Learn about Daiichi Sankyo Pipelines
Hosted by JP Morgan

Kazushi Araki
Group Leader, Oncology Clinical Development Department

June 21, 2019
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Today’s Contents

◆ Daiichi Sankyo’s ADC
  ● Feature 1: High Drug-Antibody Ratio (DAR)
  ● Feature 2: High stability linker
  ● Feature 3: Selectively cleaved linker
  ● Feature 4: Unique and potent payload
  ● Feature 5: Bystander effect
  ● Feature 6: Short systemic half-life payload

◆ About ADC Projects
  ● DS-8201, U3-1402, DS-1062

◆ Other Oncology Projects
Antibody Drug Conjugate (ADC)
ADC: Marriage of Biologics and Small Molecules

Antibody Drug Conjugates: A Marriage of Biologics and Small Molecules

Antibody drug conjugates offer a niche opportunity in drug development and contract manufacturing.

- High selectivity to target
- Less adverse events
- Efficacy may not be enough
- Potent efficacy (cytotoxicity)
- Low selectivity to target
- Issue of adverse events

Strength and weakness of low molecule drug and antibody drug are well complemented.
MOA of ADC

1. ADC bind to antigen on cancer cell surface
2. Internalization (take in ADC into cancer cell)
3. Linker cleaved in cell and release payload (drug)
4. Release payload shows efficacy
Difference between ADC and Traditional Chemotherapy

ADC

- Maximum tolerated dose
- Therapeutic range
- Minimum efficacious dose

Traditional chemotherapy

- Therapeutic range

ADC is an attractive drug delivery system with wider therapeutic window

Drug exposure in normal tissue
Drug exposure in cancer tissue
### ADC: Needs Expertize of Low Molecule and Antibody Drugs

<table>
<thead>
<tr>
<th></th>
<th>Low Molecule Drug</th>
<th>Antibody Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (size)</td>
<td>Hundreds (small)</td>
<td>About 150,000 (big)</td>
</tr>
<tr>
<td>Form</td>
<td>Simple</td>
<td>Complicated</td>
</tr>
<tr>
<td>Manufacturing methods</td>
<td>Chemical synthesis</td>
<td>Cell culture</td>
</tr>
<tr>
<td>Cost</td>
<td>Low</td>
<td>High</td>
</tr>
</tbody>
</table>

- R&D and manufacturing methods vary widely
- Each needs to improve one’s expertise and optimize processes
- Development of ADC technology requires high specialties of both
**Component and Requirement of ADC**

**A: Antibody**
- Target antigen which selectively and highly expressed on tumor
- Internalization to target cell with antigen

**B: Attachment site**
- Drug-linker can be attached
- Typically cysteine or lysine residues on antibodies

**C: Linker**
- Stable until releasing drug

**D: Payload (drug)**
- Extremely potent anti-tumor activity
- Availability of linker binding site
Launched: only 4 products
- Kadcyla®: anti-HER2 antibody (trastuzumab) + DM1*, breast cancer
- Adcetris®: anti-CD30 antibody + MMAE*, Hodgkin lymphoma
- Mylotarg®: anti-CD33 antibody + Calicheamicin*, AML
- Besponsa®: anti-CD22 antibody + Calicheamicin*, AML

Anticipated improvements
- Limited drug antibody ratio
  - Average drug antibody ratio (DAR) is limited to 2-4 and thus limitation in efficacy
- Instability of linker
  - Free payloads in blood causes toxicity and also decrease of efficacy occurs by lowered concentration of ADC in blood
- Payload
  - Most payloads are microtubule inhibitors
  - No treatment is available for patients who failed/tolerant to recent ADCs

*DM1, MMAE: microtubule inhibitor
Calicheamicin: DNA cleavage agents
DS ADC Technology
Overcoming Challenges
Daiichi Sankyo ADC Structure

ADC  =  Antibody (IgG)  +  Drug-linker

<table>
<thead>
<tr>
<th>ADC</th>
<th>Antibody (IgG)</th>
<th>Drug-linker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight :</td>
<td>Molecular weight :</td>
<td>Molecular weight :</td>
</tr>
<tr>
<td>ca. 156,000</td>
<td>ca. 148,000</td>
<td>ca. 1,000</td>
</tr>
</tbody>
</table>
DS ADC: Improved Current Challenges

Previous Generation ADC

- **Limited DAR**
  - DAR 2-4

- **Instability of linker**
  - Free payloads in blood causes toxicity and also decrease of efficacy occurs by lowered concentration of ADC in blood

- **Payload**
  - Most payloads are microtubule inhibitors
  - No treatment is available for patients who failed/tolerant to recent ADCs

Daiichi Sankyo ADC Technology

- **Feature 1: High DAR**
  - DAR is 2-4 times higher than current ADC

- **Feature 2: High stability linker**
  - Sparing non-cancerous tissue from toxicity by non-cleavable linker

- **Feature 3: Selectively cleaved linker**
  - Cancer-cell selective cleaved linker and release payload

- **Feature 4: Unique and potent payload**
  - DNA topoisomerase I inhibitor

- **Feature 5: Bystander effect**
  - Effective in heterogeneous tumor microenvironment

- **Feature 6: Short systemic half-life**
  - If payload is released, it clears rapidly due to short half-life
Feature 1: High DAR

One antibody can load 7-8 payload = 2-4 times as much as current ADC

- Cysteine residue
- Drug-linker
### Feature 1: High Drug-to-Antibody Ration (DAR)

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

Feature 2: High Stability Linker

Pharmacokinetics profile

**T-DM1, 3.6 mg/kg** (Phase 1)

- Antibody
- T-DM1
- Payload (DM1)

