WCLC 2019 Highlights
DAIICHI SANKYO CO., LTD
September 10, 2019, 7:00-8:30pm (EDT)

Antoine Yver, MD, MSc
Global Head R&D Oncology
Forward-Looking Statements

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Today’s Agenda

DS-1062: data update / what it means for Daiichi Sankyo

U3-1402: data update / what it means for Daiichi Sankyo

Recent Milestones

Upcoming Events
Today’s Agenda

DS-1062: data update / what it means for Daiichi Sankyo

U3-1402: data update / what it means for Daiichi Sankyo

Recent Milestones

Upcoming Events
DS-1062: Background

DS-1062 structure: TROP2-targeting antibody-drug conjugate\(^1\) with a novel topoisomerase I inhibitor (DXd)\(^2,3\)

Conjugation chemistry
- Tetrapeptide linker bound to a cysteine residue of the antibody
- DS-1062 is a selective DAR\(^4\) conjugate

DS-1062 Antitumor activity in lung cancer xenograft mouse models:
Stronger antitumor activity in TROP2-positive tumors\(^1,4\)

Background

Source: Heist-R \textit{et al.}, Abstract #MA25.10, WCLC 2019

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%)

DS-1062: Phase 1 Study Design (NCT03401385)

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

#### TEAEs, regardless of causality, (in ≥10% of pts), n (%) (N=52)

<table>
<thead>
<tr>
<th>TEAE</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>

- **Data cut-off:** July 3, 2019.
- **Source:** Heist-R et al., Abstract #MA25.10, WCLC 2019

**Notes:**

- DLT reached at 10.0 mg/kg; MTD at 8.0 mg/kg is also RDE, median exposure duration was 10.6 (range 3.0–43.1) weeks.
- Serious TEAEs occurred 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 organized pneumonia [8.0 mg/kg], 1 grade 2 pneumonitis [8.0 mg/kg], and 1 grade 5 [respiratory failure in a pt with disease progression; 8.0 mg/kg]).

**Definitions:**

- DLT: dose-limiting toxicity.
- MTD: maximum tolerated dose.
- TEAE: treatment-emergent adverse event.
- ILD: interstitial lung disease.
- ALT: alanine aminotransferase.
- DLT: dose-limiting toxicity.
- MTD: maximum tolerated dose.
- TEAE: treatment-emergent adverse event.
- ILD: interstitial lung disease.
- Pt: patient.
EFICACY: TUMOR RESPONSE

- 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.

Source: Heist-R et al., Abstract #MA25.10, WCLC 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.
DS-1062: Tumor Response

◆ 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: Tumor Response

Durable responses seen at multiple dose levels

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
Data cut-off: July 3, 2019.

Prior TKI treatment (ALKi; EGFRi; HER2i) shown above bars; the other 26 pts received prior I/O
6/8 pts with PR had an H score > median (vs 8/15 with SD and 4/12 with PD).

ALKi, anaplastic lymphoma kinase inhibitor; BL, baseline; C3D1, cycle 3, day 1; cfDNA, circulating free DNA; EGFRi, epidermal growth factor receptor inhibitor; EOT, end of treatment; HER2i, human epidermal growth factor receptor 2 inhibitor; IHC, immunohistochemistry; H-score, “histo” score; I/O, immuno-oncology; NE, non-evaluable; PD, progressive disease; PR, partial response; Pt, patient; SD, stable disease; SLFN11, Schlafen family member 11; TROP2, trophoblast cell-surface antigen 2; VAF, variant allele fraction.

Source: Heist-R et al., Abstract #MA25.10, WCLC 2019

TROP2 IHC score: tended to be higher in pts with PR

TROP2 and SLFN11 gene expression trended higher in pts with tumor reduction

DS-1062 reduced cfDNA in pts with SD and PR
DS-1062: Summary

- DS-1062 is well tolerated in doses up to 8.0 mg/kg
- 8.0 mg/kg dose defined as MTD and RDE
- Dose effect on anti-tumor activity observed over 2.0–8.0 mg/kg
- 12 PRs (10 confirmed, 2 too early) observed during dose escalation in heavily pretreated unselected NSCLC pts relapsed from or having progressed on standard of care, including immune checkpoint inhibitors
- This study is currently in dose expansion
  - 10 of 40 pts enrolled in dose expansion
  - 35 pts ongoing as of August 20, 2019

MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; PR, partial response; Pt, patient; RDE, recommended dose for expansion.

