mutations, post TKI and Platinum

<table>
<thead>
<tr>
<th>Phase 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS-1062 at 2 doses</td>
</tr>
</tbody>
</table>

## NSCLC combination with PD-1 / PD-L1 Inhibitor

<table>
<thead>
<tr>
<th>Phase 1b (3 studies), enabling for a first line randomized study vs SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS-1062 dose finding with IO</td>
</tr>
</tbody>
</table>

---

<table>
<thead>
<tr>
<th>Year</th>
<th>First Quarter</th>
<th>Second Quarter</th>
<th>Third Quarter</th>
<th>Fourth Quarter</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2021</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2022</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2023</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2024</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*All dates are approximative*
U3-1402 | HER3 Targeted ADC

**Conjugation Chemistry**
The drug-linker is conjugated to the antibody via cysteine residues.

**Payload MOA:** Topo I inhibitor

**High potency of payload**

**High drug-to-antibody ratio (~8:1)**

**Payload with short systemic half-life**

**Stable linker-payload**

**Tumor-selective cleavable linker**

**Bystander effect**

**Potential First-in-class Drug**
U3-1402 | Phase 1 NSCLC EGFRm

Eligibility Criteria

- Metastatic/unresectable EGFR-mutant NSCLC and:
  - T790M-negative after progression on erlotinib, gefitinib, or afatinib; or
  - Progressed on osimertinib
- Stable brain metastases allowed
- Pretreatment tumor tissue (after progression on TKIs) was required for retrospective analysis of HER3 expression

U3-1402 Dose Escalation (N = 30)

- Received ≥ 1 dose of U3-1402 IV Q3W
  - 6.4 mg/kg (n = 5)
  - 5.6 mg/kg (n = 12)
  - 4.8 mg/kg (n = 9)
  - 3.2 mg/kg (n = 4)

Patient Disposition\(^a\)

- **Ongoing**, n = 17
- **Discontinued**, n = 13
  - Progressive disease: 9
  - Consent withdrawal: 2
  - Clinical progression: 1
  - AE: 1

Objectives

- **Primary:** Safety and tolerability of U3-1402 and RDE determination
- **Secondary:** Antitumor activity of U3-1402
- **Exploratory:** Biomarkers of U3-1402 antitumor activity

A phase 1 study of U3-1402 in NSCLC (NCT03260491). \(^a\)Data cutoff of May 3, 2019.
AE, adverse event; EGFR, epidermal growth factor receptor; HER3, human epidermal growth factor receptor 3; IV, intravenously; NSCLC, non-small cell lung cancer; Q3W, every 3 weeks; RDE, recommended dose for expansion; TKI, tyrosine kinase receptor.

Source: Yu H et al., Abstract #MA21.06, WCLC 2019
A phase 1 study of U3-1402 in NSCLC (NCT03260491). Two patients had ≥ 30% reduction in SoD, which were not considered confirmed PRs; 1 experienced transient tumor size reduction and 1 had not yet been confirmed at data cutoff. Performed centrally using Oncomine Comprehensive Assay v3 from formalin-fixed, paraffin-embedded tumor tissue. Results from local testing are included for patients where tissue was unavailable for central analysis. Additional mutations detected from cfDNA in blood collected prior to treatment with U3-1402 using GuardantOMNI assay are included. For cfDNA analysis, a minor allelic frequency of 1% was used as a threshold for detection of mutations. The copy number data from cfDNA are not shown.

cfDNA, cell-free DNA; EGFR, epidermal growth factor receptor; HER3, human epidermal growth factor receptor 3; PR, partial response; SoD, sum of diameters; TKI, tyrosine kinase receptor.

Source: Yu H et al., Abstract #MA21.06, WCLC 2019
Early clinical results indicate that U3-1402 appears active in NSCLC, adding to breast cancer activity previously reported.

Targeting HER3 with U3-1402 may be a **practical approach to treat EGFR-mutant** NSCLC with diverse mechanisms of resistance to EGFR TKIs. HER3 expression post-TKI seems to be frequent and stable.