**DS-8201, 6.4 mg/kg** (Phase 1)

- Antibody
- DS-8201
- Payload (DXd)

DS-8201: High linker stability and low free payload

Feature 3: Selectively Cleaved Linker

**DS-8201**

Cleaved by cathepsin which highly expressed on tumors

The linker is connected to cysteine residue of the antibody via thioether bond

GGFG based linker cleavable

Digestion

\[ \text{DXd} \]

**Topoisomerase I inhibitor**

The linker is connected to lysine residue of the antibody via amide bond

SMCC linker non-cleavable

DM1

Cleaved by protease in lysosome

\[ \text{Lys-SMCC-DM1} \]

**Microtubule inhibitor**

\[ \text{T-DM1} \]
## Feature 4: Novel MOA and Potent Payload

<table>
<thead>
<tr>
<th></th>
<th>T-DM1</th>
<th>DS-8201a</th>
<th>SYD-985</th>
<th>XMT-1522</th>
<th>MEDI4276</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Company</strong></td>
<td>Genentech</td>
<td>Daiichi Sankyo</td>
<td>Synthon</td>
<td>Mersana</td>
<td>Medimmune</td>
</tr>
<tr>
<td><strong>Payload</strong></td>
<td>DM1</td>
<td>DXd</td>
<td>Duocarmicine</td>
<td>AF-HPA</td>
<td>Tubulysin</td>
</tr>
<tr>
<td><strong>MOA</strong></td>
<td>Tubulin</td>
<td></td>
<td>DNA alkylator</td>
<td>Tubulin</td>
<td>Tubulin</td>
</tr>
<tr>
<td><strong>Linker</strong></td>
<td>Undissociated</td>
<td>Dissociated</td>
<td>Dissociated</td>
<td>Dissociated</td>
<td>Dissociated</td>
</tr>
<tr>
<td><strong>Attachment site</strong></td>
<td>Lysine residue</td>
<td>Cysteine residue</td>
<td>Cysteine residue</td>
<td>Cysteine residue</td>
<td>Engineered cysteine</td>
</tr>
<tr>
<td><strong>Drug-to-antibody ratio (average)</strong></td>
<td>3.5</td>
<td>7-8</td>
<td>2</td>
<td>12-15</td>
<td>4</td>
</tr>
<tr>
<td><strong>Human Dose (Ph1)</strong></td>
<td>3.6mg/kg*</td>
<td>6.4mg/kg</td>
<td>1.2mg/kg**</td>
<td>0.765mg/kg***</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Yamamoto-H, Jpn J Clin Oncol. 2015 Jan;45(1):12-8
**Aftimos-PG, SABCS, 2016
***Buris-HA, Mersana homepage TPS2606
Feature 4: Novel MOA and Potent Payload

- Novel topoisomerase I inhibitor, DXd
- DXd has 10 times more potent effect than irinotecan

**SN-38**
(Active metabolite of irinotecan)

**DXd**
(Payload of DS-8201a)

Topo I IC$_{50}$: 2.78 μM

Topo I IC$_{50}$: 0.31 μM

About 1/10 amount is enough for efficacy

TOPO I IC$_{50}$: Concentration which inhibit 50% of topoisomerase I enzyme
Feature 4: Unique and Potent Payload

- T-DM1 resistant cell (N87-TDMR) has HER2 expression but low sensitivity to free payload, DM-1

- MOA of DS-8201 payload is different and therefore has superior efficacy to N87-TDMR

*Takegawa-N et al., Int J Cancer 2017*
Feature 4: Unique and Potent Payload

T-DM1 treated patient’s cancer tissue xenograft model

Remarkable efficacy of DS-8201 was seen in T-DM1 resistant or low-response cancer patient-derived xenograft model

Source: Tamura-K et al., abstract 4585 (LBA17), ESMO 2016
Feature 5: Bystander Effect

Released drug is designed to have high cell membrane cross-penetration

Heterogeneity of IHC staining in gastric cancer
All cases classify into HER2 score 3+

- Cancer tissues are group of heterogeneity
- Target expression is sometimes uneven

- Free payloads penetrate to neighbor cancer cells and have anti-cancerous effect
- Effective in heterogeneous tumor microenvironment

Doi-T et al., abstract 108, ASCO 2017
Feature 5: Bystander Effect

Bystander effect of ADC:
- Released payloads in cancer cells penetrate the cell membrane and show activity on neighboring dividing cancer cells.
- Through this effect, activity against target antigen-negative cancer cells, in other words, activity against tumors with antigen heterogeneity is observed.
Feature 5: Bystander Effect in vivo Study

Co-inoculate HER2 positive cells and HER2 negative cells (Luc tagged) to right flank of mice

Day 0

Day 14

Vehicle control

DS-8201a 3 mg/kg

T-DM1 10 mg/kg

Luciferase activity

Average radiance (p/s/cm²/sr)

Time after treatment

DS-8201a treatment clearly decreased luciferase signal

→ Luc-gene transfected HER2-negative cells was eliminated

Ogitani-Y et al., Clin Cancer Res 2016; 22:5097
**Feature 5: Bystander Effect**

- **DS-8201 bystander effect on Low HER2 (non-clin study)**

**Breast HER2 Low**

Patient-derived xenograft ST565 (IHC 1+, FISH -)

- HER2 Low (1+)
- HER2-

FISH negative (signal ratio 1.3)

**Change in tumor volume (mm³)**

Patient-derived xenograft ST565

- T-DM1
- Vehicle
- trasutuzumab
- DS-8201a 10 mg/kg IV single dose

**Source:** Ogitani-Y et al., *Clin. Cancer Res.* 2016; 22:5097-5108
Feature 6: Short Systemic Half-Life

- High concentration of free payload in blood is one of the reason of adverse events
- Released payload is designed to be excreted immediately which results in lowering occurrence of adverse events

