**CDX-527** is a bispecific antibody (BsAb) that is designed to block immune checkpoint PD-L1-PD-1-PD-L2 interactions while providing immune costimulation through CD27 signaling.

**CD27** is a key immunostimulatory molecule that enhances T cell activation, effector function, and survival.

**Combination of anti-PD-L1 and anti-CD27 mAbs** is synergistic in preclinical studies, achieving complementary cytokotytic and proliferative gene expression profiles, respectively.

**Agroin anti-CD27 mAbs** (varkimab and MK-5808) have been safely combined with checkpoint blockade in animal models of biological and clinical antitumor activity.

**Pre-clinical studies demonstrated enhanced T cell activation by CDX-527 and anti-tumor activity of a combination compared to individual mAb combinations**

- Preliminary safety, PK, and PD data are presented for the first 5 dose escalation cohorts in the CDX-527-01 Phase I study.

Methods

- First-in-human, open-label, investigator-initiated, multi-center, dose-escalation and tumor-specific expansion study to evaluate safety, PK, PD, and clinical activity of CDX-527 in patients with solid tumors refractory to SOC therapy.

Baseline Patient Characteristics

| Age, years (median) | 59 (42) | 58 (62) | 58 (60) | 54 (64) |
| Race | White | 1 (100) | 1 (100) | 1 (100) | 1 (100) |
| Ethnicity, not Hispanic or Latino | 0 | 1 (100) | 1 (100) | 3 (100) | 0 (100) |
| Prior checkpoint inhibition | 0 | 1 (100) | 1 (100) | 3 (100) | 0 (100) |
| No. prior regimens (median) | 4 | 6 | 6 (1, 11) | 9 (1, 11) | 6 (1, 11) |
| Tumor type(s)* | 1 | 1 | 1 | 1 | 1 |

*Some have primary peritoneal carcinomas and fallopian tube carcinomas. Other tumor types: leiomyosarcomas (n=2) and thymic carcinoma.

- 11 patients have been treated as of the cut-off date; 3 remain on treatment; reason for treatment discontinuation: unconfirmed progression (n=4), confirmed progression (n=2), symptomatic deterioration (n=1), median treatment cycles = 4, median treatment follow-up = 15 days (5-314).

Treatment Related AEs*

<table>
<thead>
<tr>
<th>CDX-527 Related AE(s)</th>
<th>n=11</th>
<th>n=3</th>
<th>n=3</th>
<th>n=3</th>
<th>n=3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>1 (100)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>1 (100)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Nausea</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (100)</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Paronychia</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Pruritus</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*CDX-527 related AEs occurring in 2 or more patients. CDX-527 related AE occurring in 1 patient each were mucositis, fever, pruritus, diarrhea, urticaria, dyspnea, herpes simplex reactivation, back pain, hypocalcemia, chills, pain in extremity, hand edema, paronychia, cellulitis, and pleural effusion.

- All CDX-527 related AEs were grade 1 or grade 2
- No DLTs or CDX-527 related SAEs

**RESULTS**

- **Pharmacokinetics**
  - **CDX-527 in CD27+ T cells**: CDX-527 is detected with anti-CD27 Abs. Dissociated histograms are direct-staining, red histograms are anti-CD27+ T cells with saturating amount of CDX-527. Represented histograms from 1 mg/kg and 10 mg/kg presented.
  - **Flow Cytometry on PBMC**
    - **% of Circulating Lymphocyte Populations (mean, %)***: More than 1% in all patients.
    - **% HLA-DR of Circulating Lymphocyte Populations (mean, %):** More than 1% in all patients.

**Circulating Cytokines**

Mean (± SEM) serum concentration in cycles 1 and 2

**SUMMARY & FUTURE DIRECTIONS**

- These are the first-in-human data of CDX-527, a PD-L1-CD27 bispecific antibody that combines patient CD27-dependent T cell costimulatory signaling with blockade of the PD-L1-PD-1 inhibitory pathway.
- Dose escalation of CDX-527 in patients with solid tumors has a good safety profile through 3 mg/kg.
- No DLT or treatment-related SAE
- Currently enrolling at highest dose - 10 mg/kg
- Pharmacokinetic and receptor occupancy demonstrate good exposure starting at CDX-527 doses of 1 mg/kg.
- Pharmacodynamic analysis demonstrate CDX-527 has biological activity consistent with immune activation.
- Transient increase in pro-inflammatory cytokines/chemokines
- Upregulation of activation markers in T cells and particularly NK cells
- Decrease in regulatory T cells
- Tox data support expansion into tumor specific cohorts for evaluation of clinical activity.
- Good safety, PK, and lack of immunogenicity are important hurdles for bispecific antibodies.