**Fast-to-market** US path emerging in NSCLC
Observed **frequent and durable antitumor activity** in the initial cohorts of the *metastatic breast cancer* program

- As the breast cancer study (J101) progressed, the consistency of this response pattern became variable
- Also observed frequent but transient and reversible thrombocytopenia in cycle 1, unlike with other DXd ADCs

**FTIH to August 2018 cumulative breast cancer experience** (n=42)
- ORR: 42.9% (18/42)
- Disease Control Rate: 90.5%

**August 2018 to August 2019 additional breast cancer experience** (n=82)
- ORR: 17.1% (14/82)
- Disease Control Rate: 89.0%
What have we learned

- **HER3 expression in breast cancer is more variable and heterogeneous than anticipated**
  - IHC detection, even if specific might not be sensitive enough to best select the breast cancer population most likely to benefit

- **HER3 expression in breast cancer appears to be dynamic, unlike in lung cancer or HER2 in breast cancer**
**U3-1402 | Breast Cancer: Best Overall Response by IHC**

Assessed on Pre-treatment Fresh Biopsy (N=43) *

*Source: Internal data are preliminary and on file at Daiichi Sankyo.*
HER3 Expression Variability in Breast Cancer Over Time*

HER3 Expression Level Decreases During U3-1402 Treatment in Breast Cancer*

*Source: Internal data are preliminary and on file at Daiichi Sankyo.
U3-1402 | Payload Release Profile and Thrombocytopenia Rate Distinct from DS-8201 at cycle 1*

*Source: Internal data are preliminary and on file at Daiichi Sankyo.
Sustained Internalization Rate of U3-1402 in EGFRm Lung Cancer* 
Monotherapy or in Combination with Osimertinib

*Data are preliminary
Courtesy of Dr. Pasi Janne, Dana Farber Cancer Institute
What Does It Mean for Daiichi Sankyo?

**Lung cancer:** EGFRm presents a clear opportunity
- HER3 consistently expressed and internalized post TKI
- Combination with osimertinib will be pursued

**Breast cancer:** biology of receptor (dimerization / internalization / trafficking) is substantially altered by yet unknown factor(s)
- Intensive translational research ongoing (MSKCC, MDACC, SOLTI, and others)

**Colorectal** and **Prostate** cancers: Phase 2 studies planned
Daiichi Sankyo Initiates Clinical Trial with its 4th DXd Antibody Drug Conjugate, DS-7300, in Collaboration with Sarah Cannon Research Institute

- First-in-human phase 1/2 study evaluating DS-7300, a B7-H3 targeting ADC, in patients with advanced/unresectable or metastatic solid tumors
- B7-H3 is a protein overexpressed in various types of cancers
- DS-7300 is the fourth ADC to enter the clinic utilizing Daiichi Sankyo’s proprietary DXd technology and the first being jointly developed in a strategic partnership with Sarah Cannon Research Institute
B7-H3 (CD276)

- B7-H3 is highly expressed in various solid cancers and expressed at low levels in normal tissues.
  - Anti-B7-H3 ADC antibody internalization rate 19-27%/3hr, comparable to trastuzumab
- B7-H3 is a type I transmembrane protein belonging to the B7 family which includes immune checkpoint molecules such as CTLA-4 ligands, and PD-L1.
- The function of B7-H3 yet to be elucidated.
DS-7300 | Phase 1 Study Design

**Dose Escalation**

**Key Objectives:** Finding recommended dose for Expansion and determine evidence of preliminary efficacy

**Advanced or Metastatic Solid Tumors**
Head and Neck, squamous-esophageal cancer, squamous NSCLC, Bladder, Sarcoma, Endometrial

- Regardless of B7-H3 expression (no preselection)
- mCRM, N = ~36
- Determine RDE based on safety (primary), PK, preliminary efficacy, and Biomarker

**Collection of archival and fresh tissue (pre-, on-treatment) biopsies**

**Dose Expansion**

**Key Objectives:** Preliminary efficacy, ORR, and additional safety

**Cohort 1: SCCHN**

**Cohort 2: Sq-Esophageal Ca**

**Cohort 3: Sq-NSCLC**

- N~ 40 for each cohort (1-3)
- Regardless of B7-H3 expression (no preselection)
- Additional or alternative indications may be added to expansion cohorts based on preliminary signals of activity
GPR20 is one of the ICC/GIST lineage-specific factors whose gene expression is regulated by FOXF1 and ETV1.