<table>
<thead>
<tr>
<th>Payload</th>
<th>T$_{1/2}$ in Rat (hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DXd* (payload of DXd-ADC)</td>
<td>0.9</td>
</tr>
<tr>
<td>DM1** (payload of T-DM1)</td>
<td>3.3-10</td>
</tr>
<tr>
<td>MMAE*** (payload of Adcetris)</td>
<td>5.7-11</td>
</tr>
</tbody>
</table>

* In-house report
** KADCYLA BLA
*** ADCETRIS BLA
DS ADC: Improved Current Challenges

Previous Generation ADC

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  ▶ DAR 2-4
◆ Instability of linker
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◆ Payload
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  ▪ Effective in heterogeneous tumor microenvironment
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  ▪ If payload is released, it clear rapidly due to short half-life
### Daiichi Sankyo ADC Franchise

(as of June 2019)

<table>
<thead>
<tr>
<th>Project (Target)</th>
<th>Target Indications</th>
<th>Discovery</th>
<th>Pre-Clinical</th>
<th>P1</th>
<th>Pivotal</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS-8201 (HER2)</td>
<td>Breast, Gastric, CRC, NSCLC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>U3-1402 (HER3)</td>
<td>Breast, NSCLC</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>DS-1062 (TROP2)</td>
<td>NSCLC</td>
<td></td>
<td></td>
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<tr>
<td>DS-7300 (B7-H3)</td>
<td>Solid tumors</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>DS-6157 (GPR20)</td>
<td>GIST</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>DS-6000 (undisclosed)</td>
<td>Renal, Ovarian</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>(TA-MUC1)</td>
<td>Solid tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CRC: colorectal cancer, NSCLC: non-small cell lung cancer, GIST: gastrointestinal stromal tumor
DS-8201
# DS-8201: Study Plan

## As of April 2019

<table>
<thead>
<tr>
<th>Multiple tumors</th>
<th>FY2018</th>
<th>FY2019</th>
<th>FY2020</th>
<th>FY2021</th>
<th>FY2022</th>
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</thead>
<tbody>
<tr>
<td>P1</td>
<td></td>
<td></td>
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<table>
<thead>
<tr>
<th>Breast (Global)</th>
<th>FY2018</th>
<th>FY2019</th>
<th>FY2020</th>
<th>FY2021</th>
<th>FY2022</th>
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</thead>
<tbody>
<tr>
<td>HER2 positive breast post T-DM1 pivotal P2</td>
<td>DESTINY-Breast01</td>
<td></td>
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<tr>
<td>HER2 positive breast post T-DM1 vs. phys choice P3</td>
<td>DESTINY-Breast02</td>
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<tr>
<td>HER2 positive breast vs T-DM1 P3</td>
<td>DESTINY-Breast03</td>
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<td></td>
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<tr>
<td>HER2 low breast P3</td>
<td>DESTINY-Breast04</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Gastric (Global)</th>
<th>FY2018</th>
<th>FY2019</th>
<th>FY2020</th>
<th>FY2021</th>
<th>FY2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2 expressing gastric 3rd line vs phys choice pivotal P2 (JP/Asia)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HER2 expressing gastric 2nd line vs SOC P3 (JP/Asia)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HER2 expressing gastric P2 (US/EU)</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Colorectal Lung (Global)</th>
<th>FY2018</th>
<th>FY2019</th>
<th>FY2020</th>
<th>FY2021</th>
<th>FY2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal P2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-small cell lung cancer P2</td>
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<td></td>
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</table>

<table>
<thead>
<tr>
<th>Combo</th>
<th>FY2018</th>
<th>FY2019</th>
<th>FY2020</th>
<th>FY2021</th>
<th>FY2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast/bladder with nivolumab P1b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast/NSCLC with pembrolizumab P1b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid tumor with avelumab P1b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid tumor with TKI P1b</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
## Explanation of Terms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CR</strong> (complete response)</td>
<td>Cancer disappears completely</td>
</tr>
<tr>
<td><strong>PR</strong> (partial response)</td>
<td>The size of the cancer has shrunk by more than 30% and lasted for more than 4 weeks</td>
</tr>
<tr>
<td><strong>ORR</strong> (overall response rate)</td>
<td>Percentage of patients who had a therapeutic effect. Expressed by the sum of CR and PR</td>
</tr>
<tr>
<td><strong>DCR</strong> (disease control rate)</td>
<td>Percentage of patients whose symptoms are controlled</td>
</tr>
<tr>
<td><strong>DOR</strong> (duration of response)</td>
<td>Duration of effect lasting</td>
</tr>
<tr>
<td><strong>PFS</strong> (progression-free survival)</td>
<td>Period of survival without cancer progression</td>
</tr>
<tr>
<td><strong>PD</strong> (progressive disease)</td>
<td>Cancer progression</td>
</tr>
<tr>
<td><strong>SD</strong> (stable disease)</td>
<td>Size (long diameter) of the cancer has not changed substantially before and after treatment</td>
</tr>
</tbody>
</table>
DS-8201: P1 Study HER2 Positive Breast Cancer

Data cutoff for this analysis is April 18, 2018
Iwata et al, ASCO2018 Presentation

<table>
<thead>
<tr>
<th></th>
<th>Confirmed ORR (n/N) (95% CI)</th>
<th>DCR % (n/N)</th>
<th>DOR, median (95% CI), month</th>
<th>PFS Median, (95% CI)</th>
<th>Min, max</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2 positive breast cancer</td>
<td>59.5% (66/111) (49.7, 68.7)</td>
<td>93.7% (104/111)</td>
<td>20.7 (NE)</td>
<td>22.1ヶ月 (NE)</td>
<td>0.8, 27.9</td>
</tr>
<tr>
<td>N=114</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NE: not estimable
Lancet Oncology, April 29, 2019
DS-8201: P1 Study HER2 Low Breast Cancer