Source: Heist-R et al., Abstract #MA25.10, WCLC 2019
DS-1062: What It Means for Daiichi Sankyo?

DS-1062 appears to have the characteristics of a “drug-to-be”
  • Clear activity, dose effect, durability and tolerability

**DXd portability** further established, added technology of **site-selective DAR4 conjugation** validated

Driven by emergent NSCLC Data, **Differentiation vs IMMU-132** appears credible

**Fast-to-market** US path emerging in NSCLC
Today’s Agenda

DS-1062: data update / what it means for Daiichi Sankyo

U3-1402: data update / what it means for Daiichi Sankyo

Recent Milestones

Upcoming Events
**U3-1402: Anti-HER3 ADC**

### Design Features
- **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**

### Conjugation chemistry
The drug-linker is conjugated to the antibody via cysteine residues.

**Payload MOA:** Topo I inhibitor

**Payload (DXd):** Exatecan derivative (Topoisomerase I inhibitor)

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**Potential first-in-class drug**
U3-1402: Phase 1 Dose Escalation Study Design

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

Eligibility Criteria

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
- 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). *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
# U3-1402: Baseline Demographics of Patients

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>N = 30</th>
<th>Disease Characteristics</th>
<th>N = 30</th>
<th>HER3 Expression</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median age, years (range)</strong></td>
<td>63 (44–80)</td>
<td><strong>Tumor stage (IV), n (%)</strong></td>
<td>30 (100)</td>
<td><strong>Evaluable patients</strong>, n</td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
<td>20 (67)</td>
<td><strong>Prior therapy, n (%)</strong></td>
<td></td>
<td><strong>Membrane H-score</strong>, median (range)</td>
</tr>
<tr>
<td><strong>Race, n (%)</strong></td>
<td></td>
<td><strong>EGFR TKI</strong></td>
<td>30 (100)</td>
<td>(composite score of 0–300)</td>
</tr>
<tr>
<td>White</td>
<td>18 (60)</td>
<td>Osimertinib</td>
<td>28 (93)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>8 (27)</td>
<td>Chemotherapy</td>
<td>15 (50)</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>1 (3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3 (10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ECOG performance status, n (%)</strong></td>
<td></td>
<td><strong>History of CNS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>12 (40)</td>
<td>metastases, n (%)</td>
<td>15 (50)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>18 (60)</td>
<td></td>
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</tr>
</tbody>
</table>

**EGFR mutation, n (%)**
- Ex19del: 17 (57)
- L858R: 12 (40)
- L861Q: 1 (3)

A phase 1 study of U3-1402 in NSCLC (NCT03260491). *Includes patients with tumor samples that have completed retrospective analysis. **Membrane H-score is a composite of percentage of positively staining cells and intensity of individual cell staining; for patients with multiple H-scores, the highest number was used.

ECOG, Eastern Cooperative Oncology Group; EGFR, epidermal growth factor receptor; HER3, human epidermal growth factor receptor 3; TKI, tyrosine kinase receptor.

Source: Yu-H et al., Abstract #MA21.06, WCLC 2019
U3-1402: Safety in Dose Escalation

<table>
<thead>
<tr>
<th>TEAEs &amp; AESI, n (%)</th>
<th>N = 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEAEs regardless of causality</td>
<td></td>
</tr>
<tr>
<td>Drug-related</td>
<td></td>
</tr>
<tr>
<td>29 (97)</td>
<td></td>
</tr>
<tr>
<td>28 (93)</td>
<td></td>
</tr>
<tr>
<td>Treatment-emergent SAEs regardless of causality</td>
<td></td>
</tr>
<tr>
<td>Drug-related</td>
<td></td>
</tr>
<tr>
<td>9 (30)</td>
<td></td>
</tr>
<tr>
<td>4 (13)</td>
<td></td>
</tr>
<tr>
<td>TEAEs associated with drug withdrawal/discontinuation</td>
<td></td>
</tr>
<tr>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>TEAEs associated with dose reduction</td>
<td></td>
</tr>
<tr>
<td>7 (23)</td>
<td></td>
</tr>
<tr>
<td>TEAEs associated with dose interruption</td>
<td></td>
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<tr>
<td>7 (23)</td>
<td></td>
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<tr>
<td>TEAEs associated with death</td>
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<tr>
<td>0</td>
<td></td>
</tr>
<tr>
<td>AESI</td>
<td></td>
</tr>
<tr>
<td>Interstitial lung disease</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>TEAEs in ≥ 20% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Fatigue</td>
</tr>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Platelet count decreased</td>
</tr>
<tr>
<td>Alopecia</td>
</tr>
<tr>
<td>Decreased appetite</td>
</tr>
<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose-Limiting Toxicities (N = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.2 mg/kg</td>
</tr>
<tr>
<td>4.8 mg/kg</td>
</tr>
<tr>
<td>5.6 mg/kg</td>
</tr>
<tr>
<td>6.4 mg/kg</td>
</tr>
</tbody>
</table>