- Orphan GPCR
- GIST-specific target
- Interstitial Cells of Cajal (ICCs), the cell of origin of GIST, are the only GPR20+ cells
- Function in GIST is unknown

**GPR20 Ab**
- Internalizing Ab

**GGFG linker**
- Protease cleavable

**Internalization rate**
- 72% @ 3hr

**DS-6157**
- Drug / Antibody Ratio = 8

**DXd**
- Topoisomerase I inhibitor

**GPR20 Ab**
- Internalizing Ab

**DS-6157**
- Orphan GPCR
- GIST-specific target
- Interstitial Cells of Cajal (ICCs), the cell of origin of GIST, are the only GPR20+ cells
- Function in GIST is unknown

**GIST**
- Mesenchymal tumor of GI tract, rare disease
- Stomach: 60%, Small intestine 35%
- Oncogenic mutation in KIT (78%) or PDGFRA (7.5%) gene
- Three TKIs were approved

**DS-6157**
- First in class GPR20 ADC, having different MOA than TKIs approved in GIST therapy
- Initial target indication is IM-resistant GIST
- Q3w, IV dosing regimen

Chi P. et al, Cancer Discov. 2018;8(2):146-149, 234-251. (modified)
**DS-6157 | Phase 1 Study Design**

**Dose Escalation (Part 1)**
DS-6157a IV Q3W monotherapy* in advanced GIST (2nd, 3rd, or later line) or not a candidate for imatinib

**Dose Expansion (Part 2)**
DS-6157a IV Q3W monotherapy

---

**Cohort 1***
GIST in 3rd or later line

**Cohort 2****
GIST in 2nd line

---

### Escalation

<table>
<thead>
<tr>
<th>Study Region</th>
<th>US, + (Japan)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potential Study Sites</td>
<td>DFCI, other sites, (NCCE in Japan)</td>
</tr>
</tbody>
</table>

### Expansion

<table>
<thead>
<tr>
<th>Study Region</th>
<th>US, Japan, (+ Other countries: TBD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potential Study Sites</td>
<td>DFCI, other sites, (NCCE in Japan)</td>
</tr>
</tbody>
</table>

---

GIST: gastrointestinal stromal tumors; RDE: recommended dose for expansion; BLRM: Bayesian logistic regression model; DFCI: Dana Farber Cancer Institute; NCCE: National Cancer Center Hospital

*These are planned doses. Actual dose levels will be determined by clinical toxicity findings in each dose cohort & the BLRM. Higher or intermediate doses may also be considered.

**DS-6157a dose will be determined in Dose Escalation (Part 1).

***Cohort 1 includes subjects who have been previously treated with imatinib & at least one post-imatinib treatment.

****Cohort 2 will be initiated after efficacy is demonstrated (≥20% confirmed objective response rate in a minimum of 10 subjects treated with DS-6157a at RDE) in Dose Escalation & Dose Expansion Cohort 1. Cohort 2 will be initiated in the United States only.
## Today’s Agenda

1. **Introduction**
2. **DS-8201: The Data**
3. **DS-8201: The Collaboration**
4. **ADC Portfolio: Data and CDP Updates**
5. **DXd ADC ILD**
6. **“3 and Alpha”**
7. **News Flow and Future Events**
Investigator Safe Use Campaign for ILD Detection & Management
1st Phase Campaign: Awareness (Early calendar 2019 for DS-8201)

**Goal:** Drive ILD awareness, detection, and management

<table>
<thead>
<tr>
<th><strong>HCPs</strong></th>
<th><strong>Resources for Patients</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Prioritize investigators with patients on treatment&lt;br&gt;- Ensure continuous education and ‘top of mind’ status, through numerous outlets (in-person, online)</td>
<td>- Educate patients around risk of ILD and need to self-monitor for symptoms</td>
</tr>
</tbody>
</table>

**Develop internal understanding & external communication plans**

- Comprehensive education of MSLs
- Develop tools for MSLs to use in proactive direct communication with treating physicians

**Give HCPs tools to reduce ILD severity and improve management**

**Drive awareness and give patients tools to support detection & management**

---

DS-8201: did you screen for, and mitigate against ILD today?
In HER2-positive 5.4 mg/kg, compared to safety data in submission, no significant changes in most AE and no new safety signal. Frequency of most AEs increased slightly.