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

<table>
<thead>
<tr>
<th>Study Arm</th>
<th>Confirmed ORR, n/N (%)</th>
<th>Confirmed DCR, n/N (%)</th>
<th>Duration of Response, median (range), mo</th>
<th>PFS, median (95% CI), mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (N = 51)</td>
<td>19/43 (44.2)</td>
<td>34/43 (79.1)</td>
<td>9.4 (1.5+, 23.6+)</td>
<td>7.6 (4.9, 13.7)</td>
</tr>
<tr>
<td>Subgroups</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IHC 1+ (n = 27)</td>
<td>7/21 (33.3)</td>
<td>14/21 (66.7)</td>
<td>7.9 (2.1+, 11.3)</td>
<td>5.7 (1.4, 7.9)</td>
</tr>
<tr>
<td>IHC 2+ (n = 24)</td>
<td>12/22 (54.5)</td>
<td>20/22 (90.9)</td>
<td>11.0 (1.5+, 23.6+)</td>
<td>13.6 (NA)</td>
</tr>
<tr>
<td>HR+ (n = 45)</td>
<td>18/38 (47.4)</td>
<td>31/38 (81.6)</td>
<td>11.0 (1.5+, 23.6+)</td>
<td>7.9 (4.4, 13.7)</td>
</tr>
<tr>
<td>Prior CDK4/6 inhibitor (n = 15)</td>
<td>4/12 (33.3)</td>
<td>9/12 (75.0)</td>
<td>NR</td>
<td>7.1 (NA)</td>
</tr>
</tbody>
</table>
Includes subjects who had ≥1 postbaseline scan. Dotted lines denote 20% increase and 30% reduction in tumor size, respectively.  
*Confirmed response includes subjects who had ≥2 postbaseline scans, progressive disease, or discontinued treatment for any reason prior to second postbaseline scan. Data cutoff is April 18, 2018.

<table>
<thead>
<tr>
<th></th>
<th>Confirmed ORR (n/N) (95% CI)</th>
<th>DCR % (n/N) (95% CI)</th>
<th>DOR, Median (months)</th>
<th>PFS Median, (95% CI)</th>
<th>Min, max</th>
</tr>
</thead>
<tbody>
<tr>
<td>HER2 Positive Gastric Cancer N = 44</td>
<td>43.2% (19/44) (28.3, 59.0)</td>
<td>79.5% (35/44)</td>
<td>7.0 (NA)</td>
<td>5.6 months (3.0, 8.3)</td>
<td>1.2, 19.6+</td>
</tr>
</tbody>
</table>
### DS-8201: P1 Study HER2 Mutated or Expressing NSCLC

<table>
<thead>
<tr>
<th>HER2-expressing or HER2-mutated NSCLC</th>
<th>Confirmed ORR, % (n/N)</th>
<th>Confirmed DCR, % (n/N)</th>
<th>DOR, median (range), months</th>
<th>PFS, median (range), months</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 18</td>
<td>58.8% (10/17)</td>
<td>88.2% (15/17)</td>
<td>9.9 (0.0+, 11.5)</td>
<td>14.1 (0.9, 14.1)</td>
</tr>
<tr>
<td>HER2-mutated NSCLC</td>
<td>72.7% (8/11)</td>
<td>100% (11/11)</td>
<td>11.5 (0.03+, 11.5)</td>
<td>14.1 (4.0+, 14.1)</td>
</tr>
</tbody>
</table>

Data cutoff, August 10, 2018. IHC by local laboratory testing.

E20, exon 20 insertion; EC, single base pair substitution at extracellular domain; IHC, immunohistochemistry; ISH, in situ hybridization; NSCLC, non-small cell lung cancer; NE, not examined or missing; TM, single base pair substitution in transmembrane domain.

Tsurutani et al, WCLC, 2018; Abstract #13325
DS-8201: P1 Study CRC by HER2 Status IHC/FISH

ORR 27.3% (3/11) in HER2 (IHC 2+, 3+)

<table>
<thead>
<tr>
<th>CRC</th>
<th>Confirmed ORR, % (n/N)</th>
<th>Confirmed DCR, % (n/N)</th>
<th>DOR, median (range), months</th>
<th>PFS, median (range), months</th>
<th>OS, median (range), months</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=19*</td>
<td>15.8% (3/19)</td>
<td>84.2% (16/19)</td>
<td>NR (0.0+, 5.5+)</td>
<td>3.9 (2.1, 8.3)</td>
<td>NR (1.0+, 17.9+)</td>
</tr>
</tbody>
</table>

* Evaluable patients (one IHC 0 patient was not evaluable out of 20 enrolled)
Preparation for BLA/NDA submissions is progressing to plan

**US**

- **BLA submission**
  - 1H FY2019
  - Estimated Review Period: 6M after acceptance of the application by FDA
  - Fast-track status
  - Breakthrough therapy designation

**Japan**

- **NDA submission**
  - 2H FY2019
  - Estimated Review Period: Maximum 12M after application

**EU**

- **MAA submission**
  - 1H FY2020
  - Estimated Review Period: 12M after application
HER2 Gastric Cancer Submission Plan