A phase 1 study of U3-1402 in NSCLC (NCT03260491). *Safety analysis set included all patients who received at least 1 dose of U3-1402. *For TEAEs in < 20% of patients, there were 15 grade 3 events: hypoxia and troponin increased, n = 2 each; alanine aminotransferase increased, anemia, confusional state, dyspnea, embolism, febrile neutropenia, hypokalemia, musculoskeletal chest pain, nausea, pleural effusion, psychiatric disorders, n = 1 each. AESI, adverse event of special interest; DLT, dose-limiting toxicity; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Source: Yu-H et al., Abstract #MA21.06, WCLC 2019
A phase 1 study of U3-1402 in NSCLC (NCT03260491). 12 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. aPerformed 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.

EGFR, epidermal growth factor receptor; HER3, human epidermal growth factor receptor 3; PR, partial response; SoD, sum of diameters; TKI, tyrosine kinase receptor.
U3-1402: Antitumor Activity in Patients With or Without a History of CNS Metastases

A phase 1 study of U3-1402 in NSCLC (NCT03260491). CNS, central nervous system; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease; SoD, sum of diameters.

Source: Yu-H et al., Abstract #MA21.06, WCLC 2019
U3-1402 demonstrated a manageable safety profile

HER3 expression was observed in all evaluable patients

Antitumor activity with U3-1402 was observed in patients with EGFR-mutant TKI-resistant NSCLC and across multiple resistance mechanisms

Durable systemic disease control observed in patients with and without a history of CNS metastases

The RDE of U3-1402 was determined to be 5.6 mg/kg IV Q3W

Targeting HER3 with U3-1402 may provide clinical benefit to patients with EGFR-mutant NSCLC with diverse mechanisms of TKI resistance

Enroll 45 patients

• Adenocarcinoma EGFR-mutant NSCLC
  • ≥1 prior EGFR TKI and ≥1 prior platinum-based chemotherapy regimen

Enroll 30 patients

Stage 1: Evaluate ORR and HER3 correlation

Stage 2: Enrollment based on Stage 1 analysis

Enroll up to an additional 30 patients

Source: Yu-H et al., Abstract #MA21.06, WCLC 2019
U3-1402: What It Means for Daiichi Sankyo?

U3-1402 appears active in NSCLC, adding to breast cancer activity previously reported.

- Appears to offer **option in EGFRm TKI failing patients**, without the need to select for activated pathway that putatively drives the resistance to pEGFR suppression by TKI.

- **Fast-to-market** US path emerging in NSCLC.
Today’s Agenda

DS-1062: data update / what it means for Daiichi Sankyo

U3-1402: data update / what it means for Daiichi Sankyo

Recent Milestones

Upcoming Events
**Recent Milestones**

### DS-8201

**HER2 positive mBC pivotal phase 2 study**
- **JP:** NDA submitted and accepted on September 9, 2019
- **US:** BLA completing rolling submission within 1HFY2019 on track
- Data planned to be presented at SABCS

### Pexidartinib

**Tenosynovial giant cell tumor**
- **US:** approved on August 2, 2019 and launched
Today’s Agenda

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Recent Milestones

Upcoming Events
## Upcoming Events

### FY2019 Second Quarter Results Briefing

<table>
<thead>
<tr>
<th>Date</th>
<th>October 31st (Thursday) 4:00-5:30pm (JST) @ HQ</th>
</tr>
</thead>
</table>
| Speaker | Sunao Manabe, CEO  
|        | Junich Koga, Global Head of R&D            |

### FY2019 R&D Day

| Date       | December 17th (Tuesday) afternoon @ Tokyo  
|            | December 19th (Thursday) TBD @ NY          |
| Speakers   | Sunao Manabe, CEO  
|            | Antoine Yver, Global Head of Oncology R&D  |
| What to Expect | R&D new research and development strategy  
|            | Data update (DS-8201 SABCS 2019)           
|            | Updated development plan (DS-8201, DS-1062, U3-1402) |
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