The most notable findings are:
- Discontinuation associated with TEAE increased from 8.2% to 15.2%, mainly driven by new events of low grade ILD
- Adjudicated drug-related any grade ILD increased from 8.2% to 13.5%
  - New adjudicated related ILD events included 2 grade 1, 7 grade 2 and 1 grade 3

It is important to note that after the phase 1 Safe use campaign was initiated, majority of the new cases were low grade (1 and 2) and only 1 subject was diagnosed with grade 3 ILD – no new grade 4 or 5 reported program-wide at treatment doses of 5.4 mg/kg
### U3-1402 | ILD (Adjudicated Outcomes) Summary

#### Number (% of Subjects with Each CTCAE Grade Reported by Adjudication Committee

<table>
<thead>
<tr>
<th>Grade</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjudicated&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1 (0.5)</td>
<td>7 (3.4)</td>
<td>3 (1.5)</td>
<td>0</td>
<td>1 (0.5)</td>
<td>12 (5.9)</td>
</tr>
<tr>
<td>Adjudicated as ILD</td>
<td>1 (0.5)</td>
<td>6 (2.9)</td>
<td>3 (1.5)</td>
<td>0</td>
<td>1 (0.5)</td>
<td>11 (5.4)</td>
</tr>
<tr>
<td>Adjudicated as Drug-related</td>
<td>1 (0.5)</td>
<td>4 (2.0)</td>
<td>3 (1.5)</td>
<td>0</td>
<td>1 (0.5)</td>
<td>9 (4.4)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**N = 205**

**Doses (1.6-8.0 mg/kg)**

**Median exposure 4.4 months (0.7-30.2)**

**Mean exposure (SD) = 5.76mo (4.973)**

---

<sup>a</sup> Consisted of events based on 44 PTs selected for ILD adjudication – terms adjudicated as ILD – pneumonitis, interstitial pneumonia, radiation pneumonitis

<sup>b</sup> the 2 cases considered not related to the study drug, were considered related to prior radiation therapy
All potential ILD cases as of 18 Oct 2019 have been adjudicated

<table>
<thead>
<tr>
<th>Number (%) of Subjects with Each CTCAE Grade Reported by Adjudication Committee</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=88 subj Median exposure 7.1 wks (3.0-54.0 wks)</td>
<td>Adjudicated&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
<td>3 (3.4)</td>
<td>0</td>
<td>0</td>
<td>3 (3.4)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Adjudicated as ILD</td>
<td>0</td>
<td>3 (3.4)</td>
<td>0</td>
<td>0</td>
<td>1 (1.1)</td>
</tr>
<tr>
<td></td>
<td>Adjudicated as Drug-related</td>
<td>0</td>
<td>3 (3.4)</td>
<td>0</td>
<td>0</td>
<td>1 (1.1)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Consisted of events based on 44 PTs selected for ILD adjudication – events adjudicated as ILD: pneumonitis, respiratory failure and organizing pneumonia

<sup>b</sup> The other 2 events not adjudicated as ILD were adjudicated as Disease progression per the ILD AC
What’s Next?

◆ DS and AZ have convened an advisory board consisting of oncologists and radiologists in order to discuss the ILD management algorithm and the current inclusion/exclusion criteria

◆ As a result, the management algorithm of ILD has been updated and a new phase of the Safe Use Campaign has been started across the ADC Franchise
  ➢ the algorithm is more prescriptive and will assist the treating physicians in managing their patients

◆ The inclusion/exclusion criteria have been refined to exclude patients that could be at higher risk of developing ILD
Today’s Agenda

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6  “3 and Alpha”

7  News Flow and Future Events
Evolving the Strategic Platform from “7 in 8” to “3 and Alpha”

2017 Strategic Intent

By 2025, Cancer Enterprise will be a leading world-class organization focused on 3 pillars, and will have delivered 7 valuable NMEs (approved, launched and accessed)

- Lead in Smart-Treatment with BIC & FIC ADC
  - Maximize existing Smart-Chemo portfolio
  - Develop next generation of Smart-Chemo
  - Deliver disruptive Smart-treatments

- Establish a competitive Hematology Franchise
  - Lead in the FLT3 segment
  - Expand beyond FLT3 segment
  - Expand beyond AML

- Lead with break-thru science
  - Deliver Best in Class NME or First in Class disruptive MOA NME
  - Embed new technologies to magnify the value of science