- Preparation for JNDA submission is progressing steadily

Japan

NDA submission
1H FY2020

Estimated Review Period:
6M after application

SAKIGAKE designation
# DS-8201: P1 Study *The Lancet Oncology* Breast Cancer

<table>
<thead>
<tr>
<th>Pertuzumab + trastuzumab + docetaxel (1L)&lt;sup&gt;1&lt;/sup&gt;</th>
<th>T-DM1 (1L, failed study)&lt;sup&gt;2&lt;/sup&gt;</th>
<th>T-DM1 (2L)&lt;sup&gt;3&lt;/sup&gt;</th>
<th>T-DM1 (3L+)&lt;sup&gt;4&lt;/sup&gt;</th>
<th>DS-8201&lt;sup&gt;5&lt;/sup&gt;</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>OS</td>
<td>56.5m</td>
<td>53.7m</td>
<td>30.9m</td>
<td>22.7m</td>
</tr>
<tr>
<td>ORR</td>
<td>80%</td>
<td>60%</td>
<td>43.6%</td>
<td>31%</td>
</tr>
<tr>
<td>Median prior Rx for adv. disease</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

*1CLEOPATRA (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: P1 Study *The Lancet Oncology* Gastric Cancer

<table>
<thead>
<tr>
<th></th>
<th>Trastuzumab + chemo (1L)&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Ramucirumab + chemo (2L)&lt;sup&gt;2&lt;/sup&gt;</th>
<th>T-DM1 (failed study; 3+L)&lt;sup&gt;3&lt;/sup&gt;</th>
<th>DS-8201&lt;sup&gt;4&lt;/sup&gt;</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>DoR</td>
<td>6.9m</td>
<td>4.4m</td>
<td>4.3m</td>
<td>7.0m</td>
</tr>
<tr>
<td>OS</td>
<td>13.8m</td>
<td>9.6m</td>
<td>7.9m</td>
<td>12.8m</td>
</tr>
<tr>
<td>ORR</td>
<td>47%</td>
<td>28%</td>
<td>21%</td>
<td>43.2%</td>
</tr>
<tr>
<td>Median prior LoT&lt;sup&gt;5&lt;/sup&gt;</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

m: Month,  <sup>5</sup>Line of Therapy
Investigator-Reported and Adjudicated Cases of ILD

- Median duration of treatment 108 days; 29.5% subjects on treatment for ≥180 days
  - Median time to onset of ILD 149 days

<table>
<thead>
<tr>
<th>Population</th>
<th>Adjudication status</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Investigator reported, n (%)</td>
<td>1</td>
</tr>
<tr>
<td>All subjects</td>
<td></td>
<td>30 (4.5)</td>
</tr>
<tr>
<td>All doses, N = 665</td>
<td></td>
<td>23 (3.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 (0.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 (0.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5 (0.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>66 (9.9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Population</th>
<th>Adjudicated, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases adjudicated, n</td>
<td>16 13 4 0 5</td>
</tr>
<tr>
<td>Adjudicated as drug-related ILD, n</td>
<td>11 12 3 0 4</td>
</tr>
</tbody>
</table>

Data cutoff: October 15, 2018

March 2018: ILD recognized as DS-8201 risk: key actions implemented
- Proactive awareness of subjects thru consent, to report signs or symptoms of possible ILD
- Active training of investigational sites on monitoring for, evaluation and treatment of suspected ILD cases

Spring 2019: Proactive “Safe Use Campaign”
“DS-8201: have you screened for and mitigated against ILD today?”
U3-1402
**U3-1402: HER3 Targeted ADC**

**Product concept**

**Highly-internalized ADC:**
Patritumab (anti-HER3 mAb) armed with topoisomerase I inhibitor, to target HER3 expressing tumors

**Antibody:** Patritumab

**Linker and payload:**
Same as DS-8201

**Internalization rate:** 50-80%

**Drug-antibody ratio:** = 8

**Potential first-in-class drug**
U3-1402: HER3 Positive Refractory/Metastatic Breast Cancer Efficacy

ClinicalTrials.gov Identifier: NCT02980341

Best Percentage Change in Sum of Diameters From Baseline in Target Lesions*

ORR†: 15/32 (47%)
DCR†: 30/32 (94%)

Percentage Change in Sum of Longest Diameters

*Analysis set: Efficacy-evaluable patients with at least 1 scan.
Baseline is defined as the last measurement taken before the first dose of study drug.
†Investigator assessment. For each patient, the best percentage change from baseline in the sum of diameters for all target lesions is represented by a vertical bar.
DCR = disease control rate; ORR = objective response rate.

Potential against HER3-positive, advanced/unresectable, or metastatic breast cancer

Source: Kogawa-T et al., Abstract #2512, ASCO 2018
Safety Summary of Patients Treated with U3-1402

Median duration of exposure was 105 days (range: 21–336)

<table>
<thead>
<tr>
<th>Summary</th>
<th>Dose escalation, n (%) (N = 23)a</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TEAEs regardless of causality</strong></td>
<td>23 (100.0)</td>
</tr>
<tr>
<td>Drug-related</td>
<td>22 (95.7)</td>
</tr>
<tr>
<td><strong>Treatment-emergent SAEs regardless of causality</strong></td>
<td>6 (26.1)</td>
</tr>
<tr>
<td>Drug-related</td>
<td>3 (13.0)</td>
</tr>
<tr>
<td><strong>TEAEs leading to drug withdrawal/discontinuation</strong></td>
<td>1 (4.3)</td>
</tr>
<tr>
<td><strong>TEAEs leading to dose reduction</strong></td>
<td>7 (30.4)</td>
</tr>
<tr>
<td><strong>TEAEs leading to dose interruption</strong></td>
<td>6 (26.1)</td>
</tr>
<tr>
<td><strong>TEAEs leading to death</strong></td>
<td>0</td>
</tr>
</tbody>
</table>

Data cutoff date of February 25, 2019. aSafety analysis set included all patients who received ≥1 dose of U3-1402. SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Source: Jänne-P et al., Abstract #9010, ASCO 2019
### U3-1402 Antitumor Activity Across Diverse EGFR-TKI Resistance Mechanisms

Data cutoff date of February 25, 2019. Dotted lines denote 20% increase and 30% decrease in tumor size. Sixteen patients received ≥1 dose of U3-1402 and had pre- and post-treatment evaluable tumor assessments.

