CDX-585 was generated from novel aPd-5 (7B1) and gL4T-7 (871) mAbs.

- 7B1 is a novel aPd-5 humab mAb that potently inhibits PD-1 signaling by PD-L1.
- A7B1 and gL4T-7 (871) mAbs exhibit high binding activity to HLA-G.

CDX-585 retains comparable potency to parental mAbs in blocking PD-1 signaling and HLA-G ligand binding.

CDX-585 exhibits synergistic effects in mixed lymphocyte reaction.

- The combination of CD8+ T cells and CD8+ T cells activates CDX-585 on both aPd-5 and gL4T-7.
- The activity of CDX-585 on both aPd-5 and gL4T-7 is significantly enhanced by the combination treatment with parental mAbs.

CDX-585 has sub-nanomolar affinity for human PD-1 and ILT4 and cross-reacts with cynomolgus macaque receptors.

- CDX-585 has sub-nanomolar affinity for both human and cynomolgus macaque PD-1.
- CDX-585 cross-reacts with cynomolgus macaque ILT4 with lower affinity, but activates similar saturation on murine receptors.

CDX-585 In Vivo Activity

- Enhanced anti-tumor activity demonstrated in humanized mouse model of melanoma relative to parental mAbs below or in combination.

CDX-585 Potentiates Proinflammatory Phenotype in Myeloid and T Cells.

- Enhanced cytokine production through ILT4 blockade by human macrophages and DCs in response to LPS.
- Full activation by CDX-585 on dual inhibition of ILT4 and PD-1.

CDX-585 Toxicology Study

- 4-week GLP toxicology study in cynomolgus macaques.

Conclusions

- Simultaneous inhibition of ILT4 and PD-1 checkpoints with CDX-585 leads to myeloid and T-cell activation with enhanced activity relative to combination of mAbs.

Clinical Study Design

- A Phase 1 dose-escalation and expansion study of the PD-1 x ILT4 bispecific antibody CDX-585 in patients with advanced malignancies.

- Open-label, non-randomized, multicenter, dose-escalation study with cohorts to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and clinical activity of CDX-585 in patients with advanced or metastatic solid tumors that have progressed during or after standard of care (NCT01728066).

- CDX-585 will be administered intravenously every 2 weeks until confirmed disease progression, intolerance, or for a maximum of 1 year.

- GAVY-CMC activities have been successfully executed.

- CDX-585 demonstrates good safety profile in a GLP-compliant toxicology study supporting initiation of clinical development.

- A toxicity study demonstrated that the administration of CDX-585 by once weekly intravenous infusion (5 mg/kg over 30 minutes) on Day 1, 8, 15, 22, and 29 resulted in well-tolerated monoclonal antibody elevations with a continuous rise in serum concentration over time.

Simultaneous inhibition of ILT4 and PD-1 checkpoints with CDX-585 leads to myeloid and T-cell activation with enhanced activity relative to combination of mAbs.

- Inhibition of ILT4 on myeloid cells promotes a pro-inflammatory phenotype.
- CDX-585 has sub-nanomolar affinity and potentially inhibits both PD-1 and ILT4.
- CDX-585 promotes T-cell activation as measured by mixed lymphocyte reactions in a manner not achieved by the combination of ILT4 and PD-1 mAbs.
- CDX-585 demonstrated anti-tumor activity in a humanized mouse model of melanoma.
- CDX-585 effectively combines ILT4 and PD-1 blockade into one molecule with favorable biophysical and immunologic characteristics which supported the initiation of development activities including manufacturing.
- GAVY-CMC activities have been successfully executed.

CDX-585 demonstrates good safety profile in a GLP-compliant toxicology study supporting initiation of clinical development.

- A toxicity study demonstrated that the administration of CDX-585 by once weekly intravenous infusion (5 mg/kg over 30 minutes) on Day 1, 8, 15, 22, and 29 resulted in well-tolerated monoclonal antibody elevations with a continuous rise in serum concentration over time.

Simultaneous inhibition of ILT4 and PD-1 checkpoints with CDX-585 leads to myeloid and T-cell activation with enhanced activity relative to combination of mAbs.

- Inhibition of ILT4 on myeloid cells promotes a pro-inflammatory phenotype.
- CDX-585 has sub-nanomolar affinity and potentially inhibits both PD-1 and ILT4.
- CDX-585 promotes T-cell activation as measured by mixed lymphocyte reactions in a manner not achieved by the combination of ILT4 and PD-1 mAbs.
- CDX-585 demonstrated anti-tumor activity in a humanized mouse model of melanoma.
- CDX-585 effectively combines ILT4 and PD-1 blockade into one molecule with favorable biophysical and immunologic characteristics which supported the initiation of development activities including manufacturing.
- GAVY-CMC activities have been successfully executed.

CDX-585 demonstrates good safety profile in a GLP-compliant toxicology study supporting initiation of clinical development.

- A toxicity study demonstrated that the administration of CDX-585 by once weekly intravenous infusion (5 mg/kg over 30 minutes) on Day 1, 8, 15, 22, and 29 resulted in well-tolerated monoclonal antibody elevations with a continuous rise in serum concentration over time.