7 NMEs in 8 years
A Science Machine and a X-functional Value Creation Team

2019 Realities

- ADCs meeting / exceeding expectations in the clinic, leading to expanded resource needs
- Quizartinib at risk of not achieving broad approval (RR or 1st line)

2019 Strategic Intent

- Fully optimize the three ADCs (DS-8201, DS-1062, U3-1402)
- Keep critical attention on the potential of the alpha assets to contribute to a robust science and technology driven portfolio
## Maximizing Development of 3 ADC’s with Breadth & Depth Expansions

<table>
<thead>
<tr>
<th>Maximize</th>
<th>Swift and independent development of the next ADCs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DS-8201</strong></td>
<td><strong>DS-1062</strong></td>
</tr>
<tr>
<td>Co-development partnership with AZ</td>
<td>Fast to market as late line NSCLC patient population</td>
</tr>
<tr>
<td>Accelerated and broadened geographical coverage</td>
<td>Potential expansion into first line NSCLC (IO Combo) and indications with high TROP-2 level</td>
</tr>
<tr>
<td>Expansion into multiple indications</td>
<td>Massive scale up of our manufacturing capacity which creates relief on supply access</td>
</tr>
</tbody>
</table>

### Science-informed precision medicine

Full development of 3 ADC’s based on the unique biology of both the DXd technology and the vector/receptor.
Maximizing Value of Development

Top 17 indications for DS-1062 and U3-1402 give ~90% of the value and require ~60% of clinical supplies (& ~55% of RD costs)

Indication prioritization ensures focused and optimized use of resources

- We are actively prioritizing our indications based on potential value and clinical development requirements
- Potential risk cannibalization across assets on the same indication is considered if and only if the biology is truly overlapping
What is the “3 and Alpha” Strategy?

3 lead ADCs

- **DS-8201**: maximize value with co-development partnership with AZ

- **DS-1062**: Substantial opportunities across multiple indications

- **U3-1402**: fast to market

Science-informed precision medicine:
three ADCs based on the unique biology of DXd technology and the vector/receptor

**Alpha**

- Alpha = angle of attack and speed of elevation
- Alpha = Performance far exceeding benchmark index

**Alpha** = **the cutting edge and power of true innovation**
delivering drugs changing SOC
## Major R&D Pipeline

**As of December 2019**

### 3 ADCs

<table>
<thead>
<tr>
<th>Generic Name/Project Code/ MOA</th>
<th>Target Indication</th>
<th>Region</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>[fam-] trastuzumab deruxtecan/DS-8201/anti-HER2 ADC</td>
<td>Breast cancer (HER2 positive post T-DM1)</td>
<td>JP/US/EU/Asia</td>
<td>BLA/NDA P3</td>
</tr>
<tr>
<td></td>
<td>Breast cancer (HER2 positive vs T-DM1)</td>
<td>JP/US/EU/Asia</td>
<td>P3</td>
</tr>
<tr>
<td></td>
<td>Breast cancer (HER2 low expression)</td>
<td>JP/US/EU/Asia</td>
<td>P3</td>
</tr>
<tr>
<td></td>
<td>Gastric cancer (HER2 positive, 3L)</td>
<td>JP/Asia</td>
<td>P2</td>
</tr>
<tr>
<td></td>
<td>Colorectal cancer (HER2 expressing)</td>
<td>JP/US/EU</td>
<td>P2</td>
</tr>
<tr>
<td></td>
<td>NSCLC (HER2 expressing/mutant)</td>
<td>JP/US/EU</td>
<td>P2</td>
</tr>
<tr>
<td></td>
<td>Breast and bladder cancer (with nivolumab)</td>
<td>US/EU</td>
<td>P1</td>
</tr>
</tbody>
</table>

| | Breast cancer (HER2 positive post T-DM1) | JP/US/EU/Asia | BLA/NDA P3 |
| | Breast cancer (HER2 positive vs T-DM1) | JP/US/EU/Asia | P3 |
| | Breast cancer (HER2 low expression) | JP/US/EU/Asia | P3 |
| | Gastric cancer (HER2 positive, 3L) | JP/Asia | P2 |
| | Colorectal cancer (HER2 expressing) | JP/US/EU | P2 |
| | NSCLC (HER2 expressing/mutant) | JP/US/EU | P2 |
| | Breast and bladder cancer (with nivolumab) | US/EU | P1 |