*Local testing as reported by the investigator. *Performed centrally using Oncomine Comprehensive assay v3 from formalin-fixed, paraffin-embedded tumor tissue.

#### Source: Jänne-P et al., Abstract #9010, ASCO 2019

<table>
<thead>
<tr>
<th>EGFR activating mutations&lt;sup&gt;a&lt;/sup&gt;</th>
<th>L858R</th>
<th>L858R</th>
<th>L858R</th>
<th>L858R</th>
<th>Ex19del</th>
<th>Ex19del</th>
<th>Ex19del</th>
<th>L858R</th>
<th>Ex19del</th>
<th>Ex19del</th>
<th>Ex19del</th>
<th>L858R</th>
<th>Ex19del</th>
<th>Ex19del</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR resistance mutations&lt;sup&gt;b&lt;/sup&gt;</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td>T790M</td>
<td>NE</td>
<td>NE</td>
<td>T790M</td>
<td>T790M</td>
<td>T790M</td>
<td>T790M</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>Amplifications&lt;sup&gt;b&lt;/sup&gt;</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td>CDK4</td>
<td>NE</td>
<td>CDK4</td>
<td>HER2</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
</tr>
</tbody>
</table>

<sup>a</sup>Confirmed partial response

<sup>b</sup>Not evaluable for mutation analysis

Genomic alteration not detected
U3-1402 Antitumor Activity Over Time

Data cutoff date of February 25, 2019. Sixteen patients received ≥1 dose of U3-1402 and had pre- and post-treatment evaluable tumor assessments. Dotted lines denote 20% increase and 30% decrease from baseline in tumor size over time.

Source: Jänne-P et al., Abstract #9010, ASCO 2019
Data cutoff date of February 25, 2019. Safety analysis set included all patients who received ≥1 dose of U3-1402. *Membrane H-score is a composite of percentage of positively staining cells and intensity of individual cell staining. Scores range from 0–300. For patients with multiple H-scores, the highest number was used.

Source: Jänne-P et al., Abstract #9010, ASCO 2019
U3-1402 Patient Case

65-year-old male NSCLC patient

Tumor biopsy analyses:

- EGFR Ex19del 2012
- EGFR Ex19del/T790M 2017
- EGFR Ex19del/T790M; MET amp 2018
- EGFR Ex19del/T790M/G724S; low MET copy gain; plasma EGFR C797S 2019

Treatment:

- Cisplatin + etoposide + RT 2012
- Erlotinib 2013-2015
- Osimertinib 2016
- Carboplatin + pemetrexed + pembrolizumab 2017
- Osimertinib 2018
- Osimertinib + crizotinib 2019
- Osimertinib + necitumumab 2019

Baseline

- Adrenal Glands
- Anterior Left Shoulder
- Posterior Left Shoulder

12 Weeks

- Adrenal Glands
- Anterior Left Shoulder
- Posterior Left Shoulder

Source: Jänne-P et al., Abstract #9010, ASCO 2019
DS-1062: Efficacy and Safety Balanced by Selecting DAR4

TROP2 ADC is designed to be best in class

- Antibody: Humanized anti-TROP2 monoclonal antibody (hIgG1)
- Cys conjugation
- GGFG cleavable
- Payload: Topoisomerase I inhibitor

Selective-DAR4 to protect safety margin

Non-selective DAR*4

Selective DAR4

*drug-antibody ratio
## DS-1062: Comparison to Sacituzumab Govitecan

<table>
<thead>
<tr>
<th></th>
<th><strong>DS-1062a</strong> (Daiichi Sankyo)</th>
<th><strong>Sacituzumab Govitecan-hziy</strong> (Immunomedics)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibody</strong></td>
<td>MAAP-9001a (humanized IgG1)</td>
<td>hRS7 (humanized IgG1)</td>
</tr>
<tr>
<td><strong>Payload</strong></td>
<td>DXd (TopoI inhibitor)</td>
<td>SN38 (TopoI inhibitor)</td>
</tr>
<tr>
<td><strong>DAR</strong></td>
<td>4</td>
<td>7.6</td>
</tr>
<tr>
<td><strong>Linker cleavage</strong></td>
<td>Enzymatic</td>
<td>pH-dependent and enzymatic</td>
</tr>
<tr>
<td><strong>Human PK (T&lt;sub&gt;1/2&lt;/sub&gt;)</strong></td>
<td>TBD</td>
<td>11.7 h at 10 mg/kg dosing*</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>q3w regimen</td>
<td>10 mg/kg at day1 and 8 of 3 weeks</td>
</tr>
<tr>
<td><strong>Dose Limiting Toxicity in Human</strong></td>
<td>TBD</td>
<td>Neutropenia, MTD=12mg/kg**</td>
</tr>
<tr>
<td><strong>Stage</strong></td>
<td>Phase I NSCLC</td>
<td>Phase 3</td>
</tr>
</tbody>
</table>

* Reported in ASCO 2015 and AACR 2017
** Clin Cancer Res; 21(17) September 1, 2015
DS-1062: Relapsed NSCLC P1 Study Design

NSCLC ≥ 3rd line

Dose Escalation

No selection based on TROP2 expression. TROP2 (IHC) is examined retrospectively

Dose Expansion

n=40 in RDE

Assess efficacy and safety for GO/NO-GO decision

Following NSCLC POC
• Open 2 other expansion cohorts for other TROP2 positive tumors

