Interim Data from the First Clinical Study of ADCT-301, a Novel Pyrrolobenzodiazepine-Based Antibody Drug Conjugate, in Relapsed/Refractory Hodgkin/Non-Hodgkin Lymphoma

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BACKGROUND
• Expression of CD25 (IL-2R-α) occurs in many lymphomas, including Hodgkin lymphoma (HL), peripheral T-cell lymphoma, cutaneous T-cell lymphoma, and diffuse large B-cell lymphoma (DLBCL).

Figure 1. CD25 immunohistochemical staining of tissue micromasses of lymph node tissue from a patient with ADCLL and B. Classical HL. Black arrows indicate Reed-Sternberg cells.

• ADCT-301 is an antibody drug conjugate (ADC) comprising a human monoclonal antibody against CD25, stochastically conjugated via a cathepsin-cleavable valine-alanine linker to a potent pyrrolobenzodiazepine (PBD) dinar toxin.

Figure 2. IL-2R complex that includes CD25 (left). ADCT-301 structure (right).

ADCT-301 is currently enrolling patients (pts) with relapsed HL and Non-Hodgkin lymphoma (NHL).

RESULTS

Table 1. ADCT-301-001 patient baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (N=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>27 (66.7)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>9 (22.0)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (12.2)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>34 (82.9)</td>
</tr>
<tr>
<td>Non-Hispanic or Latino</td>
<td>7 (17.1)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>11 (26.8)</td>
</tr>
<tr>
<td>Male</td>
<td>26 (63.4)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>57.0</td>
</tr>
<tr>
<td>n</td>
<td>27</td>
</tr>
<tr>
<td>SD</td>
<td>17.4</td>
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<tr>
<td>Min, Max</td>
<td>19, 79</td>
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<tr>
<td>Body Mass Index (BMI)</td>
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<tr>
<td>n</td>
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</tr>
<tr>
<td>Median</td>
<td>25.79</td>
</tr>
<tr>
<td>Min, Max</td>
<td>16.5, 34.2</td>
</tr>
</tbody>
</table>

Key Inclusion Criteria
• Age 18 years or older
• Pathologically confirmed relapsed or refractory lymphoma
• Failure, or intolerant to any established therapy known to provide clinical benefit at current state of disease
• Measurable disease, defined by the 2014 Lugano Classification Criteria

Figure 2. Targeted PBD delivery to CD25+ B- and T-cells.

STUDY OBJECTIVES

• This first-in-human clinical trial of ADCT-301 is currently enrolling patients (pts) with relapsed HL and Non-Hodgkin lymphoma (NHL).

INTERIM data from the latest data cut are reported here.

ADCT-301 has demonstrated potential anti-tumor activity against CD25-expressing hematological malignancies in mouse xenograft models.1

This first-in-human clinical trial of ADCT-301 is currently enrolling patients with relapsed HL and Non-Hodgkin lymphoma.

Key Exclusion Criteria
• Active graft-versus-host disease
• Evidence of myelodysplasia or myeloid leukemia
• Known history of positive serum human anti-drug antibody

ADCT-301 Safety Data
• 5 pts have reported DLTs:
  - 1 with maculopapular rash at 8 µg/kg
  - 1 with oral mucositis and small bowel enteritis at 20 µg/kg
  - 1 with elevated creatinine phosphokinase at 20 µg/kg
  - 1 with maculopapular rash and pruritis at 30 µg/kg
  - 1 with lip ulceration and skin infection at 45 µg/kg

The most commonly reported treatment-emergent adverse events (TEAEs) were:
• Fatigue (8 [21.9%] pts)
• Rash (7 [17.1%] pts)
• Anemia (6 [16.6%] pts)
• Maculopapular rash (6 [16.6%] pts)

CONCLUSIONS
• This dose escalation and expansion study will identify the MTD of ADCT-301 and provide a preliminary assessment of its single-agent anti-tumor activity and toxicity profile in HL and NHL.

ADCT-301 Exposure and Pharmacokinetics
• The median number of ADCT-301 cycles received to date is 2 (range 1–4).
• The median duration of treatment is 43 days (range 1–298 days).

The ADCT-301 PK exposure increased with dose. Accumulation was not apparent with multiple doses. ADCT-301 was below quantifiable limits before the end of the 3-week cycle.

As expected, variability increased at ADCT-301 exposure.

Figure 4. ADCT-301-001 study design

The ADCT-301 PK exposure increased with dose.

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REFERENCES