### Alpha Oncology

<table>
<thead>
<tr>
<th>Generic Name/Project Code/ MOA</th>
<th>Target Indication</th>
<th>Region</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quizartinib/FLT3 inhibitor</td>
<td>AML (relapsed/refractory)</td>
<td>Asia</td>
<td>P3</td>
</tr>
<tr>
<td></td>
<td>AML (1st line)</td>
<td>JP/US/EU/Asia</td>
<td>P3 LCM</td>
</tr>
<tr>
<td>Pexidartinib/CSF-1/KIT/FLT3 inhibitor</td>
<td>Tenosynovial giant cell tumor</td>
<td>EU</td>
<td>P3</td>
</tr>
<tr>
<td>Axicabtagene ciloleucel/Axi-Cell®/anti-CD19 CAR-T</td>
<td>B-cell lymphoma</td>
<td>JP</td>
<td>P2</td>
</tr>
<tr>
<td>DS-1647(G47Δ)/oncolytic HSV-1</td>
<td>Malignant glioma</td>
<td>JP</td>
<td>P2</td>
</tr>
</tbody>
</table>

### Specialty Medicines

<table>
<thead>
<tr>
<th>Generic Name/Project Code/ MOA</th>
<th>Target Indication</th>
<th>Region</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valemetostat/DS-3201/EZH1/2 inhibitor</td>
<td>Adult T-cell leukemia/lymphoma</td>
<td>JP</td>
<td>P2</td>
</tr>
<tr>
<td></td>
<td>Non-Hodgkin’s Lymphoma (PTCL)</td>
<td>JP/US</td>
<td>P1</td>
</tr>
<tr>
<td></td>
<td>AML, ALL</td>
<td>US</td>
<td>P1</td>
</tr>
<tr>
<td></td>
<td>Small cell lung cancer</td>
<td>US</td>
<td>P1</td>
</tr>
</tbody>
</table>

### Vaccine

<table>
<thead>
<tr>
<th>Generic Name/Project Code/ MOA</th>
<th>Target Indication</th>
<th>Region</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>VN-0107/MEDI3250/live attenuated influenza vaccine nasal spray</td>
<td>Prophylaxis of seasonal influenza</td>
<td>JP</td>
<td>NDA</td>
</tr>
<tr>
<td>VN-0105/DPT-IPV/Hib</td>
<td>Prevention of pertussis, diphtheria, tetanus, poliomyelitis and Hib infection</td>
<td>JP</td>
<td>P3</td>
</tr>
<tr>
<td>VN-0102/JVC-001/Measles-mumps-rubella vaccine</td>
<td>For measles, mumps, and rubella prophylaxis</td>
<td>JP</td>
<td>P2</td>
</tr>
</tbody>
</table>

ADC Development Coalition with a Selected CRO
Integrated Delivery Model meeting both Companies’ needs

Daiichi Sankyo Needs

• **Innovative** – Changing the CRO/sponsor dynamic with concentrated effort on innovation & early integration, joint tactical decisions
• **DS core competency retention** – enables Daiichi Sankyo to retain & develop core competencies
• **Financial alignment** – that aligns CRO/sponsor objectives and supports CRO accountability
• **Efficient & predictable operational delivery** – commitment to driving/reducing clinical development timelines
• **Site & Patient Centric Approach** – early engagement from protocol development through market access
• **Flexibility and scalability** – ability to adapt and adjust strategy and resource in a dynamic research environment
• **Assurance of quality** – robust quality management plan & access to transparent portfolio data enabling DS “Right” touch

CRO Needs

• **Science** – involved in world-class science which in turns motivate CRO employees
• **Respect and Trust** – CRO’s voice to be considered and heard by sponsor will result in CRO employee retention and performance
  • i.e. not be considered “a service provider” to a sponsor
• **Financial alignment and incentives** – that align CRO/sponsor and supports CRO accountability for performance based on regulatory approval(s)
Today’s Agenda

1 Introduction

2 DS-8201: The Data

3 DS-8201: The Collaboration

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5 DXd ADC ILD

6 “3 and Alpha”

7 News Flow and Future Events
Upcoming News

DS-8201

HER2 Positive mBC Pivotal Phase 2 Study – DESTINY-Breast01
• JP: NDA submitted and accepted on September 9, 2019
• US: PDUFA date: April 29, 2020
• EU: MAA submission planned for 1H FY2020