IHC : immunohistochemistry, RDE: Recommended Dose for Expansion, POC : Proof of Concept, Q3W: every 3 weeks
Safety Summary: number of patients with TEAEs (in ≥10% of patients), regardless of causality

<table>
<thead>
<tr>
<th>TEAE, n (%)</th>
<th>All grades</th>
<th>Grade ≥3&lt;sup&gt;a,b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any TEAE</td>
<td>34 (87.2)</td>
<td>16 (41.0)</td>
</tr>
<tr>
<td>TEAE, by preferred term (in ≥10% of patients)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>13 (33.3)</td>
<td>2 (5.1)</td>
</tr>
<tr>
<td>Nausea</td>
<td>12 (30.8)</td>
<td>0</td>
</tr>
<tr>
<td>Anemia</td>
<td>9 (23.1)</td>
<td>0</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>9 (23.1)</td>
<td>0</td>
</tr>
<tr>
<td>Alopecia</td>
<td>8 (20.5)</td>
<td>0</td>
</tr>
<tr>
<td>Infusion related reaction</td>
<td>8 (20.5)</td>
<td>0</td>
</tr>
<tr>
<td>Constipation</td>
<td>6 (15.4)</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6 (15.4)</td>
<td>0</td>
</tr>
<tr>
<td>Cough</td>
<td>5 (12.8)</td>
<td>0</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>5 (12.8)</td>
<td>1 (2.6)</td>
</tr>
<tr>
<td>Rash</td>
<td>5 (12.8)</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (10.3)</td>
<td>0</td>
</tr>
<tr>
<td>Pain</td>
<td>4 (10.3)</td>
<td>1 (2.6)</td>
</tr>
<tr>
<td>Weight decreased</td>
<td>4 (10.3)</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>a</sup>TEAEs include ‘uncoded (all grades: n=5, 12.8%; grade ≥3, n=1, 2.6%); <sup>b</sup>The majority of TEAEs were grade 3 (n=8; 20.5%), except for one grade 2 and 1 grade 5 TEAE (grade 5 sepsis; 6.0 mg/kg treatment group).

TEAE, treatment-emergent adverse event.
Objective responses emerging at >2mg/kg dose

Best percent change in sum of longest dimension from baseline in target lesions (N=33)

ASCO 2019 Abstract #9051
DS-1062: TROP2 Targeted ADC

Dose / Effect Spider Plot (preliminary data April 12, 2019)

<table>
<thead>
<tr>
<th>Cohort 1</th>
<th>Cohort 2</th>
<th>Cohort 3</th>
<th>Cohort 4</th>
<th>Cohort 5</th>
<th>Cohort 6</th>
<th>Cohort 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.27 mg/kg</td>
<td>0.5 mg/kg</td>
<td>1.0 mg/kg</td>
<td>2.0 mg/kg</td>
<td>4.0 mg/kg</td>
<td>6.0 mg/kg</td>
<td>8.0 mg/kg</td>
</tr>
</tbody>
</table>

*3 additional PRs were confirmed after data cut-off

ASCO 2019 Abstract #9051
DS-3201
DS-1001
## AML / HEM Franchise Progress

### Quizartinib
- QuANTUM-First study (Newly Diagnosed FLT3-ITD AML) continues to accrue ahead of expectations; >90% enrolled

### DS-3201
- EZH1/2 inhibitor
- Granted SAKIGAKE designation for PTCL in Japan in April 2019
- Small-Cell Lung Cancer (SCLC) Phase 1 study initiated

### DS-1001
- IDH1m inhibitor
- Phase 1 results reported at ASCO (Abstract # 2004)

### DS-3032
- MDM2 inhibitor (milademetan)
- Dose escalation of P1 combination studies with quizartinib and azacitidine have started
DS-3201 (valemetostat): Dual EZH 1/2 Inhibitor

DS-3201

Potent and selective dual inhibitor of the histone methyltransferases (histone-modifying enzymes) EZH1 and EZH2 at histone H3 (H3K27)

A promising new epigenetic approach

- Tri-methylation of H3K27 (H3K27me3) is negative regulator of tumor suppressor genes or cell differentiation genes
- Dual inhibition of EZH1 and EZH2 is hypothesized to allow more potent blockade of hypermethylation of H3K27 and overcome compensatory mechanism between EZH1 and EZH2
SAKIGAKE Designation: DS-3201 PTCL

- Potential first-in-class EZH1/2 dual inhibitor
- Received SAKIGAKE Designation for relapsed/refractory peripheral T-cell lymphoma (PTCL) treatment based on the preliminary result of Phase 1 Non-Hodgkin lymphomas trial including PTCLs

Preliminary results in relapsed or refractory Non-Hodgkin Lymphoma

PTCL
- Non-Hodgkin lymphoma arising from T cells
- Tend to be aggressive and associated with poor prognosis, particularly for relapsed disease
- High unmet medical needs (very few treatment options)

DS-1001 : Mutant IDH1 Inhibitors

◆ MOA

\[
\alpha\text{-ketoglutarate (}\alpha\text{-KG)} \quad \text{DS-1001} \quad \text{(R)-2-hydroxyglutarate (2-HG)} \quad m\text{ IDH1/2}
\]

◆ Annual incidence of diseases with IDH1 mutation

- AML / Myelodysplastic syndrome
  - 7500/yr
  - 5-10% in total

- Glioma
  - 11000/yr
  - ~50% in total glioma
  - 85% in low-gr glioma and secondary GBM

- Cholangiocarcinoma
  - 1500/yr
  - 15% in total

- Chondrosarcoma
  - 4600/yr
  - 70% in total

Numbers and circle sizes indicate the estimated number of patients with IDH1m (annual incidence/year in JP/US/EU: our estimates)
Antitumor activity was observed in recurrent gliomas. High response rates were also observed in contrast-enhanced and non-contrast-enhanced tumors.