HER2 Positive mGC Pivotal Phase 2 Study – DESTINY-Gastric01
• JP/S. Korea TLR anticipated for 4Q FY2019

ASCO 2020 Planned Presentations
• DESTINY-Breast01 Update
• DESTINY-Gastric01 Results
• Colorectal Phase 2
• NSCLC Phase 2
• Breast/Bladder – Nivolumab Combo – Phase 1
• Translational Research

DS-1062

ASCO 2020 Planned Presentation
• NSCLC Phase 1 Expansion Update
Upcoming News

U3-1402

WCLC 2020 Planned Presentation

• NSCLC Phase 1 Expansion Update

Pexidartinib

Tenosynovial Giant Cell Tumor

• EU: under review for 1H FY2020 decision

DS-1647 (G47Δ)

Malignant Glioma

• JP: NDA submission in 2H FY2019
# FY2019 R&D Major Milestones (As of December 2019)

<table>
<thead>
<tr>
<th>Project</th>
<th>Target Indications and Studies</th>
<th>FY2019</th>
<th>FY2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS-8201</td>
<td>P2 pivotal: breast cancer (HER2 positive post T-DM1)</td>
<td>Q1: JP/US submitted</td>
<td>Q2: EU submission</td>
</tr>
<tr>
<td></td>
<td>P2 pivotal: gastric cancer (HER2 positive, 3L) (JP/Asia)</td>
<td>Q3: JP submission</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P2: gastric cancer (HER2 positive post trastuzumab) (US/EU)</td>
<td>Q4: Study started</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P1: breast cancer and NSCLC with pembrolizumab</td>
<td>Q1~: Study start planned</td>
<td></td>
</tr>
<tr>
<td>U3-1402</td>
<td>P1: NSCLC</td>
<td>Q1: Started dose expansion</td>
<td></td>
</tr>
<tr>
<td>DS-1062</td>
<td>P1: NSCLC</td>
<td>Q2: Started dose expansion</td>
<td></td>
</tr>
<tr>
<td>3 ADCs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project</th>
<th>Target Indications and Studies</th>
<th>FY2019</th>
<th>FY2020</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quizartinib</td>
<td>P3: AML (relapsed/refractory)</td>
<td>JP approved US CRL</td>
<td>JP launched EU received EMA CHMP negative opinion</td>
</tr>
<tr>
<td>Pexidartinib</td>
<td>P3: tenosynovial giant cell tumor (US/EU)</td>
<td>US approved/ launched</td>
<td>EU decision</td>
</tr>
<tr>
<td>DS-1647</td>
<td>IIS: malignant glioma (JP)</td>
<td>Submission</td>
<td></td>
</tr>
<tr>
<td>DS-3201</td>
<td>P1: small cell lung cancer (US)</td>
<td>Study started</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P2: Adult T-cell leukemia/lymphoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DS-1205</td>
<td>P1: NSCLC with osimertinib (Asia)</td>
<td>Study started</td>
<td>Study started</td>
</tr>
<tr>
<td>DS-7300</td>
<td>P1/2: solid tumors</td>
<td>Study started</td>
<td></td>
</tr>
<tr>
<td>DS-6157</td>
<td>P1: gastrointestinal stromal tumors (GIST)</td>
<td></td>
<td>Study start planned</td>
</tr>
<tr>
<td>Laninamivir</td>
<td>P3: influenza (nebulizer formulation) (JP)</td>
<td>Approved</td>
<td>Launched</td>
</tr>
</tbody>
</table>


Underlined in red: new or updated from FY2019 Q2, blue: achieved
### DS-8201 | Breast Cancer CDP | Comprehensive Plan