Source: Natsume-A et al., Abstract #2004, ASCO 2019
DS-1001: Efficacy Treatment Duration and Time to Response
As of May 7, 2019

Non-enhancing (n=12)

Enhancing (n=35)

ORR = 33% (4MR), DCR = 100%
Median treatment duration: 9.1 months
67% of patients continue on treatment

ORR = 17% (1CR, 5PR), DCR = 49%
Median treatment duration: 2.3 months
20% of patients continue on treatment

• Extended disease control was observed in the non-enhancing glioma (median treatment period 9.1 months, 67% of patients continued)
• Once responded, the duration of the reaction was quite long

Source: Natsume-A et al., Abstract #2004, ASCO 2019
Summary
## Major R&D Pipeline (Oncology)

### As of June 2019

<table>
<thead>
<tr>
<th>Generic name/Project number (drug efficacy/mechanism of action)</th>
<th>Target Indication</th>
<th>Region</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ADC Franchise</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>DS-8201 (anti-HER2 ADC)</td>
<td>BC (HER2 positive post T-DM1)</td>
<td>JP/US/EU/Asia</td>
<td>Phase 1, Phase 2, Phase 3, NDA/BLA</td>
</tr>
<tr>
<td></td>
<td>BC (HER2 positive vs T-DM1)</td>
<td>JP/US/EU/Asia</td>
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<td></td>
<td>BC (HER2 low)</td>
<td>JP/US/EU/Asia</td>
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<td>GC (HER2 expressing post trastuzumab)</td>
<td>JP/Asia</td>
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<tr>
<td></td>
<td>CRC</td>
<td>JP/US/EU</td>
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<td></td>
<td>NSCLC</td>
<td>JP/US/EU</td>
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<td></td>
<td>BC and bladder cancer (with nivolumab)</td>
<td>US/EU</td>
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<tr>
<td><strong>U3-1402 (anti-HER3 ADC)</strong></td>
<td>BC</td>
<td>JP/US</td>
<td></td>
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<tr>
<td></td>
<td>NSCLC</td>
<td>US</td>
<td></td>
</tr>
<tr>
<td><strong>DS-1062 (anti-TROP2 ADC)</strong></td>
<td>NSCLC</td>
<td>JP/US</td>
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<tr>
<td><strong>Quizartinib/AC220 (FLT3 inhibitor)</strong></td>
<td>AML (relapsed/refractory)</td>
<td>JP/US/EU/Asia</td>
<td>Phase 1, Phase 2, Phase 3, NDA/BLA</td>
</tr>
<tr>
<td></td>
<td>AML (1st line)</td>
<td>JP/US/EU/Asia</td>
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<tr>
<td><strong>DS-3032 (MDM2 inhibitor)</strong></td>
<td>Solid tumor</td>
<td>JP/US</td>
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<tr>
<td></td>
<td>AML</td>
<td>JP/US</td>
<td></td>
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<tr>
<td><strong>DS-3201 (EZH1/2 inhibitor)</strong></td>
<td>PTCL</td>
<td>JP</td>
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<td></td>
<td>ATL/L</td>
<td>JP</td>
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<td>AML, ALL</td>
<td>US</td>
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<tr>
<td></td>
<td>SCLC</td>
<td>US</td>
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<tr>
<td><strong>PLX2853 (BRD4 inhibitor)</strong></td>
<td>AML, solid cancer</td>
<td>US</td>
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<tr>
<td><strong>DS-1001 (IDH1m inhibitor)</strong></td>
<td>Glioma</td>
<td>JP</td>
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<tr>
<td><strong>Axi-Cel® (anti-CD19 CAR-T cells)</strong></td>
<td>BCL</td>
<td>JP</td>
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<tr>
<td><strong>Pexidartinib (CSF-1/KIT/FLT3 inhibitor)</strong></td>
<td>TGCT</td>
<td>US/EU</td>
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<tr>
<td><strong>DS-1647 (G47Δ virus)</strong></td>
<td>Glioblastoma multiforme</td>
<td>JP</td>
<td>Phase 1, Phase 2, Phase 3, NDA/BLA</td>
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<tr>
<td><strong>DS-1205 (AXL inhibitor)</strong></td>
<td>NSCLC [with osimertinib (Asia) gefitinib (JP)]</td>
<td>JP/Asia</td>
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</tr>
</tbody>
</table>


★: Projects in the field of oncology which are planned for registration application based on the results of P2 studies, designated as breakthrough therapy (FDA)/SAKIGAKE (JP)

As of June 2019

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Upcoming Milestones

**DS-8201**
- **Breast**
- **DESTINY-Breast01**
- Pivotal Phase 2 in HER2 positive mBC
  - US: BLA submission in 1H FY2019
  - JP: NDA submission in 2H FY2019

**Quizartinib**
- **AML**
- **QUANTUM-R**
- Relapsed/Refractory *FLT3*-ITD AML
  - US: FDA PDUFA August 25, 2019
  - JP: expecting approval in June 2019
  - EU: review on track for 2H FY2019 approval

**Pexidartinib**
- **TGCT**
- **ENLIVEN**
- Tenosynovial Giant Cell Tumor
  - US: FDA PDUFA August 3, 2019
  - EU: review on track 1H FY2020

**DS-1647 (G47Δ)**
- **GBM**
- Glioblastoma multiforme
  - JP: NDA submission in 1H FY2019
Thank you for listening

Daiichi Sankyo / DS Cancer Enterprise is a Global Pharma Innovator with strengths in Science and Technology, and will have a pipeline to meet various UMN's of patients.
Inquiries about this document

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