As of Nov 15, 2019

<table>
<thead>
<tr>
<th>Neoadj. only 60k</th>
<th>Adj 120k</th>
<th>Adjuvant only 425k</th>
<th>Adv/Met 1st line 135k</th>
<th>2nd line 90k</th>
<th>3rd line 45k</th>
<th>4th-5th 25k</th>
</tr>
</thead>
<tbody>
<tr>
<td>10k mAb ± mAb + Chemo</td>
<td>25k Mono/Combo (post-neoadj)</td>
<td>50k mAb ± mAb + Chemo</td>
<td>30k Mono/Combo</td>
<td>20k DESTINY-Breast03 Mono</td>
<td>10k DESTINY-Breast01/02 Mono</td>
<td>5k mAb/TKI ± Chemo</td>
</tr>
<tr>
<td>~20% HER2+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HER2-null</th>
<th>HR+</th>
<th>~65% of &quot;HER2-&quot; HER2-low</th>
<th>TNBC</th>
<th>HER2-null</th>
</tr>
</thead>
<tbody>
<tr>
<td>35k Chemo</td>
<td>85k Endocrine therapy</td>
<td>335k Endocrine therapy ± chemo</td>
<td>40-60% PDL1+ + chemo</td>
<td>15k Chemo</td>
</tr>
<tr>
<td>~65%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Simplified view of SOC in G7 shown above – not meant to be patient flow or full representation of regimen shares; biomarker overlap not well characterized
- Drug-treated patients G7 markets in 2025 (source: Kantar, rounded to nearest 5k). 80% of Stg IIIbc patients included in metastatic as not resectable with curative intent (to be validated in MR)
- *Multi-indication basket*
<table>
<thead>
<tr>
<th>Ongoing P3</th>
<th>P2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potential P3</td>
<td>P2</td>
</tr>
</tbody>
</table>

**Early disease**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Patients</th>
<th>1st line</th>
<th>2nd line</th>
<th>3rd line</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastric</strong> (20% West / 12% East HER2+)</td>
<td>13k</td>
<td>Chemo ± RT</td>
<td>Combo</td>
<td>Trastuzumab + Chemo</td>
</tr>
<tr>
<td><strong>Gastric</strong> (HER2-low 24%)</td>
<td>18k</td>
<td>Chemo ± RT</td>
<td>Combo</td>
<td></td>
</tr>
<tr>
<td><strong>NSCLC</strong> (2% HER2+ / 10% HER2+)</td>
<td>1k 8k</td>
<td>CRT</td>
<td>post-CRT</td>
<td>Mono</td>
</tr>
<tr>
<td></td>
<td>2k 10k</td>
<td>RT ± Chemo</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CRC</strong> (5% HER2+)</td>
<td>12k</td>
<td>Chemo ± RT</td>
<td>Combo</td>
<td>Chemo ± VEGF or EGFR mAb</td>
</tr>
<tr>
<td><strong>Other / Tumor Agnostic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Drug-treated patients G7 markets in 2025 (source: Kantar for total patients, rounded to nearest 1k; Prevalence per below; Gastric includes GEJ adeno, rates sourced from DRG)
- Wide range of HER2+ prevalence reported in literature. Same prevalence assumed across lines of therapy given limited data; may differ between early & metastatic
- *Registrational Ph2 in Japan/Korea, with exploratory cohort in IC 2+/1+; †Multi-indication basket

![Diagram](image-url)
# Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>AE</td>
<td>Adverse event</td>
</tr>
<tr>
<td>BTD</td>
<td>Breakthrough therapy designation</td>
</tr>
<tr>
<td>CR</td>
<td>Complete response</td>
</tr>
<tr>
<td>CRL</td>
<td>Complete response letter</td>
</tr>
<tr>
<td>DCR</td>
<td>Disease control rate</td>
</tr>
<tr>
<td>DLT</td>
<td>Dose limiting toxicity</td>
</tr>
<tr>
<td>DOR</td>
<td>Duration of response</td>
</tr>
<tr>
<td>EGFR</td>
<td>Epidermal growth factor receptor</td>
</tr>
<tr>
<td>MTD</td>
<td>Maximum tolerated dose</td>
</tr>
<tr>
<td>ORR</td>
<td>Overall response rate Objective response rate</td>
</tr>
<tr>
<td>OS</td>
<td>Overall survival</td>
</tr>
<tr>
<td>PD</td>
<td>Progress disease</td>
</tr>
<tr>
<td>PFS</td>
<td>Progression-free survival</td>
</tr>
<tr>
<td>PR</td>
<td>Partial response</td>
</tr>
<tr>
<td>SD</td>
<td>Stable disease</td>
</tr>
<tr>
<td>TEAE</td>
<td>Treatment emergent adverse event</td>
</tr>
</tbody>
</table>
Contact address regarding this material

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Q&A 2
Q&A 3
Q&A 4
Q&A 6
Q&A 7
Q&A 8
Q&A 9
Q&A 10
Q&A 11
Q&A 12